NINETEENTH HEALTH SCIENCES CENTRE POSTER CONFERENCE 2014

Under the Patronage of
The President of Kuwait University

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19th HSC Poster Conference 2014

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Special Acknowledgements

- Prof. Adel K Ayad, *Dean, Faculty of Medicine*
- Mr. Adel Al-Moosad, *Director, Service Department*
- Mrs. Teena Sadan, *Technical Staff, CRC, Faculty of Medicine*

Photograph of Organizing Committee

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

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Message from the Dean, Faculty of Medicine

It gives me great pleasure to write the introductory remarks of the Abstract book for the 18th Poster Conference 2013. The Poster Conference throughout the years has continued to achieve the goals of fostering high quality medical research, stimulation of scientific endeavor and collaboration and interaction of faculty and students. This meeting is important as it provides a forum for all researchers to present and discuss basic and clinical research conducted in Kuwait.

We are extremely fortunate for this year to have one of the pioneers in the field of neural stem cells, Professor Freda D. Miller from the Department of Molecular Genetics, University of Toronto, as our keynote speaker who will present to us "Stem Cells: Building and Rebuilding the Nervous System". This talk will address: One, how neural stem cells are regulated both during normal development and in genetic disorders? Second, can we provide therapies for the injured or degenerating adult nervous system?

The total number of research abstracts accepted this year is 236, which reflects the good progress in research in the Health Sciences in Kuwait. I am grateful to the Vice Dean Research and Postgraduate Studies Prof. Widad Al-Nakib for his continuing support for the Poster Conference. I also thank the Chairman of the 18th Poster Conference Organizing Committee, Prof. Peter Lucas, and the Organizing Committee from HSC Faculties. They have all worked so hard to ensure the good quality of selecting abstracts and to make this conference successful.

Professor Adel K. Ayed

Dean, Faculty of Medicine

Message from the Vice Dean for Research & Postgraduate Studies
Faculty of Medicine

The first Poster Conference was introduced in April 1996 in the Faculty of Medicine. We have since 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 18 years ago, in April 1996, in the Faculty of Medicine. The founders of Poster Day started with a premise that scientific knowledge and therefore progress depends on investigation and critical analysis, and that exchange of ideas and information is an essential part of this continuous process. 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. Samuel Achilefu, Director of Optical Radiology Lab., Professor of Radiology, Professor of Biochemistry & Molecular Biophysics & Professor of Biomedical Engineering, Washington University School of Medicine, Mallinckrodt Institute of Radiology, USA, who will give the keynote speech on “Image-guided surgery from bench to bedside”. This year we have 209 poster abstracts and I have no doubt that the 19th HSC Poster Conference will be a great success. I thank Kuwait University for the continuing support and sponsorship of the Poster Conference and Prof. Samuel Achilefu for accepting our invitation as a keynote speaker in this year Poster Conference. I would like 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-Attiyah
Vice-Dean for Research & Postgraduate Studies
Faculty of Medicine

Message from the Chairman,
19th HSC Poster Conference Organizing Committee

It is my great pleasure to welcome you all to the 19th Annual Health Sciences Centre Poster Conference, a HSC tradition since April 1996! The conference receives enthusiastic support from all faculties within the Health Sciences Centre and other faculties at Kuwait University. Submission of abstracts from other countries adds an international flavor and also indicates its true vitality. This year 209 posters, that cover a wide range of biomedical topics, are presented. This is a place for basic and clinical sciences to meet. The conference forms the central bond that ties the HSC together. It is an important venue for our students to present and we hope that the event stimulates even more exciting research.

This year, we welcome Professor Samuel Achilefu as our keynote speaker. Professor Achilefu obtained PhD in Molecular/Materials Chemistry from University of Nancy in France and did postdoctoral training in Oxygen Transport Systems at Oxford University, England. He is one of the leading names in the use of nanomaterials as probes for identifying aberrant genes and proteins. His laboratory is active in designing and developing specific ways to image delivery of drugs to target tissues and cell organelles. Professor Achilefu is an ideal person to speak on the aspect of basic research that leads to clinical practice as he started his career as a Research Chemist at Mallinckrodt, Inc. before moving into the academia. He has an enviable track record and wears several hats. Currently he is Professor of Radiology, Professor of Biomedical Engineering, Professor of Biochemistry & Molecular Biophysics, Director of Optical Radiology

Lab, Director of Washington University Molecular Imaging Center and Leader of Oncologic Imaging Program, Siteman Cancer Center, Washington University. He is a widely travelled scientist and has given over 100 invited lectures. He has several patents to his name and an impressive list of research publications.

Organizing of an event is team work. 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 in their category. On behalf of the organizing committee I offer our deepest thanks to Kuwait University for financing the event. But my biggest debt is to the Centre for Research Support and Conferences under the leadership of the past and present Vice Deans for Research & Postgraduate Studies for the infrastructure that made this work so pleasurable. Ms. Teena Sadan and her team have worked tirelessly, efficiently and enthusiastically to make this event such a big success. Lastly, thanks to everyone for coming and joining in. It is the enthusiasm of the participants make this conference the success that it is.

Professor Khalid M. Khan

Chairman, 19th HSC Poster Conference Organizing Committee

Keynote Speaker: Professor Samuel Achilefu

Professor of Radiology, Mallinckrodt Institute of Radiology, Washington University School of Medicine

Professor Samuel Achilefu is the Director, Optical Radiation Laboratory, Mallinckrodt Institute of Radiology, Washington University, St. Louis, Missouri, USA. He has secondary appointments as Professor of Biochemistry and Molecular Biophysics and Professor of Biomedical Engineering. Professor Achilefu has an international reputation has been invited all around the globe and has delivered over 100 lectures in addition to innumerable presentations at international conferences. He was conferred with "Overseas Distinguished Expert Award by the Chinese Ministry of Education. He is a Trustee of Loma Linda University. He is a fellow of SPIE, International Society for Optics and Photonics.

Professor Achilefu is a pioneer in the field of use of nanomaterials for imaging the expression of aberrant genes, proteins, and other pathophysiologic processes. He has over 50 patents in the field of molecular optical imaging. He is particularly interested in developing molecular systems and methods to detect diseases at early stages. He is a member of editorial boards of several

scientific journals He has authored more than 250 scientific papers in addition to book chapters and books.

Professor Achilefu has been in his current position since 2001 and has a distinguished career. He is an excellent teacher and has trained scores of undergraduate and graduate students. He is a mentor par excellence and several postdoctoral fellows have been trained in his multidisciplinary laboratory.

Keynote Abstract:
Image-guided surgery – from bench to bedside

Professor Samuel Achilefu,

Washington University School of Medicine, USA

Nanotechnology has emerged as enabling platform for using nanofabrication and nanoparticle formulations to improve human health. These capabilities has ushered a new era of molecular nanomedicine, where miniaturization of clinical imaging devices has come of age from rudimentary small animal imaging studies to recent efforts in clinical translation. Equally important is the development of molecular imaging probes that can identify primary and metastatic cancer cells. Together, these approaches can address the overarching need to provide real-time image guidance in the operating room.

Here, we demonstrate the astute use of nanotechnology to develop a simple goggle device for image-guided cancer resection, molecular probe to light up cancer cells, and a novel class of nanoparticles to eradicate cancer. The synergistic effect of these technologies promises to improve patient outcomes.

Best Poster Award Winners -2013; 18th HSC Poster Conference

PhD, MSc and Undergraduate

- **Rapid and accurate identification of *Candida dubliniensis* and *Candida albicans* by real-time PCR and melting curve analysis**

  **Asadzadeh M, Ahmad S, Theyyathel A, Khan ZU*

  Department of Microbiology, Faculty of Medicine, Kuwait University

- **Neuron and astrocyte protection against lead toxicity by [(-)-Epigallocatechin-3-Gallate - (EGCG)] in hippocampal primary cell culture**

  **Al Shimali HM, Rao MS, Renno WM, Smitha S.*

  2nd Year Medical Student, Faculty of Medicine Kuwait University; Department of Anatomy, Faculty of Medicine, Kuwait University, Kuwait

- ***Nigella sativa* seeds extract protects hippocampal neurons, enhances neurogenesis and increases astrocytes in kainic acid model of temporal lobe epilepsy**

  Hedaya OM, Rao MS, Renno WM, Smitha S

  3rd Year pharmacy student, Faculty of Pharmacy, Kuwait University; Department of Anatomy, Faculty of Medicine, Kuwait University, Kuwait

- **Lead Imparts Cytotoxic and Mitogenic Effects on Hepatocytes in a Dose and Time-dependent Manner in the Rat Liver**

  **Mujaibel LM , Narayana K*

  Department of Anatomy, Faculty of Medicine, Kuwait University;

  Environmental Science, College of Graduate Studies, Kuwait University

- **Profiling the expression of 84 genes related to the Th17 Regulatory Network in SLE Patients**

  Al-Failakawi AT[1], Al-Fadhli SM[2], Al-Muhana AG[3]

  Department of Biochemistry, Kuwait University Faculty of Sciences; Department of Medical Laboratory Sciences, Kuwait University Faculty of Allied Health Sciences; Department of Rheumatology, Ministry of Health Mubarak Al-Kabeer Hospital.

Graduate Resident Original Research and Case

- **Vernix Caseosa Peritonitis after vaginal delivery- A case report**

  **Sadath SA, Abo Diba FI, Nayak S, Al Shamali I, Diejomaoh MFE.*

  Dept of Obs and Gynae, Faculty of Medicine, Kuwait University, Kuwait; Dept of Obs and Gynae, Maternity Hospital, Kuwait; Dept of Pathology, Maternity Hospital, Kuwait

Past Poster day Keynote Speakers and Lectures

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 21stcentury; 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 Medicien, University of Oxford, UK

Past Poster Day Keynote Speakers and Lectures, Cont.

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 Enviornmental 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

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*Alotaibi N: Investigation into health science students awareness of occupational therapy and implications for inter-professional education

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* Al-Sayegh N, Al-Obaidi SM, Al-shuwai N, Ramadan S, Al-Qurba T, Dean E: Benchmarking Health of the Health Sciences Community of Kuwait University: Health Inventory and Database Development

Anatomy

3

*Abdel Ali A A, Al Sabah AM, Faid IM, Smitha S, Rao MS: Nigella sativa oil enhances neurogenesis, learning and memory in epileptic rats treated with antiepileptic drug

4

*AL-Herz AS, Abu-Sharkh FA, Al-Musaieed SM, Sadek HL, Renno WM: Neuroprotective Effect of Nigella Sativa Oil on Multiple Sclerosis in Rats

5

*Al-Hussaini H, Kilarkaje N: Diabetes-induced retinal pigment epithelial cell proliferation occurs concomitantly with up-regulated ERK and down-regulated JNK signaling in rat retina

6

*Al-Shimali HM, Al-Musaileem, AF, Rao MS, Khan KM: Low-dose exposure to lead during pregnancy effects spatial learning and neurogenesis in hippocampus in young rats

7

*Eid M M Kh E A, Almohri SFA, Shahreyari HAH, Brito AS, Smitha S, Rao MS: Simvastatin decreases hippocampal neurogenesis, learning and memory in rats

8

*Faid I, Abdel Ali A, Verghese S, Narayana K: Resveratrol modulates diabetes-induced alterations in c-Jun N-terminal kinase signaling in the testis

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*Khan KM, Memon I, Siddiqui S, Perveen S, Ishaq M: Expression and immunohistochemical localization of the G beta gama-activated and calcineurin-inhibited adenylyl cyclase isoforms in rat articular chondrocytes

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Khraishah H, Renno WM, Al-Maghrebi M, Rao MS: Green tea (-)-epigallocatechin-3-gallate extract protects the spinal neurons from degeneration by enhancing GAP-43, Bcl-2 and decreasing Bax expression in spinal cord in sciatic nerve crush model of nerve injury

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Narayana K, Al-Hussaini H, Al-Bader M: DNA damage and apoptosis in the testis are associated with poly (ADP-ribose) polymerase-1 inhibition in diabetic rat

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*Rao MS, Raihanah Al-Sayegh, Smitha S: Nigella sativa oil prevents the hippocampal neuronal and dendritic loss and improves learning and memory in kainic acid model of temporal lobe epilepsy

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*Al-Asfoor A, Cheng B, Kilarkaje N: Adrenal distributions of ATP-binding cassette transport A1 and G1

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*Al-Desoky MM, Al-Al-Johar WY, Al-Mufty SA: Determination of trans fatty acids in food samples in Kuwait market

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Alrefaee S, Hattab M, Abdul Hakim E, Mohammad T: A Study in Total Vitamin D Assay

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*Charara M, Benov L, Craik J: Shedding some light on Zn (II) N-alkylpyridylporphyrin-based photosensitizers

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*Hedaya OM, *Qureshi MA, J Craig: Using the ribosome to sythesize polyethylene glycol and polyester biopolymers

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*Moghnieh S, Benov L, Craik J: Antifungal photodynamic activity of Zn (II) N-alkylpyridylporphyrins

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Thomas M, Benov L*: Fe(III) porphyrins cannot act as superoxide scavengers in vivo

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*Thomas M, Benov L: Superoxide dismutase mimetics act as chain-breaking antioxidants

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*Al-Awadi A, Al-Mahmeed A, Ramadan F, Dashti G, Al-Mazeedi I, Al-Asfour M: Anxiety, driving behavior, and road traffic accidents among Public Authority of Applied Education and Training Students

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*Al-Mutawa S, Nazar H, Ariga J, Al-Menezaa E, Al-Duwairy Y, Soparker P: Assessment of Tooth Brushing and Flossing among Adults.

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*Honkala E, El Salhy M, Soderling E, Varghese A, Honkala S: Association between ICDAS Scores in Primary and Permanent Teeth

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*Shyama M, Al-Mutawa SA, Honkala E, Honkala S: Daily Consumption of Soft drinks and Sweets among Disabled Schoolchildren in Kuwait

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Original Research Abstracts By Subject Area

Allied Health
Category: Basic Sciences

1

Investigation into health science students awareness of occupational therapy and implications for inter-professional education

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Introduction:
As the Kuwait University Department of Occupational Therapy graduates its first class, the purpose of this study was to ascertain the level of awareness of the occupational therapy profession among final year health sciences students at Kuwait University.

Methods:
This descriptive study utilized a survey targeting the population of final year students in the Health Sciences Center at Kuwait University schools of Medicine, Pharmacy, Dentistry and Allied Health Sciences. The survey addressed awareness of occupational therapy, its scope of practice, work environments, and preference for learning more about the profession.

Results:
Of the 244 surveys distributed, 132 were returned for a 54% response rate. The proportion of those who knew about occupational therapy ranged from 94% (radiologic science) to a low of 17% (medicine). Most respondents learned about occupational therapy from colleagues (47%), rather than from their academic programs (17%). Results indicated that almost half of the students (41.7%) were unsure about the role of occupational therapists as members of the health care team. Preferences for learning more about the profession were consistent with inter-professional opportunities such as observing an occupational therapy session (65.1%), and attending a workshop (63.3%) or a presentation (59.6%).

Conclusions:
Although the majority of Health Sciences Center students at Kuwait University had some awareness of occupational therapy as an autonomous health care profession, specifics about its scope of practice and relevance to the health care team were lacking. Preferences for learning more about occupational therapy were consistent with the current trend for inter-professional education in health care. Implications for inter-professional education and collaborative practice are presented.

Key Words: Health Care center; Kuwait University; Collaborative practice
Funding Agency: NONE

Allied Health
Category: Clinical

2

Benchmarking health of the health sciences community of Kuwait University: Health inventory and database development

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Introduction:
An important mechanism for addressing Kuwait's leading health care priorities is through health care professionals providing excellent role models with respect to health and wellbeing. Faculty members and support staff can help future health care professionals fulfill this role by serving as exemplary health role models themselves for the student body. In this way, Kuwait University. The aim of this study was to benchmark the health of students, academic faculty members, and support staff across faculties at the Health Science Center of Kuwait University, to inform the need for campus health services.

Methods:
A cross sectional design using a convenience sample of the campus community was used. Health assessment included a health questionnaire and objective measures (heart rate, blood pressure, waist-to-hip ratio, and random blood glucose testing).

Results:
Students, faculty/staff had evidence of sub-optimal health, e.g., overweight/obesity (45%, 74% respectively, $p<0.001$), high blood pressure (16.3%, 33% respectively, $p= 0.009$), and abnormal blood glucose (3.4%, 20% respectively, $p<0.001$). Significant differences between students and faculty/staff were observed for BMI (median (IQR) 24.4 (21.4-27.6) vs 26.8 (24.9-29.5), $p<0.001$); resting heart rate (median (IQR) 84 (14) vs 78 (14), $p=0.003$); systolic blood pressure (mean (SD) 122.6 (15.7) vs 129.7 (19.1), $p=0.001$) diastolic blood pressure (mean (SD) 72.9 (8.7) vs 79.5(9.8), $p<0.001$), and blood sugar (median (IQR) 5.4 (4.9-6.0) vs 6.3 (5.3-7.3), $p<0.001$). Morbidity was more prevalent among faculty/staff compared to students (61.1% and 36.5% had more than one morbidities, $p=0.001$).

Conclusions:
Our findings support the need for general health education targeted at differentially to students, and to faculty and staff to promote a culture of health on campus. Further, a commitment to healthy living will increase the likelihood students will serve as credible role models to their patients upon graduation.

Key Words: Obesity/overweight; Diabetes; Hypertension
Funding Agency: Kuwait University, NP01/10

Anatomy
Category: Graduate MSc (Basic Science)

3

Nigella sativa oil enhances neurogenesis, learning and memory in epileptic rats treated with antiepileptic drug

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Introduction:
Studies have associated brain inflammation as a cause for neural excitability and decreased neurogenesis in epilepsy. Antiepileptic drug, carbamazepine(CBZ), has been shown to weaken the cognitive functions. Nigella sativa oil (NS) has anti-inflammatory and antiepileptic properties and shown to enhance the neurogenesis. Aim of the present study was to investigate the effects of oral treatment with NS oil on neurogenesis, learning and memory in epileptic rats treated with CBZ.

Methods:
Status epilepticus was induced in Wistar rats by injecting kainic acid(0.5µg) into the lateral ventricles and were divided into four groups. i. Remained without any treatment - Lesion only (LO), ii. Lesioned and treated with NS for 30 days (400mg/kg, L+NS), iii. Lesioned and treated with CBZ (30mg/kg, L+CBZ), iv. Lesioned and treated with NS and CBZ (L + NS + CBZ, n=12 in all groups). Six rats from each group were subjected to passive avoidance (PA) test after treatment. The other 6 rats were subjected to long term memory test in Morris water maze (MWM). After behavioral tests rats were sacrificed, brain was dissected, brain sections were immunostained with doublecortin to assess neurogenesis. Data were analyzed with one way ANOVA.

Results:
PA test revealed significant deficit in memory retention in LO and L+CBZ groups compared to normal controls(NC, $P<0.001$); memory was unimpaired in L+NS and L+NS+CBZ groups. MWM test showed a significant learning and memory deficit in LO, L+CBZ group compared to NC($P<0.001$); memory retention of L+NS group was comparable to NC. Memory in L+CBZ+NS group was significantly better than L+CBZ group ($P<0.001$). Neurogenesis was significantly decreased in LO compared to NC($P<0.001$) and significantly increased in L+NS and L+ NS+CBZ compared LO group($P<0.001$).

Conclusions:
Our data suggest that treatment with CBZ deteriorates the cognitive functions and NS restores it, possibly by increasing neurogenesis.

Key Words: Carbamazepine; Spatial learning; Neurogenesis
Funding Agency: NONE

Anatomy
Category: Undergraduate

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Neuroprotective effect of *Nigella sativa* oil on multiple sclerosis in rats

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Introduction:
Multiple sclerosis (MS) is a chronic demyelinating disease in which the myelin around the axons in the CNS are damaged, leading to axonal injury with a broad spectrum of neurological signs and symptoms. A combination of genetic, environmental and infectious factors contributes to the development of MS. Several studies showed that Nigella sativa and its active ingredient, thymoquinone, have neuroprotective effects against many degenerative diseases, such as diabetic neuropathy and frontal cortical degeneration. The aim of this study is to investigate the role of Nigella Sativa oil (NSO) neuroprotection and remyelination following MS. Previous studies have shown strong association between NSO and the fundamental biological processes that facilitate regeneration, such as anti-oxidant, anti-inflammatory, and anti-apoptotic effects.

Methods:
Fifteen Wistar female rats aged 21 days were randomly divided into three groups: Group A was a control group; Group B and C were given 0.6% cuprizone in food chow for two weeks to induce demyelination. Group B was treated orally with 400 mg/kg of NSO; while group C were given equal volume of saline. Behavioral tests were conducted during the experimental period including tail flick, hot plate, and rota-rod followed by morphological assessment of the brain tissues at the end of the experiment.

Results:
Animals treated with NSO showed significant ($P<0.000$) improvement on rota-rod test compared to saline treated group. Tail flick ad hot plate results were insignificant. In cuprizone fed rats many oligodendrocytes showed morphological characteristics of apoptosis such as condensed and fragmented nuclei. In contrast, NSO-treated group revealed less abnormal oligodendrocytes and noticeable preservation of the white matter area of corpus callosum.

Conclusions:
NSO may be a useful adjunct therapeutic regimen to alleviate neurobehavioral symptoms as well as speed up the remyelination process in MS rat model.

Key Words: Black seeds; cuprizone; neurobehavior
Funding Agency: FOM

Anatomy
Category: Basic Sciences

5

Diabetes-induced retinal pigment epithelial cell proliferation occurs concomitantly with up-regulated ERK and down-regulated JNK signaling in rat retina

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Introduction:
Diabetes causes retinal microvascular changes and disruption of blood-retinal barrier leading to retinopathy. However, the influence of diabetes on proliferative ability of retinal pigmented epithelium (RPE) and factors responsible for the proliferation under hyperglycemic state are not clear. The present study investigated the role of extracellular-signal regulated kinases 1 and 2 (ERK1/2) and c-Jun-N terminal kinases 1/2/3 (JNK1/2/3) in diabetes-induced RPE proliferation.

Methods:
Diabetes was induced in male dark Agouti rats (12-week-old) by streptozotocin and the RPE was dissected out on day 7 (N=9), 21 (N=7) and 35 (N=6) from the eyeball and used as a monolayer for BrdU labelling by immunofluorescence. The ERKs, JNKs and c-Myc were quantified by Western blotting (N=10) on day 15 as a pilot study showed highest cell proliferation on this day. The data were statistically analyzed by Mann-Whitney 'U' test and Kruskall-Wallis test with significance set at $P<0.05$.

Results:
In diabetic groups, the RPE cell proliferation was observed on day 7 and continued to remain as such up to day 21 ($P<0.05$), but on day 35, the proliferation was subsided to the control level. The levels of ERK1/2 and total ERKs were significantly increased ($P<0.05$) and that of JNK p54 isoform was almost completely abrogated in diabetic group ($P<0.05$), with border line significant increase in p46 isoform ($P=0.05$). The level of c-Myc, a downstream target of JNK, showed a trend to up-regulate in diabetic group although the effect was not significant.

Conclusions:
Our results indicate that diabetes enhances the proliferation of RPE cells in an ERK- and JNK-dependent manner. The ERK inhibition may be a new avenue of research to alleviate the RPE proliferation in diabetics.

Key Words: Blood-retinal barrier; Diabetic retinopathy; MAPKs, RPE proliferation
Funding Agency: Kuwait University, MA02/09

Anatomy
Category: Undergraduate

6

Low-dose exposure to lead during pregnancy effects spatial learning and neurogenesis in hippocampus in young rats

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Introduction:
Lead (Pb) is toxic to all organ systems. The severity of toxicity depends on the dose, duration of exposure, and developmental stage of the subject. Central nervous system has received much attention because of the impact of Pb exposure on cognitive and behavioral development in children. The aim of this study was to investigate the effects of in utero low-dose exposure to Pb on spatial learning and neurogenesis in hippocampus of young rats.

Methods:
Wistar rats were mated and after pregnancy was established, animals (N=10) were given drinking water with 0.1% lead acetate from day one of pregnancy until parturition. Control animals (N=10) received deionized water. Spatial learning and memory of two pups from each dam were determined with Morris water maze on postnatal days 21 and 30. Animals were later sacrificed and Pb level in hippocampus was measured by atomic absorption spectrophotometer. Sections of hippocampus were stained for doublecortin (marker for neurogenesis). Data were analyzed with Student's t-test.

Results:
Pb in hippocampus of Pb-exposed rats were significantly ($P<0.001$) higher in 21-day group but not in the 30-day group. Water maze test revealed significant($P<0.01$) memory deficit when tested on day 21, but not when tested on day 30. When retested for memory retention after 10 days both control and Pb-exposed rats failed to locate the platform. However, after a session of relearning and retesting 24 hours later, only the rats from the control group located the platform. Pb-treated rats showed significantly decreased number of doublecortin positive neurons in the hippocampus in comparison to control rats ($P<0.0001$).

Conclusions:
Our data show that low-dose exposure to Pb during pregnancy results in impairment of spatial learning correlated with decreased neurogenesis in the hippocampus.
Acknowledgements: We acknowledge the use of Research Core Facility (SRUL 02/13) and technical help of S. Jacob, S. Joe and S. Shivanandan.

Key Words: Lead neurotoxicity; Spatial learning; Neurogenesis
Funding Agency: None

Anatomy
Category: Graduate MSc (Basic Science)

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Simvastatin decreases hippocampal neurogenesis, learning and memory in rats

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Introduction:
Statins are a group of drugs (3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors) used for treating hypercholesterolemia and coronary artery diseases. Experiential studies showed that statins have adverse psychiatric effects, amnesia and anxiety. Aim of the present study was to investigate the effects of simvastatin on neurogenesis, spatial learning and memory in rats.

Methods:
Wistar rats (3 months) were divided into two groups: -normal control group (NC, n=6) and simvastatin group (ST, n=6). Rats in both groups were subjected for learning and memory ability screening in Morris water maze (MWM). NC rats were intubated with saline(1ml) for 30 days. ST rats were treated orally with simvastatin (1mg/kg) for 30 days. All rats were subjected to MWM learning and memory test from 31st day. From 38th day onwards rats were subjected to new learning sessions and memory test in the same water maze. Finally all rats were sacrificed and brain was dissected. Brain sections were immunostained for doublecortin to assess neurogenesis. Data were analyzed with Student's t-test.

Results:
Screening test revealed a good learning ability and memory in both groups. Escape latency was significantly increased in ST group after treatment with simvastatin compared to NC ($P<0.001$); during memory retention test, 24hrs and 48hrs after last learning session, ST rats spent significantly less time in the target quadrant compared to NC rats ($P<0.001$. In new learning sessions escape latency was significantly high in ST rats ($P<0.001$); during memory retention test 24hrs and 48hrs after new learning session, ST rats spent significantly less time in the target quadrant compared to NC rats ($P<0.001$). There was a significant decrease in neurogenesis in the hippocampus of ST treated group.

Conclusions:
Our data suggests that simvastatin affects the cognitive function. Impaired learning and memory may be due to decreased neurogenesis.

Key Words: Simvastatin; Hippocampus; Neurogenesis
Funding Agency: NONE

Anatomy
Category: Graduate MSc (Basic Science)

8

Resveratrol modulates diabetes-induced alterations in c-Jun N-terminal kinase signaling in the testis

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Introduction:
Background & Objectives: Although diabetes (DM) induces male hypogonadism, the early molecular changes in the testis leading to gonadal dysfunction have not been investigated. In this study, we investigated the modulatory effects of Resveratrol (RES) on DM-induced alterations in c-Jun N-terminal kinase (JNK) signaling in the rat testis.

Methods:
Adult male Wistar rats (N=6-8) were segregated into a) control; b) RES-treated (20 mg/kg; ip); c) Streptozotocin-induced DM; and d) DM + RES-treated groups. The b and d groups received RES (20 mg/kg; ip) from day 8-14. All animals were sacrificed on day 14 after the confirmation of DM. In the testis, total antioxidant (TAS) and oxidant (TOS) levels (plate reader assays), and JNK, p-JNK, c-Jun, and p-c-Jun activities (immunohistochemistry and Western blotting) were measured. Data were analyzed by Mann-Whitney 'U' test with the level of significance set at $P<0.05$.

Results:
RES exacerbated DM-induced decrease in body weight gain ($P<0.05$), but neither DM nor RES affected reproductive organ weights and sperm parameters, except that RES recovered reduced prostate weight in DM rats ($P<0.05$). In contrast to our hypothesis, RES, when given to normal or DM rats, has induced oxidative stress as indicated by reduced TAS/TOS ratio. DM up-regulated JNK and p-JNK expression, but RES normalized only JNK expression to control level, but not that of p-JNK. RES inhibited both c-Jun and p-c-Jun expression, on the other hand, DM stimulated c-Jun and inhibited p-c-Jun expression, which were normalized to control level by RES in DM rats ($P<0.05$).

Conclusions:
Our results indicate that RES up-regulates oxidative stress, but down-regulates JNK signaling in DM rat testis. It appears that the inhibition of JNK signaling by RES in DM rats may not be mediated by oxidative stress, but by some other unknown mechanisms and that the normalization of JNK signaling by RES in DM rats is related to germ cell survival in the testis.

Key Words: Hyperglycemia; Antioxidants; Male reproductive system
Funding Agency: SRUL02/13

Anatomy
Category: Basic Sciences

9

Expression and immunohistochemical localization of the G beta gama-activated and calcineurin-inhibited adenylyl cyclase isoforms in rat articular chondrocytes

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Introduction:
Cross-talk between signal transduction pathways is essential to maintain normal homeostasis. cAMP mediated pathway is archetypical in mammalian cells and adenylyl cyclase (AC) is the effector enzyme that converts ATP into cAMP. We believe that AC/cAMP mediated pathway is involved in homeostasis of the articular cartilage. In this study we report the expression of Gβγ-activated AC isoforms 2, 4, and 7 and calcineurin-inhibited AC isoform 9 in rat articular chondrocytes.

Methods:
Fresh slices of articular cartilage were taken from various synovial joints of rat (N=5). Total RNA was extracted through modified single step RNA extraction method using Tri Reagent and the expression of AC isoforms was determined by RT-PCR. Immunohistochemical localization of AC isoforms in articular chondrocytes was performed by using specific antibodies.

Results:
All AC isoforms studied were found differentially expressed in the articular cartilage. Generally, expression of all AC isoforms increased with age from week 0-6. Immunoreactivity for all AC isoforms was detected in all zones of the articular cartilage but age-related differences were noted which were similar to the RT-PCR results.

Conclusions:
These data add to the information about signaling cascades possibly involved in articular chondrocytes. Presence of AC isoforms 2, 4, 7, and 9 suggest a role for the AC/cAMP mediated 2nd messenger signaling cascades in articular chondrocytes. Further studies, such as measuring the AC and cAMP levels during development and differentiation of articular chondrocytes would confirm our results and help in understanding the signaling mechanisms in articular chondrocytes.

Key Words: Articular chondrocytes; cAMP signaling
Funding Agency: NONE

Anatomy
Category: Graduate MSc (Basic Science)

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Green tea (-)-epigallocatechin-3-gallate extract protects the spinal neurons from degeneration by enhancing GAP-43, Bcl-2 and decreasing Bax expression in spinal cord in sciatic nerve crush model of nerve injury

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Introduction:
EGCG, the active ingredient in green tea, has been shown to display many beneficial actions on different tissues due to its anti-oxidant, anti-inflammatory, anticholesterolemic effects, and various modulating effects on apoptosis. The goal of this study is to test the central effects of ECGC on spinal cord motor neurons after sciatic nerve injury.

Methods:
Forty Wistar rats were randomly assigned to one of four groups: Naïve control group, Sham operated animals, saline-treated sciatic nerve crushed animals, and EGCG-treated sciatic nerved injured group. The rats were tested using various behavioral, histological and Immunohistochemical methods. Moreover, the expression of GFAP, GAP-43, Bax, Bcl2, and surviving were measured using real time PCR.

Results:
Our study showed that administering 50 mg/kg i.p.of EGCG to sciatic nerve injured rats improved their performance on different behavioral tests checking for the motor functions and mechanical hyperesthesia. Histological examination of the spinal cords of sciatic nerve injured and EGCG-treated animals showed an increase in the number of neurons in the anterior horn when compared to sciatic nerve injured and saline treated animals. Additionally, immunohistochemical examination of spinal cord sections revealed that EGCG reduced the expression of GFAP and increased the expression of GAP-43. Finally, EGCG reduced the ratio of Bax: Bcl2, and increased the expression of survivin gene.

Conclusions:
This study suggests future clinical use of EGCG and its constituents in the treatment of peripheral nerve injury due to its neuroprotective and neuroregenerative properties.

Key Words: EGCG; Neuroprotection; Spinal cord
Funding Agency: None

Anatomy
Category: Basic Sciences

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DNA damage and apoptosis in the testis are associated with poly (ADP-ribose) polymerase-1 inhibition in diabetic rat

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Introduction:
Although diabetes induces infertility, molecular mechanisms responsible for the onset of diabetes-induced testicular dysfunction are not clear. In this study, we investigated the relationship between DNA damage and expression of poly (ADP-ribose) polymerase-1 (PARP1) in diabetic rat testis.

Methods:
Diabetes was induced in adult male SD rats (N=6) by streptozotocin treatment and the testes were retrieved at the end of first (DM1) and third (DM3) month. In the testis, the total oxidant and antioxidant (plate reader assay) and 8-Oxo-dG (ELISA and immunohistochemistry) levels were measured. The PARP1 activity was measured by Western blotting and immunohistochemistry. The TUNEL assay was used to label DNA double-strand breaks. The data were analyzed by Mann-Whitney 'U' test and Kruskall-Wallis test with a significance level set at $P<0.05$.

Results:
Diabetes increased oxidative stress status along with upregulation of deoxyguanosine oxidation in a stage-dependent manner ($P<0.05$). In DM1, all germ cell types and Sertoli cells in stage VII-IX tubules showed more cytoplasmic expression of 8-Oxo-dG than did the other stage tubules indicating mitochondrial DNA damage. In DM3, mainly nuclear expression of 8-Oxo-dG was observed in germ cells, but not in Sertoli cells, in a stage-dependent manner indicating genomic DNA damage. The levels of full length PARP1 (116 kDa) and its 89 kDa large-cleaved fragment were decreased in both DM groups. The level of 24 kDa small-cleaved fragment was decreased in DM1 and increased in DM3 ($P<0.05$). A stage-dependent nuclear expression of the protein was observed in germ and Sertoli cells, which decreased from DM1 to DM3. Increases in oxidative DNA damage and PARP1 cleavage led to DNA double-strand breaks with 3'OH ends in a stage-independent manner ($P<0.05$).

Conclusions:
DM-induced oxidative stress, single and double strand DNA breaks occur along with PARP1 inhibition in the testis.

Key Words: Hyperglycemia; Hypogonadism; DNA damage
Funding Agency: General Facility Grant # SRUL 02/13

Anatomy
Category: Basic Sciences

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Nigella sativa oil prevents the hippocampal neuronal and dendritic loss and improves learning and memory in kainic acid model of temporal lobe epilepsy

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Introduction:
Nigella sativa seeds oil (NSO) is shown to have many therapeutic effects. Chronic temporal lobe epilepsy leads to neuronal loss, decrease in dendritic length in hippocampus and subsequent memory loss. Present study was aimed to investigate the effects of NSO on learning, memory, hippocampal neuronal number and dendritic length (in CA1, CA3, dentate hilus (DH) and dentate gyrus) in rats which had status epilepticus.

Methods:
Temporal lobe epilepsy (TLE) was induced by injecting kainic acid (0.25µg) into the lateral ventricles in 4 months old Wistar rats. These rats were divided into two groups: i) Lesion only (LO, n=12) - received 1ml of saline orally for three week, ii) Lesion + nigella sativa oil (L+NSO, n=12) - received NSO (400mg/kg) in saline orally for three weeks. A group of age matched normal control rats were also maintained (n=12). Rats in all groups were subjected to Morris water maze learning test after 3 weeks of treatment. Rats were sacrificed and brain was processed for cresyl violet, NeuN and Golgi staining. Number of neurons, dendritic length and branching points in different regions of hippocampus were quantified. Data were analyzed with one way ANOVA followed by Bonferroni's test.

Results:
Rats treated with NSO spent significantly more time in target quadrant during probe test in water maze suggesting better memory retention compared to LO group. NeuN staining revealed significantly more number (~20%) of neurons in CA1, CA3, DH and DG regions in lesion + NSO group compared to LO group ($P<0.001$). Golgi staining showed significantly increased dendritic length and branching (~30%) in all regions in L+NSO group ($P<0.001$).

Conclusions:
Results of our study revealed that treatment with NSO prevents the neuronal and dendritic loss and improve learning and memory in chronically epileptic rats. Hence NSO may be used along with antiepileptic drugs to prevent neuronal degeneration and memory loss in epileptic patients.

Key Words: Nigella Sativa; Hippocampus; Memory
Funding Agency: NONE

Biochemistry
Category: Graduate MSc (Basic Science)

13

Adrenal distributions of ATP-binding cassette transport A1 and G1

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Introduction:
Adrenal gland has two distinct structures the cortex and the medulla. The cortex comprises three zones: glomerulosa (ZG), fasciculata (ZF), and reticularis (ZR). Adrenocortical ZG and ZF/ZR synthesize aldosterone and cortisol, respectively. In circulation, the molar ratio of aldosterone to cortisol is about 1 to 250-3,300. Thus, it takes a very small quantity of cholesterol to synthesize aldosterone in the ZG, as compared to the quantity of cholesterol needed for cortisol production in ZF/ZR. However, animal studies revealed that the ZG not only contains rich cholesterol and actively expresses lipoprotein receptors, but also accumulates lipid droplets for storage of cholesterol esters. Thus, the ZG should express a comparable level of ATP-binding cassette transporter (ABC) to facilitate cholesterol efflux in parallel.

Methods:
ABCA1 and ABCG1 are the principal ABCs that mediate cholesterol efflux. Adrenal distributions of ABCA1 and ABCG1 in male Wistar rats were investigated by a histochemical technique using commercially available specific antibodies as probes. Aldosterone synthase (CYP11B2) and 11-beta-hydroxylase (CYP11B1) were employed as specific markers for ZG and ZF/ZR, respectively.

Results:
The immunostaining results show that CYP11B2 is enriched only in the ZG, whereas CYP11B1 resides in ZF/ZR. No immunostains of either marker were seen in the medulla. The ZG and its adjacent portion of ZF contain the highest concentrations of both ABCA1 and ABCG1 than the inner portion of ZF, ZR, and medulla.

Conclusions:
The ZG expresses ABCA1 and ABCG1. Conceivably, both transporters provide a fine tuning mechanism to adjust cholesterol availability for aldosterone synthesis. We thank F. Sequeira, G. Thakkar and S. Varghese for technical advices. This work is supported by a Research Grant No. YM13/04 of the University.

Key Words: ABC transporter; Adrenal Cortex; Aldosterone
Funding Agency: Kuwait University, YM 04/13

Biochemistry
Category: Basic Sciences

14

Determination of trans fatty acids in food samples in Kuwait market

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Introduction:
Humans need edible fats to provide energy and to sustain growth. Vegetable oils contain a mix of saturated, monounsaturated, and polyunsaturated fatty acids. The mono- and polyunsaturated fatty acids have double bonds, all in the normal "cis" formation. Food manufacturers go to convert the vegetable oils to hydrogenated vegetable oils by hydrogenation process which increases the shelf life, flavor stability and improve the texture of foods. Hydrogenation will convert "cis" double bonds to "trans" double bonds, producing trans fatty acids. Trans fatty acids affect human health by raising the low density lipoprotein (LDL) cholesterol (bad blood cholesterol) and lowers the high density lipoprotein (HDL) cholesterol (good blood cholesterol), which leads to increase the total blood cholesterol level. A high total blood cholesterol level is a major risk factor for coronary heart disease. The objective of this study is to determine and quantify trans fatty acids in food samples.

Methods:
A total of 720 samples including vegetable oils, hydrogenated vegetable oils, margarine, butter, ghee, cheese, cake and biscuits from 15 countries were collected during the period of January 2011 and December 2013. They were analyzed and quantified using gas chromatography with flame ionization detector (GC-FID).

Results:
We determined and quantified different types of trans fatty acids such as elaidic acid, which is the major type of trans fatty acid, linoelaidic acid and palmitelaidic acid. There were 331 sample (46%) contain less than 0.2% (w/w, gram of trans fatty acids per 100 gram of total fatty acid), while 296 sample (41.1%) ranged from 0.2-2.5%, 79 samples (11%) ranged from 2.5-10% and 14 samples (1.9%) more than 10% of trans fatty acid.

Conclusions:
The study highlight that a lot of food sample in local Kuwait markets contain trans fatty acids ranged from 0.01 to 25% according to the different types of fats and oils and there degree of hydrogenation.

Key Words: Trans fatty acid; Gas chromatography; Hydrogenated vegetable oil
Funding Agency: none

Biochemistry
Category: Clinical

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AQt90 analyzer as a point of care

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Introduction:
A lot of interest toward point-of-care (POC) testing for biochemical markers of myocardial cell necrosis in addition to traditional testing is found in clinical field, since this technology introduced a wide range of tests to be performed simply and quickly. However, rapid patient triage, decreased length of stay and improvement in turnaround time, combined with lack of precision, sensitivity, increased cost and no demonstration in improvement in patient outcomes gave a mixed opinion regarding the issue of POC that precludes their routine use and recommendation. We tested AQt90 analyzer / Radiometer as a random access immunoassay system "whole blood" for patients presented with cardiac like symptoms. Troponin I, CKMB, Myoglobin, NT- pro BNP and D-Dimer were the markers to be tested.

Methods:
Blood samples from suspected cardiac patients or coagulation abnormalities were collected using EDTA as sampling tube. Citrated tube was used for D-Dimer to be compared with latex agglutination method" DIMERTEST, American Diagnostica" and EDTA samples. Comparison with Beckman access for Troponin I was also done. Controls tested before each run for tests specified above.

Results:
147 patients "75 males and 72 females" were involved randomly. Citrated and EDTA D-Dimer tests correlated significantly P=0.0001. D-Dimer levels >1000 ng/ml showed positive results with latex agglutination. Interestingly, D-Dimer correlated with NT-pro BNP; p=0.001. Troponin correlated with CKMB; p= 0.035, NT-pro BNP; p=0.03 but not Myoglobin; p=0.4 or D-Dimer; p=0.9. Troponin I; n=39 (medianAQT90 0 ng/ml), however, failed to show correlation with Beckman access (median Access 0.01 ng/ml); p=0.9.

Conclusions:
AQT90 could be a valuable point of care testing in addition to traditional testing for cardiac patients using EDTA samples. More samples needed for Troponin comparison.

Key Words: AQT90; POINT OF CARE; TROPONIN
Funding Agency: TAREQ COMPANY

Biochemistry
Category: Clinical

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A study in total vitamin D assay

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Introduction:
A renewed interest in vitamin D reflects almost the high prevalence of vitamin D deficiency worldwide and the increased publication connecting its deficiency to other clinical conditions than bone health. In most assays underestimation of the vitamin levels observed even with the new measurement of total vitamin D (D3+ D2) assays. Therefore, the combination of total vitamin D levels with other tests should be considered when studying certain clinical conditions such as bone diseases and diabetes mellitus.

Methods:
We tested total vitamin D results in randomly selected 243 patients attending J.A. armed forces hospital. Total vitamin D levels were measured for the samples using two different instruments located at two different hospitals. LIAISON, diaSorin at our hospital and ROCHE, COBAS 6000 in MOH hospital. We studied the link between serum total vitamin D levels and levels of serum calcium, parathyroid hormone, glucose, HbA1c all measured at j.A armed forces hospital.

Results:
Descriptive statistics for whole population involved that include 41 males and 202 females are shown in the table. No statistically significant difference was found in total vitamin D levels between both sexes (Mann-Whitney; P=0.6). LIAISON & COBAS total vitamin D levels correlated significantly (P=0.001, R2=0.87; linear regression). No Correlations (spearman) were found between total vitamin D, ca (P=0.9), PTH (P=0.4), Glucose (P=0.6) or HbA1C (P=0.2).

Conclusions:
Measurement of total vitamin D alone provides crude assessment of its status but may give inaccurate indication of its deficiency's effect on certain clinical conditions.

	Vitamin D	Ca	PTH	glucose	HBA1C
	nmol/l	mmol/l	pmol/l	mmol/l	%
median	22.3	2.3	26.4	5.4	7.1
25 % I.Q.R	19.03	2.2	17.8	5	6.2
75% I.Q.R	58.1	2.4	60.5	6.3	9.1

Key Words: Vitamin D; LIAISON, DiaSorin; ROCHE, COBAS 6000
Funding Agency: none

Biochemistry
Category: Graduate MSc (Basic Science)

17

Shedding some light on Zn (II) N-alkylpyridylporphyrin-based photosensitizers

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Introduction:
Photodynamic therapy (PDT) is emerging as a promising medical treatment for both neoplastic and non-neoplastic disorders. In PDT, cell destruction is accomplished by the production of cytotoxic reactive species upon illumination of light-sensitive compounds called photosensitizers (PSs). It has been determined that the location and extent of damage determines the mode of cell death and consequently the outcome of PDT. The aim of this study was to investigate the relationship between the structure of specially designed Zn(II) N-alkylpyridylporphyrin photosensitizers (ZnPs) and their cellular localization, cell death mechanisms and consequently their PDT efficacy.

Methods:
A homologous series of isomeric ZnPs with increasing length of alkyl chains were synthesized. Their effect on PII cells' viability and proliferation was tested using MTT and SRB assays, respectively. Flow cytometry (Annexin kit) was used to determine the mechanism of cell death. Experiments were repeated at least twice, with 3 replicates.

Results:
The photoefficiency of amphiphilic hexyl ZnPs depended on the position of the meso substituent. At 0.5 uM the ortho isomer demonstrated the highest PDT efficiency followed by the meta and para isomers, in parallel with photodependent yield of reactive species. Minimal loss of viability was observed during the illumination period (20 min), but as a result of PDT-triggered cell death mechanisms, less than 50% of the cells survived for 48 h.

Conclusions:
The anti-proliferative activity and the pattern of cell killing by ZnP PSs depended on their concentration, the time of illumination and the spatial orientation of alkyl substituents at meso position on the porphyrin ring.

Key Words: Photodynamic therapy; Photosensitizer; Zn-porphyrin
Funding Agency: Kuwait University College of Graduate Studies (Grant YM09/13)

Biochemistry
Category: Basic Sciences

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Phytanic acid activates NAPDPH oxidase in vascular smooth muscle cells

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Introduction:
Phytanic acid (PA), a branched fatty acid derived from chlorophyll, is of great significance in human health as its defective metabolism leads to life threatening conditions such as Refsum disease. To explore molecular mechanisms of phytanic acid-induced cellular pathology, we investigated its effect on NADPH oxidase (NOX), major enzyme system responsible for producing cytotoxic superoxide radical, and epidermal growth factor receptor (EGFR), a significant player in free radical-induced intracellular signaling effects, in rat aortic smooth muscle cells (RASMC).

Methods:
Smooth muscle cells were isolated from rat aortae using enzymic digestion with collagenase and elastase. Cultured RASMC were treated with varying concentrations (0.5-10 µg/ml) of phytanic acid in the presence / absence of fetal bovine serum (FBS). Following treatment with experimental agents, NOX activity was assayed in RASMC cultures by luminescence method using lucigenin. Protein levels of NOX-1 and, phosphorylated and total EGFR were measured in cell homogenates by Western blot.

Results:
Treatment of RASMC with physiological levels (1.0 µg/ml) of PA did not affect NOX activity, however supraphysiological concentrations (> 10µg/ml) of PA significantly ($p < 0.01$) increased the NOX activity. Interestingly, PA (1-10 µg/ml) markedly (2-3 folds) increased the phosphorylation of EGFR.

Conclusions:
These results suggest for the first time that phytanic acid induces NOX activity in vascular smooth muscle cells which possibly involves activation of EGFR phosphorylation.

Key Words: Phytanic acid; NOX; EGFR
Funding Agency: Research Sector Kuwait University Grant MK 01/12

Biochemistry
Category: Undergraduate

19

Using the ribosome to synthesize polyethylene glycol and polyester biopolymers

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Introduction:
Polymers have a variety of medical use such as, in drug delivery and biomaterials, but the main problem with polymers is their synthesis, which is tedious and inefficient, resulting in low yields of imperfectly sequenced polymers. In the cells, ribosomes synthesize proteins, which is by facilitating a nucleophilic attack from the aminoacyl-tRNA onto the peptidyl-tRNA, yielding a growing peptide. In this study we intend to assess the ability of this system to catalyze polyester and ethylene glycol polymerization.

Methods:
Alpha-hydroxyacyl-tRNAs were prepared by the deamination the aminoacyl-tRNA mixture after nitrous acid treatment. The ethylene glycol sulfonate ester of the tRNA was also prepared by reacting tRNA-sulfonyl chloride and ethylene glycol in the presence of pyridine. To guide the polymerization, artificial mini genes coding for methionine-alanine and methionine-alanine-phenylalanine were then synthesized by a DNA synthesizer. Each of the tRNAs were then incubated with each of the mini genes in a transcription and translation mixture for 4 hours at 37ºC. This reaction was then stopped by freezing the samples. The products were then analyzed by liquid chromatography mass spectroscopy (LC-MS).

Results:
After the incubation with the different tRNA derivatives, the produced polymers matched the predicted mass, depending on the mini gene used.

Conclusions:
The ribosome can successfully be used to catalyze the formation of non-protein biopolymers, but require the presence of an attacking nucleophilic group and a suitable leaving group. This reaction requires further investigation to find out the yield and the perfect conditions required for this reaction to work.

Key Words: Ribosome; Non-protein; Biopolymers
Funding Agency: None

Biochemistry
Category: Graduate MSc (Basic Science)

20

Antifungal photodynamic activity of Zn (II) N-alkylpyridylporphyrins

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Introduction:
The increase in antibiotic resistance among pathogenic bacteria, viruses, and fungi has stimulated research for alternative treatment strategies. Photodynamic inactivation (PDI) is one of the novel antimicrobial approaches that avoids resistance. In PDI, light activates a photosensitizer (PS) which in the presence of molecular oxygen generates singlet oxygen and other reactive oxygen species that damage and kill the target cells. The aim of this study was to investigate the antifungal activities of newly synthesized Zn-porphyrins (ZnPs) and commercially available PSs with different structures and lipophilicity.

Methods:
The PDI efficiency of PSs was assessed by investigating their effect on cell viability using the MTT surrogate assay. Yeast suspensions of S. cerevisiae and C. albicans were grown to A600~ 0.1. Aliquots of 100µl were incubated with different concentrations of PSs for 90 minutes and illuminated for 60 min. Cell viability was then determined. Experiments were repeated at least 3 times with 3 replicates. Results were expressed as means ±S.E.

Results:
The antifungal PDI efficiency of ZnPs increased as their lipophilicity increased; the long-chain amphiphilic ZnPs were more efficient than the short-chain hydrophilic analogs. Increasing the hydrophobicity of ZnP molecules increases their cellular accumulation. There was no significant difference between the ortho, meta, and para isomers. Chlorin e6, a hydrophobic PS, at 5 and 10 µM demonstrated lower photoefficiency than the ZnP hexyl derivative.

Conclusions:
ZnPs antifungal efficiency depends on chain length and the nature of meso-substituent groups present in the macrocycle periphery. Increase in the amphiphilic character of the photosensitizer assists its accumulation in the cell and is accompanied by an increase in the photocytotoxic antifungal activity. The amphiphilic hexyl-substituted ZnP is a promising PS for antifungal photodynamic therapy.

Key Words: Photodynamic antifungal therapy; Photosensitizer; Photodynamic inactivation
Funding Agency: Grant YM 03/13, Kuwait University

Biochemistry
Category: Basic Sciences

21

Fe(III) porphyrins cannot act as superoxide scavengers in vivo

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Introduction:
Para cationic Fe(III) N-methylpyridylporphyrin was the first metalloporphyrin to possess high catalytic rate constant for superoxide (O_2^-) dismutation [log $k_{cat}(O_2.^-) = 7.20$)]. This encouraged the synthesis of other Fe-porphyrins (FePs), which were tested as potential medications in various pathological conditions. No proof, however, has been provided so far that such compounds scavenge superoxide in vivo. In an attempt to fill this gap, the present study explores the mechanism of FePs in vivo action.

Methods:
The efficiency of FePs in scavenging superoxide was determined by their ability to replace the missing superoxide dismutases (SOD) in mutant strains of Escherichia coli and Saccharomyces cerevisiae. Information about the intracellular state of the FePs was obtained by growing SOD deficient cell cultures with fixed concentrations of FePs and analyzing cell lysates. Fe liberated from the FePs, free porphyrin ligand content, and the ability of the lysate to suppress/induce lipid peroxidation were determined. All experiments were repeated at least 3 - 5 times with 3 replicates. Results are expressed as means ± S.E.

Results:
None of the tested Fe(III) N-alkylpyridylporphyrins could replace SOD in SOD-deficient strains. Analyses of cell lysates demonstrated that in cells, the FePs exist as metal-free porphyrins and that cells incubated with FePs accumulate Fe unbound to porphyrin. While the FePs suppressed lipid peroxidation, lysates obtained from cells incubated with FePs induced lipid peroxidation.

Conclusions:
Irrespective of their high catalytic rate constant for superoxide dismutation, FeP-based compounds cannot act as catalytic superoxide scavengers in vivo due to their instability. Caution should be applied, and before such compounds are proposed for pharmaceutical use, their metabolic stability should be thoroughly checked.

Key Words: Iron-porphyrin; Superoxide dismutase; Antioxidant
Funding Agency: Grant MB02/12 from Kuwait University

Biochemistry
Category: Basic Sciences

22

Superoxide dismutase mimetics act as chain-breaking antioxidants

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Introduction:
The central role of superoxide ($O2^-$) as a mediator of oxidative stress and source of other reactive oxygen species has triggered great interest in artificial compounds capable of performing catalytic removal of $O2^-$. In many cases, such superoxide dismutase (SOD) mimetics have catalytic activity that is too low to explain their in vivo beneficial action. This suggests that activities other than scavenging of $O2^-$. should be considered. The aim of this study was to explore the ability of a series of SOD mimetics to act as chain-breaking antioxidants.

Methods:
Rat brain homogenate was used as a model system. Series of SOD mimetics including Mn(III) porphyrins, Mn(III) salens, Mn(II) cyclic polyamines, nitrones, and nitroxides were tested at concentrations of 0.1 – 50 uM. Cell-free extracts of cells cultures incubated with the compounds were used in order to obtain information about the intracellular state of the SOD mimetics. The chain-breaking activity of the compounds was determined by assaying the amount of malondialdehyde produced by the brain homogenate. All experiments were repeated at least 3 - 5 times with 3 replicates. Results are expressed as means ± S.E.

Results:
Depending on their redox potentials, most of the tested SOD mimetics more or less efficiently suppressed the spontaneous lipid peroxidation of the brain homogenates. The only totally inefficient compounds were a negatively charged Mn(III) porphyrin, MnTBAP, and a nitrone, NXY-059.

Conclusions:
Very few of the SOD mimetics, designed in various laboratories around the world, have the required kinetic, electrochemical and thermodynamic characteristics in order to act as true SOD mimetics. Most of the compounds that show beneficial effects in vivo act as chain-breaking antioxidants scavenging lipid, peroxyl and alcoxyl radicals instead of O_2^-.

Key Words: Chain-breaking antioxidant; Superoxide dismutase mimetic; Lipid peroxidation
Funding Agency: Grant MB02/12 from Kuwait University

Community Medicine
Category: Undergraduate

23

Anxiety, driving behavior and road traffic accidents among Public Authority of Applied Education and Training students

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Introduction:
Background and Objectives: This cross-sectional study assessed the association between anxiety levels, driving behaviors, and the prevalence of road traffic accidents (RTAs).

Methods:
Students from the Public Authority of Applied Education and Training (PAAET) were enrolled in the study. A sample of 593 students was selected purposively from the five colleges of PAAET. A questionnaire of 52 questions was developed to collect data on socio-demographic characteristics, driving behavior, anxiety level and information about the most recent accident. Scores for safety of driving behavior and anxiety level were developed. The association between variables was analyzed by chi-square analysis. Relationships of selected variables with RTAs were further quantified by multivariate logistic regression.

Results:
It was found that more females (41%) had higher anxiety levels compared to males (25.1%) ($p<0.001$). Unsafe driving behaviors were reported by more males than females. A strong association was found between level of anxiety and unsafe driving behavior as the percentages of unsafe behavior increased from 22.8% to 26.2% to 35.8% as anxiety level increased from low, moderate, to high respectively. Among all PAAET students 56.8% reported experiencing at least one accident, 72.4% among males and 46.8% among females. Unsafe driving behaviors such as tailgating, speeding and using mobile phones while driving were also strongly associated with RTAs. Level of anxiety was not significantly associated with experience of RTA before and after adjusting for driving behavior.

Conclusions:
The results confirm our expectations that RTAs are related to gender and unsafe driving behavior. We found that anxiety level was positively associated with unsafe driving behaviors which in turn were associated with RTAs while anxiety level did not have a significant independent association with RTA occurrence.

Key Words: Anxiety; RTA; behaviors
Funding Agency: None

Community Medicine
Category: Clinical

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Smoking patterns and smoking cessation counseling practices among medical students in Kuwait

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Introduction:
The prevalence of smoking and practice of smoking cessation (SC) counseling among medical students is important because of their future role in health promotion. This study aimed to assess the prevalence and factors associated with smoking among medical students in Kuwait, to evaluate their SC experiences and to assess their SC counseling practice.

Methods:
This cross–sectional study enrolled 310 medical students at Kuwait University. A written questionnaire was used to collect data on smoking experience and SC counseling. A score based on 5 SC counseling practices was developed to assess the level of SC counseling practice.

Results:
The prevalence of smoking was 5.8%, and past smoking was 1.3%. Current smoking was associated with non-Kuwaiti nationality (OR=3.8;p<0.01) and male gender (OR=8.7;p<0.001) but not with age, phase of medical studies, childhood exposure to secondary smoking within the family, or living with a smoker. Close proximity to smokers was the most cited barrier to SC (27.8%). The students reported asking a median of 10 (IQR=1) of the last 10 patients about their smoking status. Students also reported advising a median of 2 (IQR=5) out of 10 smoking patients to quit, to provide a median of 1 (IQR=5) with reasons to quit, a median of 0 (IQR=0) with a quit date, and a median of 0 (IQR=0) with a referral to a SC clinic. High SC counseling scores were associated with older age (OR=3.8;p<0.001), non-Kuwaiti nationality (OR=2.4; p<0.05) and awareness of SC clinics in Kuwait (OR=3.1; p<0.001).

Conclusions:
The prevalence of smoking among medical students in Kuwait was low, although it should be decreased further among male students. Reported SC counseling practices showed good identification of patient smoking status but poor attempts to help them quit. Improved training in SC counseling and increased awareness of SC clinics are recommended to strengthen the preparation of medical students to provide smoking cessation counseling.

Key Words: Smoking; Medical Students; Kuwait
Funding Agency: none

Community Medicine
Category: Clinical

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Practice of smoking cessation counseling among physicians in Kuwait

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Introduction:
Physician smoking cessation (SC) counseling is known to increase quitting rates among smokers. However, little is known aboutthe practice of SC counseling among physicians in Kuwait.This study aimed at measuring the level ofphysicians' practice of SC counseling and identifying physician characteristics associated with higher practice of SCcounseling.

Methods:
This cross-sectional study enrolled 499 physicians from primary, secondary and tertiary governmental medical centers from all governorates in Kuwait. Convenient sampling was used in sampling the participants within the centers. Participants were asked to fill a 30 item questionnaire which recorded their socio-demographic characteristics, smoking behaviors and practice of SC counseling.A score was developed to assess the level of SC counseling practice.

Results:
Physicians reported asking a median of 8 (interquartile range [IQR]=5) of the last 10 patients about their smoking status. Physicians also reported advising a median of 7 (IQR=7) out of 10 smoking patients to quit, providing a median of 7 (IQR=6) with reasons to quit, helping a median of 0 (IQR=3) to set a quit date, and referring a median of 0 (IQR=2) to SC clinics. Factors associated with better SC counseling included older age (p-value for trend= 0.005) and being aware of SC clinics in Kuwait (odds ratio [OR]=11.5; p<0.001). Family medicine physicians had higher practice of SC counseling compared to other specialties (OR=8.7; p=0.005). Surgeons had lower practice compared to other specialties (OR=0.2; p<0.001). Only 56.7% knew about the presence of SC clinics in Kuwait, and 17.8% had previously received training in SC counseling.

Conclusions:
The low practice of SC counseling among physicians in Kuwait is concerning in face of the increased prevalence of smoking in the population. Efforts should be made to improve physicians' training in SC counseling and their awareness of SC clinics in the country.

Key Words: Smoking cessation; Counseling; Kuwait
Funding Agency: none

Community Medicine
Category: Undergraduate

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Comparison of health effects between shisha and cigarette smoking in young adults in Kuwait

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Introduction:
Shisha smoking is a growing public health problem, especially in young people in Kuwait. There is a popular myth that smoking shisha is less harmful than smoking cigarettes; however, there are very little data to support this myth. Our study aimed to demonstrate the health effects of shisha smoking compared to those of cigarette smoking among young adults.

Methods:
This cross-sectional study was conducted from September to October 2013 among male university students aged 16 to 32 years in Kuwait. Information on demographics and self-reported health problems were collected using a pretested questionnaire. Respiratory function was measured by the peak expiratory flow rate (PEFR). Body weight and height were measured by standard methods and BMI was computed.

Results:
Of the 525 participants, 411 (78%) were Kuwaitis (aged 21 ± 2 years), and 213 (40%) were current smokers. Among them, 13% smoked cigarettes, 10% smoked shisha only, and 23% smoked both cigarettes and shisha. Frequent respiratory infections ($p = 0.046$), persistent cough ($p < 0.001$), shortness of breath ($p = 0.002$), chest pain ($p < 0.001$), and fast heart beat ($p < 0.001$) were significantly higher among those who smoked both shisha and cigarettes, compared to the other smokers (either shisha alone or cigarette alone) and non-smokers. The people who smoked both shisha and cigarette also had more frequent sleep disturbances ($p = 0.011$) and breathing problems during sleep ($p = 0.004$) than the other groups. PEFR was highest among non-smokers (524.88 ± 99.91 L/min), and lowest among those who smoked both shisha and cigarettes (502.22 ± 102.15 L/min).

Conclusions:
This study demonstrated that shisha smoking is as harmful as cigarette smoking, and that the people who smoked both cigarettes and shisha were more likely to report respiratory symptoms and sleep disturbances than people who were non-smokers.

Key Words: Shisha; Cigarette smoking; Health effect
Funding Agency: None

Community Medicine
Category: Clinical

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Patterns of tobacco smoking among physicians in Kuwait

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Introduction:
Patterns of tobacco smoking among physicians in Kuwait are not well documented. The objectives of this study were to assess the prevalence and factors associated with smoking patterns among doctors in Kuwait and the smoking cessation experiences of past and present smokers.

Methods:
This cross–sectional study enrolled, via convenience sampling, 499 physicians in governmental medical centers at the primary, secondary and tertiary levels from all governorates in Kuwait. Data were collected using a self-administered anonymous questionnaire. The Fagerstrom score (Range 0-10) was used to assess the level of nicotine dependence among the participants who smoke.

Results:
The prevalence of current, past and never-smoking was 15.6%, 10.2%, and 74.1%, respectively. Prevalence among male physicians was 22.3% vs. 0.6% in female physicians. Current smoking was associated with male gender (OR= 44.0; p-value= <0.001), but not with age, nationality, professional specialty, or living with a smoker. Generally, participants were found to have low levels (≤4) of nicotine dependence based on the Fagerstrom score. Emotional disturbance or irritability (32.5%), and close proximity to smokers (19.5%) were the most cited barriers to smoking cessation. Prevalence of successful smoking cessation was 39.1% among smoking doctors. Successful smoking cessation among smoking physicians was not significantly associated with any characteristics.

Conclusions:
The prevalence of smoking among physicians in Kuwait was high among male physicians and low among females. A substantial percent of smoking physicians who attempted to quit, had succeeded. Given the important role of physicians in providing smoking cessation counseling, health promotion programs should target the smoking physicians in Kuwait.

Key Words: Smoking; Physicians; Kuwait
Funding Agency: none

Community Medicine
Category: Graduate MSc (Basic Science)

28

Middle East Respiratory Syndrome Coronavirus (MERS-CoV): Knowledge, risk perceptions and precautions among physicians in Kuwait

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Introduction:
A novel corona virus (CoV) emerged during 2012 in the Middle-East, reportedly had a low spread rate with a high case-fatality and regarded as a causative agent of Middle East Respiratory Syndrome (MERS). This cross-sectional study aimed to assess MERS-CoV knowledge, risk perception, and precautions among physicians working at tertiary-care hospitals in Kuwait.

Methods:
During October, 2013, we enrolled 600 physicians from all six tertiary-care hospitals as a sample of convenience in this study. A structured, self-administered questionnaire was used to collect the data. The questionnaire comprised questions about physicians' socio-demographic variables, their MERS-CoV knowledge, risk perception, and potential preventive measures that can be undertaken while dealing with a MERS case. Data were analyzed using Chi-square analysis, univariate, and multivariate logistic regression.

Results:
The prevalence of MERS-CoV unawareness among the physicians in the study sample was 15•2% (91/600). The multivariate logistic regression showed that trainee physicians were significantly more likely to be unaware of MERS-CoV (adjusted OR = 3•1; 95%CI: 1•2 -7•8). Whereas, physicians working at Al-Jahra hospital were significantly less likely to be un-aware of MERS-CoV (adjusted OR = 0•1; 95% CI: 0•01 -0•4).

Conclusions:
This study underscored a high prevalence of unawareness of MERS-CoV among physicians working at public sector tertiary-care hospitals and identified trainee physicians as significantly more likely to be unaware of this new syndrome and its causative agent. Physicians need to educate and prepare themselves for any probable MERS-CoV epidemic in Kuwait.

Key Words: MERS; Kuwait; Awareness
Funding Agency: None

Community Medicine
Category: Undergraduate

29

Age at menarche in relation to digit ratio and breastfeeding among high school girls in Kuwait

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Introduction:
Background: Early age at menarche has been linked to various adverse health outcomes such as, obesity, type 2 diabetes and breast cancer. Many factors are thought to be linked to early age at menarche, one of which is breastfeeding, but this remains under intense debate.
Objectives: To estimate the age at menarche among high school girls in Kuwait and to explore the association between age at menarche and breastfeeding or digit ratio.

Methods:
A cross-sectional study was conducted on 810 randomly selected female high school students from all governorates in Kuwait. Data on age at menarche was collected by self-administered questionnaire by the students; while the data on breastfeeding was collected by self-administered questionnaire sent to their mothers. To calculate digit ratio (2D:4D), finger lengths were measured using a digital caliper. Weight and height of students were measured using digital scale and stadiometer. Multiple linear regression was used to investigate the association between age at menarche and breastfeeding or digit ratio.

Results:
Out of the 810 students selected, 50 (6.2%) were absent or refused to participate, and out of the 761 mothers to whom the questionnaire was sent, 433 (56.9%) responded. The mean (SD) age at menarche was 12.32(1.21) years (95%CI: 12.23-12.41). There was no significant association between age at menarche and breastfeeding in the first four months of life before and after adjusting for potential confounders. There was no significant association between age at menarche and digit ratio in either hand before and after adjusting for potential confounders.

Conclusions:
The estimated age at menarche among contemporary girls in Kuwait is similar to that in industrialized countries. Trends in age at menarche should be monitored because of their public health implications; and cohort studies are recommended to investigate if breastfeeding has a spinoff benefit in terms of delaying sexual maturity.

Key Words: Age at menarche; Digit ratio; Breastfeeding
Funding Agency: none

Community Medicine
Category: Undergraduate

30

Microbiological contamination of mobile phones of clinicians in intensive care units and neonatal care units in public secondary care hospitals in Kuwait

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Introduction:
Objectives: This study aimed to explore the prevalence of microbiological contamination of mobile phones that belong to clinicians in intensive care units (ICUs), pediatric intensive care units (PICUs), and neonatal care units (NCUs) in all public secondary care hospitals in Kuwait.

Methods:
This is a cross-sectional study that included all clinicians with mobile phones in ICUs, PICUs, and NCUs in all secondary care hospitals in Kuwait. Samples for culture were collected from mobile phones and transported for microbiological identification using standard laboratory methods. Self-administered questionnaire was used to gather data on mobile phones disinfection practices.

Results:
Out of 213 mobile phones, 157 (73.7%, 95% CI [67.2%-79.5%]) were colonized. Coagulase-negative staphylococci followed by Micrococcus were predominantly isolated from the mobile phones; 62.9% and 28.6% of all mobile phones, respectively. Methicillin-resistant Staphylococcus aureus (MRSA) and Gram-negative bacteria were identified in 3 (1.4%) and 15 (7.0%) mobile phones, respectively. Sixty-eight clinicians (33.5%) reported ever having disinfected their mobile phones, with the majority disinfecting their mobile phones only when they get dirty. The only factor that was significantly associated with mobile phone contamination in multivariate analysis was whether a clinician has ever disinfected his/her mobile phone; odds ratio 2.42 (95% CI [1.08-5.41]).

Conclusions:
The prevalence of mobile phone contamination is high in ICUs, PICUs, and NCUs in public secondary care hospitals in Kuwait. Although some of the isolated organisms can be considered non-pathogenic, various reports described their potential harm particularly among patients in ICU and NCU settings. Isolation of MRSA and Gram-negative bacteria from mobile phones is of great concern, and calls for efforts to consider guidelines for mobile phone disinfection.

Key Words: Mobile phones; Contamination; Hospitals
Funding Agency: None

Community Medicine
Category: Undergraduate

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Public knowledge and attitudes regarding organ donation in Kuwait

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Introduction:
In Kuwait, the rate of organ donation is relatively low. The aims of this study included: 1) to evaluate public knowledge and attitudes on organ donation; and 2) to determine factors which predict public knowledge regarding organ donation.

Methods:
A cross-sectional study was conducted among 630 participants recruited from 27 randomly selected public cooperative societies and private supermarkets in Kuwait from December 2013 to January 2014. A self-administered questionnaire was used to collect data on demographics, public knowledge, attitudes, and their perceived barriers. The study was approved by the ethics committee, and an informed consent was taken from each participant before enrollment.

Results:
68% knew about organ donation; however, more females than men knew about it (73% vs. 63%, respectively, $p = 0.01$). A composite score of knowledge was also higher among females than males (8.4 ± 5.8 vs. 6.8 ± 5.8, respectively, $p = 0.001$). People with a higher education had a better perception about organ donation ($p < 0.001$), and were more willing to donate an organ ($p = 0.04$). Among the barriers, more females mentioned about health complications after organ donations (77% vs. 67%, $p = 0.011$) and a fear of the operation itself (83% vs. 69%, $p < 0.001$). In a multiple logistic regression analysis, female gender (OR = 1.7; 95% CI = 1.2, 2.4), and an educational level of bachelor's degree or higher (OR = 2.6, 95% CI = 1.7, 3.9) were significant predictors of the knowledge about organ donation.

Conclusions:
In this study, females and people with bachelor's degree or a higher educational level were more knowledgeable about organ donation. Acceptance of organ donation was not correlated with socio-demographic factors; however, the willingness to donate organs was higher among people with higher educational level. Fear of the operation itself, health complications, and lack of proper knowledge were the most common perceived barriers of organ donation.

Key Words: Organ donation; Knowledge; Attitudes
Funding Agency: None

Community Medicine
Category: Clinical

32

Critical use of *Origanum majorana* as an organic food preservative in milk products

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Introduction:
Many food products are perishable require protection from spoilage despite the use of usual food preservatives with their adverse effects.
We aimed to evaluate the use of origanum majorana forms-oil, hydrosol and leaves-as an organic food preservative in milk products and cereals after their storage for 6 months.

Methods:
In such prospective controlled study, origanum leaves were washed, air-dried and cut into small pieces and mixed with food. Hydrosol and oil were prepared by hydrodistillation.. Different concentrations of different origanum forms were added to milk products(white, ras and kareesh cheeses) in concentrations of (5,10,20 g/kg for leaves ;25,50,100ml/kg for hydrosol and 62,125,250ugm/kg for oil) but only leaves were mixed with cereals(wheat and corn).Samples with and without additive (control) were assessed microbiologically and organoleptically every month for 6 months.

Results:
High concentration of origanum forms was successful in suppressing mesophilies below the limit of detection in all cheese samples except kareesh. Moreover, the oil was significantly better compared to the control and other forms at different intervals of storage. Medium and high concentrations of leaves showed significant reduction in mesophiles compared to that detected in the control after the 1st month of storage until it could not be detected at the 5th month of corn storage and 6th month of wheat storage. Color of milk products treated with oil or hydrosol was more or less similar to the control samples. Moreover, the lowest acceptance % was in leaves treated samples (medium and high concentrations). Taste, texture and odor of milk products treated with high concentrations of different origanum forms and concentrations showed significantly lower mean score and acceptance % compared to the control.

Conclusions:
We recommend origanum majorana-medium concentration of its oil form- as an organic food bio-preservative in milk products.

Key Words: Origanum majorana; Food preservation; Biological
Funding Agency: None

Dentistry
Category: Undergraduate

33

Informed consent in dentistry: What would patients really need to know?

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Introduction:
Patients have the right to be informed about the important aspects and potential complications of any dental procedure and to make a final decision. Each patient has a different personality that may influence their decisions regarding treatment options. The bjective of this study is to assess individual's response to different levels of details regarding a hypothetical dental implant surgery and to evaluate socio-demographic and personality traits that affect candidate's decision regarding this procedure to help design a new more comprehensive informed consent forms for dental implants in the HSC dental clinic.

Methods:
A cross-sectional survey among students and staff at the Health Science Center in Kuwait University utilizing a purpose specific questionnaire was conducted with IRB approval in 2013. The Faculty of Dentistry students and staff were excluded from the study. Personality was assessed using the Zuckerman-Kuhlman Personality scale(ZKPQ-50-CC). Data were entered using SPSS program and descriptive statistics with appropriate tests, such as ANOVA, t-test and Chi-square were used in analysis.

Results:
A total of 263 participants completed the survey. Different socio-demographic characteristics were significantly associated with pre-operative, intra-operative, post-operative, outcome, timing, and requested personal to discuss the consent document. Personality traits have no significance on the decision making, except for individuals with impulsive trait who had specific choice of health care professionals requested to discuss the informed consent.

Conclusions:
Informed consent process and documentation are integral elements of the patient-dentist relationship. Several factors can affect candidate's decision regarding an implant procedure. These factors may help clinical students to create a more comprehensive consent form for implant surgery that focuses on all important information that patients need.

Key Words: Informed; Consent; Dental procedures
Funding Agency: Final year dental students

Dentistry
Category: Clinical

34

Prescription of antibiotics and analgesics during endodontic treatment

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Introduction:
Surgical and non-surgical root canal treatment of involved teeth can necessitate prescription of analgesics and antimicrobials. The literature suggests a confusion amongst practitioners regarding need for adjunctive medication, mainly during non-surgical root canal treatment, often leading to over-prescription. Aim: This project aimed to establish if problems alluded to in the literature were also reflected in the dental community during non-surgical endodontic management in Kuwait.

Methods:
Prescription patterns for antibiotics and analgesics were analyzed by the responses to self-administered questionnaire. Information was collected based on different clinical endodontic diagnostic scenarios. Statistical analysis was performed with SPSS software version 17.0 to determine relationships between prescription patterns, age, gender, dental qualification (specialists and general dentists).

Results:
Ninety-two per cent of dentists prescribed analgesics for the management of endodontic pain. While Sixteen percent prescribed antibiotics for severe dental pain. Sixty-two percent prescribed antibiotics for an acute apical abscesses. Significantly more male dentists prescribed antibiotics for dental pain than female dentists. No significant difference was found between general dental practitioners' and specialists' attitude toward drug prescriptions. Amoxicillin and ibuprofen were the most commonly prescribed medications.

Conclusions:
While the majority of dentists appeared to prescribe antibiotics and analgesics appropriately, many did not. This research confirmed previous studies and established a need for imparting information of evidence-based prescriptions protocols for the dentists surveyed in this study in Kuwait.

Key Words: Endodotics; Analgesics; Antibiotics
Funding Agency: None

Dentistry
Category: Clinical

35

A pharmacokinetic study of a topical anesthetic (EMLA®) in mouse soft tissue laceration

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Introduction:
The use of topical anesthesia instead of injection of local anesthetics for managing soft tissue lacerations in the emergency situations may be a relief for both patients and surgeons. Topical anesthesia in the form of a cream (EMLA®, Astrazeneca, Karlskoga,Sweden) containing 2.5% lidocaine and 2.5% prilocaine has been reported as efficient as anesthetic on skin before venipuncture anesthesia and as an alternative to injection anesthesia in some minor surgery situations. The aim of the study was to compare the pharmacokinetics of EMLA® when applied in a laceration in comparison with topical skin application in the mouse.

Methods:
A total of 120 BALB/c male mice were divided into three groups with regards to application mode of EMLA®. Group A: with laceration, 48 mice, Group B: on intact shaved skin, 48 mice, Group C: control group, 24 mice, with same procedures but without application of EMLA®. Blood levels were collected at 0, 10, 20, 30, 45, 60, 75 and 90 minutes post EMLA® application. Plasma samples analysis was carried out employing liquid chromatography coupled with tandem mass spectrometric (LC-MS/MS) method and the pharmacokinetic analysis of the mouse plasma samples was estimated by standard non-compartmental methods.

Results:
The absorption of lidocaine and prilocaine was rapid following application of EMLA® to lacerated and intact mouse skin. Cmax and AUC values of lidocaine were significantly increased following application of EMLA to lacerated mouse skin by 448.6% and 161.5%, respectively in comparison with intact skin. Similarly, prilocaine's Cmax and AUC values were also increased by 384% and 265.7%, respectively, following lacerated mouse skin, in contrast to intact skin.

Conclusions:
Further pharmacokinetic studies on different carriers of lidocaine/prilocaine are warranted before any conclusions for the clinic can be drawn

Key Words: EMLA®; anesthesia; pharmacokinetics
Funding Agency: ds01/13

Dentistry
Category: Clinical

36

Sources of oral health information and received instructions among parents of disabled school children in Kuwait

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Introduction:
Regular visits to a dentist are very important for the prevention of oral diseases in disabled children. The objective of this study was to obtain the sources of oral health information and received instructions among parents of disabled schoolchildren in Kuwait.

Methods:
A total of 308 parents of children with a physical disability (n=211) and developmental disability; Down syndrome (n=97) and 112 parents of normal children, participated in the study. Information was collected by structured anonymous questionnaires. The chi-square test was used in the analysis.

Results:
Dentists were the most common source of oral health information among the parents of disabled children (36%), more than for parents of normal children (26%). Less than a quarter of the parents of disabled (16%) and normal children (19%) stated that they had received information about the importance of regular dental visits. Disabled children had received more instructions for tooth brushing (52%) compared to normal children (43%); and less advice for avoiding sugary foods (17% vs 26%) than normal children. Advice to use fluorides was received by only 16% of the parents of disabled and 12% of the normal children. The majority of the parents of the disabled (69%) and normal children (64%) stated that the dentist should check the teeth of their children regularly. Less than a quarter (19%) of the parents of the disabled children expressed a wish that the dentist should give oral health education. A smaller proportion (10%) stated that the dentist should teach parents about oral health and only 2% felt that the dentist should teach school teachers about oral health

Conclusions:
The majority of parents of disabled children had inadequate information on the importance of regular dental visits. Dentists were the main source of oral health information. There is a need for strengthening the oral health education for the parents of the disabled children.

Key Words: Oral health information; Dental visits; Parents, Disabled children
Funding Agency: none

Dentistry
Category: Graduate PhD (Basic Science)

37

Assessment of tooth brushing and flossing among adults.

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Introduction:
The aim of this study was to assess the level of tooth brushing and flossing of adults in Kuwait.

Methods:
A cross- sectional study was done among adults working at the Ministries Complex in Kuwait during 2011-2012. A self-reported questionnaire was distributed. A convenience sample (N=1001) participated in this study. The questionnaire had six sections. One section was about the oral hygiene that consisted of eight questions.

Results:
The mean age of adults was 35.7±10.2. Females were 30% and 68% were males. Most of participants were healthy. Sixty four percent of participants had college or higher than college level of education. Approximately, two third (67%) were married with the mean number of children was 3.3±2.1. Almost all participants brushed their teeth (91.5%) of which half of them brushed twice a day (56%). Approximately, most used toothpaste to clean their teeth (90%). Thirty six percent of participants used fluoride toothpaste, 38% used toothpaste containing whitening or anti-sensitive agent, and 18% did not know the type of toothpaste. More than half of participants (62%) replaced their tooth brush every 6-months or less than 6-months. Only 25% of participants flossed their teeth of which 9% of them flossed once a day.

Conclusions:
Oral hygiene behavior among adults in Kuwait was unsatisfactory. Though most brushed their teeth once a day, only half brushed twice and only one quarter used dental floss. More efforts should be laid in educating the public about the importance of proper oral hygiene practices.

Key Words: Tooth brushing; Flossing; Tooth paste
Funding Agency: None

Dentistry
Category: Graduate (Resident)

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Parental knowledge and behavior of children towards use of fluoride containing toothpastes

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Introduction:
Fluoride containing toothpaste is an important adjunct in prevention of dental caries in children. Objective: This study was done to assess parental knowledge and behavior of their children towards the use of fluoride containing toothpastes.

Methods:
A cross-sectional study was carried out at the School Oral Health Program centers. A convenience sample of 485 parents from five different governorates participated. Self- reported questionnaire was used which included 7 questions. The questions were about tooth brushing, tooth paste ingredients, fluoride containing tooth paste, and children's oral hygiene behavior.

Results:
The total number of parents participated in this study was (N=485) from five governorates. Fifty two percent were males and 46% were females with the mean age 39.7±6.9. Among the children, 45% were males and 47% were females with the mean age 9.5±2.5. Almost all children brushed their teeth (95%) and half of them brushed only once a day (51%). Sixty seven percent of parents were aware that the toothpaste used by their children contained fluoride and 42% chose the toothpaste according to the presence of fluoride. Half of parents knew that fluoride in toothpaste prevent caries (53%). Most parents participating in this study did not have any knowledge about the appropriate concentration of fluoride in their children's toothpaste (90%).

Conclusions:
Though most of the children brushed their teeth only half of them brushed twice a day. Parental knowledge about fluoride in toothpaste was not satisfactory. More emphasis should be laid in future towards educating the parents and children in proper oral hygiene practices with focus on the importance of fluoride containing toothpastes.

Key Words: Fluoride toothpaste; Tooth brushing; Caries prevention
Funding Agency: None

Dentistry
Category: Clinical

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The effect of 5 weeks xylitol consumption on some members of oral microflora

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Introduction:
Xylitol is a naturally occurring polyol shown to have anti-caries effects on Str.mutans. However its effects on other oral bacteria are less well-known .The aim of this study was to evaluate the short-term effects (5 weeks) of xylitol chewing gum consumption (three times a day)on some oral bacteria.

Methods:
Altogether 122 children aged 12-13 years were screened with Dentocult® Orion Diagnostica, Turku, Finland) test. Those children with high (>100000 CFU/ml) MS counts in saliva or plaque were included in the intervention. The children were randomly allocated to the Xylitol and Control (Sorbitol) groups, using classrooms as clusters. The following bacterial species were quantified from stimulated saliva samples using Real time PCR: Streptococcus mutans, Streptococcus sobrinus, Lactobacillus plantarum, Lactobacillus paracasei, and Aggregatibacter-actinomycetemcomitans. Species-specific forward and reverse primers were used. Changes in the salivary microbes before and after the intervention were evaluated.

Results:
There were no statistically significant differences between the groups at the beginning or at the end of the study . However the saliva samples showed statistically significant reduction in the counts of all 5 studied bacteria both in the Xylitol and the Control groups, but none of them were statistically significant.

Conclusions:
It seems that both groups were benefiting from the chewing gum interventions. The study associated improved oral hygiene in both groups might explain the significant reduction in the determined bacteria.

Key Words: Xylitol; Oral bacteria; Real Time PCR
Funding Agency: Kuwait University grants No: DD02/10, GD01/11, SRUL02/13.

Dentistry
Category: Clinical

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Association between ICDAS scores in primary and permanent teeth

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Introduction:
Dental caries in primary dentition is a risk factor for caries of the permanent teeth. Objective: This study aimed to determine the association between International Caries Detection and Assessment System (ICDAS) scores in the primary teeth and permanent ones among the schoolchildren.

Methods:
Male children (122) aged 12-13 years with positive informed consent were clinically examined in a mobile dental clinic with a standard spot light. One examiner (EH) with an experience on ICDAS method conducted all the examinations. The intra-examiner reproducibility was high (kappa>0.9).

Results:
The mean number of enamel caries surfaces was 0.14 (SD=0.5) and dentinal caries surfaces 0.90 (3.0) in the primary teeth. The respective means were 2.12 (2.5) and 1.07 (3.0) in the permanent teeth. The mean number of surfaces with the different ICDAS scores in primary teeth were: 1) 0.3, 2) 1.1, 3) 0.7, 4) 0.6, 5) 0.3, 6) 0.3 and in permanent teeth: 1) 0.0, 2) 0.1, 3) 0.0, 4) 0.1, 5) 0.2, 6) 0.5. The correlations between the mean numbers of enamel and dentinal caries surfaces between the primary and the permanent teeth were very low. The only statistically significant correlation (r=0.37) was between the number of enamel and dentinal caries lesions in the permanent dentition.

Conclusions:
The mean ICDAS score of the primary teeth does not correlate with the ICDAS score of the permanent teeth, but number of enamel caries surfaces has high correlation with the number of dentine caries surfaces in the permanent teeth.

Key Words: Dental caries; Mixed dentition; ICDAS
Funding Agency: Kuwait University grants N:o DD02/10, GD01/11, SRUL02/13.

Dentistry
Category: Undergraduate

41

Sodium fluoride as adjuvant in pharmacological management of dental implants osseointegration

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Introduction:
It is known that the achievement of dental implants (DI) primary stability in porous and soft bone is one of the unresolved challenges of implant dentistry. Other problem is that the overload-induced bone loss around DI is not uncommon in patients with implant-supported dentures. One way to improve the osseointegration is pharmacological management of bone-to-implant response. It is reported that strontium ranelate (Str) stimulates remodeling of bone tissue around implants in osteoporotic animals, but influence of other minerals on this process has not been studied enough. Research purpose is to study the influence of sodium fluoride (NaF) co-administration on the effect of Str on mandible bone after dental implantation.

Methods:
Dental implantation was performed in female Wistar rats with corticosteroid osteoporosis or without it immediately after the extraction of low molar under the general anesthesia. Str with NaF were administered to animals orally in standard effective doses during 20 days after the intervention with following Ro-investigation of mandible bones.

Results:
At the moment of investigation DI osseointergation is not complete both in normal and osteoporotic animals and bone tissue around implant has signs of inflammation. Treatment by Str improves formation of secondary bone around DI, but causes the hypertrophy of alveolar process. Mandible bone after the combined treatment by Str and NaF has the best characteristics and the density of bone is more than in other groups. Hypertrophy of bone is absent. Around DI bone tissue has clear trabecular structure with no signs of degradation or inflammation. Such development of reparative processes under the combined action of Str and NaF is observed in rats with osteoporosis as well as in animals with normal bone mineral density.

Conclusions:
Thus, addition of NaF to the therapy of osseointegrative processes with Str is characterized by more intensive maturation of bone around DI and prevents the hypertrophy of bone tissue caused by Str.

Key Words: Sodium fluoride; strontium ranelate; dental implantation
Funding Agency: None

Dentistry
Category: Clinical

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Real-time PCR quantification of periodontal pathogens in diabetic Kuwaiti children

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Introduction:
Background: Prevalence of type-1 diabetes in children is increasing worldwide. A link has emerged between diabetes and periodontal diseases. Although diabetes in Kuwaiti children is common no information is available of their periodontal microbiota. Objectives: To assess the levels of major periodontal pathogens in diabetic and non-diabetic Kuwaiti children with gingivitis.

Methods:
6 children (14-18 years old) were included; 3 diabetics (HbA1C >7%) and 3 controls (HbA1C ≤5.5%). None had received antibiotics during the preceding 3 months. 8 subgingival paper point samples were collected per child. Bacterial DNA was purified using DNeasy kit (Qiagen) and quantified on ABI Fast 7900 HT RT-PCR machine using Power SYBR Green' kit and species-specific primers. The detection limit for all target species was 10e+02 CFU/ml.

Results:
The detection rates among diabetics vs controls were for Aggregatibacter actinomycetemcomitans (Aa; 2 vs 3), Porphyromonas gingivalis (Pg; 2 vs 3), Prevotella intermedia (Pi; 2 vs 1), Prevotella nigrescens (Pn; 2 vs 2), Fusobacterium nucleatum (Fn; 3 vs 3), Campylobacter rectus (Cr; 3 vs 3), and Parvimonas micra (Pm; 2 vs 2). Pg, Fn and Cr quantities were low (≤10e+03 CFU/ml) in all children and did not significantly (P>0.05) differ between the groups. Neither Aa and Pm differed (P>0.05) between the groups, although their mean quantities were higher in children with [(Aa: 1.15e+05 (1.9e+05), Pm: 2.4e+04 (3.4e+04) CFU/ml] than without [(Aa: 1.6e+04 (7.3e+03), Pm: 1e+04 (9e+03) CFU/ml] diabetes. Mean (SD) quantities of Pi and Pn were elevated [5e+05 (7e+05) and 5.6e+05 (7e+05) CFU/ml] in 2 of 3 patients in the diabetes group, but the difference from the non-diabetes group did not reach statistical significance. The diabetic with the lowest number of target bacteria also had the lowest HbA1C.

Conclusions:
While the target species seem common, diabetics may support the peak quantities. The results encourage analyzing larger study populations.

Key Words: Gingivitis; Periodontitis; RT-PCR
Funding Agency: Kuwait University, GF projects GD01/11; GM 01/01, SRUL02/13

Dentistry
Category: Clinical

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Daily consumption of soft drinks and sweets among disabled school children in Kuwait

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Introduction:
The aim of this study was to describe the use of soft drinks and sweets among disabled schoolchildren in Kuwait.

Methods:
A total of 308 parents of children with a physical disability (n = 211) and developmental disability; Down syndrome (n = 97) and 112 parents of normal children completed the questionnaire about the frequency of sugar consumption of their children. Information was collected by structured anonymous questionnaires. The chi-square test was used in the analysis.

Results:
About one-half of the Down syndrome children (53%); and physically disabled children (41%) had twice or more daily sugar exposures as compared to normal children (30%) (p = 0.001). A large proportion of Down syndrome children (48%) reported consuming soft drinks and beverages containing sugar several times a day, compared to physically disabled (28%) and normal children (23%) (p = 0.012). More than one-thirds of Down syndrome children and normal children (38%) consumed sweets and chocolates several times a day compared to physically disabled children (28%) (p = 0.012). More than once-a-day consumption of soft drinks was more prevalent in the disabled children (34%) compared to once-a-day consumption (22%). Also, more than once-a-day consumption of sweets was more common in the disabled children (31%) compared to once-a-day consumption (27%). Consumption of soft drinks several times a day was more prevalent in the disabled children whose parents had no university education (40%) compared to those with a university education (22%) (p = 0.028). There were no differences in the proportions of frequent consumers of sugar products according to gender, nationality or residence of the disabled children.

Conclusions:
Daily consumption and the frequency to use sugar products were very common among disabled schoolchildren and should be focused on by oral health education concerning prevention of dental caries.

Key Words: Soft drinks; Sweets; Disabled children
Funding Agency: None

Ethics
Category: Undergraduate

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Ethics in Disaster Medicine and Public Health: The first 24 hours after the accidental release of hydrogen sulphide in Kuwait

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Introduction:
Health crises are highly unpredictable. They can hit communities at any time, causing substantial human suffering and loss of life. If national systems, particularly health systems, are ill prepared to deal with a crisis in an ethical, transparent and evidence-based manner, individuals and communities will be at risk. In this study, "health crises" refer to the health threats associated with the accidental release of hydrogen sulphide gas (H_2S) from oil drilling operation in Kuwait on 17 October 2012.The objective of this study is to assess the information about this crisis among a sample of adult workers and students at the Health Sciences Center (HSC) within the first 24 hours.

Methods:
A purpose specific questionnaire was used with IRB approval within two hours of reports about the release of (H2S) gas in the social media. The questionnaire consisted of four parts: sociodemographics, sources of information, reliability of information, consequences and preventive measures taken.

Results:
A total of 202 adults participated in this study. Among them, 83% females, 78% Kuwaiti, and 86% students. The majority reported hearing about this crisis in the first 24 hours from different sources: social media 50% (Twitter, Instagram, and Facebook) followed by telephone calls from family and friends 17%, word of mouth 15%, television and radio 13%. Reliability was confirmed through smelling the gas themselves in 69%,while 20% reported having no confidence in the information. As a consequence to hearing about this gas release, the used precautions varied from covering mouth and nose in 26%, eating specific food items, switching air conditions on/off, and moving to higher floors.

Conclusions:
The sources, content, and consequences of information varried significantly with serious potential implications on health and wellbeing. It is essential therefore that all stakeholders' efforts during any crisis be conducted in a transparent and coordinated manner.

Key Words: Ethics; Crises; Public Health
Funding Agency: 5th year Medical Students

Forensic Medicine
Category: Basic Sciences

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DNA degradation during forensic investigations in Kuwait

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Introduction:
DNA degradation can occur when samples have been exposed to several environmental insults and chemical factors. These include: Light (UV), humidity, elevated temperatures and moisture and fungal contamination. The survival of DNA depends on several factors and environmental conditions. The aim of the present study was to investigate the effect of various temperatures on DNA survival over time.

Methods:
The present project investigated 28 samples of human blood, saliva and semen. The saliva and semen samples were collected by buccal swab but the blood samples were collected by Bode SecurSwab S.I.T. Collector. The experiments were done at four different temperatures (55°C, 37°C, 24°C and 4°C), which are the most Kuwaiti weather conditions in summer, spring and winter times.

Results:
The results showed that, DNA quantity in blood and saliva samples remained more or less the same at temperature of 4°C and 24°C compared to values for day1 with all other days. Typically, DNA quantification of human blood following extraction at 37°C was 46.14 ± 0.22 ng/µl at day1 then started to decrease until it reached 36.05 ± 0.07 ng/µl at day 28. In contrast, the result obtained from real-time PCR showed that when the temperature was raised to 55°C, the DNA started to degrade with time until it reached zero at day 12. The results clearly show that DNA in saliva and blood samples is extremely sensitive to heat. In contrast, the study also revealed that DNA quantity in semen samples remained more or less same.

Conclusions:
Environmental temperature of 55 0C could denature DNA within 12 days of exposure for saliva and blood samples. But exposure of semen samples to 55 0C over a period of 28 days failed to degrade DNA.

Key Words: DNA degradation.; Temperature; Humidity
Funding Agency: None

Forensic Medicine
Category: Clinical

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Thromboembolism and incidentally discovered vascular emboli in the forensic autopsy in the State of Kuwait

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Introduction:
One of the medico-legal issues that the forensic pathologist may face is the discovering of thromboembolic phenomenon and/ or incidentally discovered unexpected impacted emboli during autopsy performance. Hence, a great debate and opened discussion usually raised regarding the relation between such findings and the cause of death.

Methods:
This study was carried out retrospectively on all autopsy cases performed in the mortuary of the forensic medicine department in the State of Kuwait during the period from l/1/2010 to 31/12/2013 which followed by histopathological study. Cases which had findings of thromboembolism and/or intravascular emboli were selected aiming to assess the pathological findings and their relation to the cause of death.

Results:
Twenty three cases have been collected from a total of 437 autopsies which followed by histopathological study. Fourteen cases (61%) were women, and nine cases (39%) were men. The source of emboli in nine cases (39%) were considered to be from DVT, four cases (17%) from septic emboli, two cases (9%) from bone marrow embolism, two cases (9%) from hydrophilic emboli, one case (4%) from fat embolism, one case (4%) from air embolism and one case (4%) from amniotic fluid embolism, all leading to massive pulmonary embolism and the remaining three cases (13%) from dislodged mural thrombus leading to coronary thrombosis and myocardial. In four cases (17%) there were malpractice claims and two cases (9%) concluded that claims without evidence of medical error. The most common predisposing factors for embolism were injury, surgical intervention and immobility in bed.

Conclusions:
This study highlights the importance of studying the correlation between medical history, circumstances of death and autopsy findings to determine the cause of death. Also, the assessment of medical management that had been provided to patient before death is essential to identify the presence or absence of any medical malpractice.

Key Words: Thromboembolism; Histopatholgical study; Autopsy
Funding Agency: none

Forensic Medicine
Category: Clinical

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Estimation of the age of Kuwaiti males by radiological examination of the wrist and hand

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Introduction:
Age estimation of living individuals often represents a forensic challenge with important legal and social implications. Epiphyseal union of the distal ends of the radius and ulna, along with the small hand bones are considered as reliable mark for reaching the age of 18 years. There is no published data of the age of epiphyseal union for the Arabian Gulf populations.

Methods:
Hand radiographs from 486 Kuwaiti male subjects, whose ages ranged between 12-20 years, were assessed. Epiphyseal union of selected elements of the hand skeleton was recorded.

Results:
Radius: Partial epiphyseal union was recorded as early as 14 years (14/51; 27%) with highest incidence at 15 years (60/72; 83%), while all subjects above 18 years did not show evidence of partial union. Complete union was demonstrated as early as 16 years (22/59; 37%) with highest incidence at 18 years (38/46; 83%), while all subjects above 18 years showed complete union. Ulna: Partial union was recorded as early as 14 years (28/51; 55%), with highest incidence at 15 years (58/72; 81%), while all subjects above 18 years did not show evidence of partial union. Complete union was demonstrated as early as 16 years (26/59; 44%), with highest incidence at 18 years (41/46; 89%), while all subjects above 18 years showed complete union. Metacarpal Bones: Partial union was recorded as early as 13 years (6/66; 9%), with highest incidence at 15 years (31/72; 53%), while all subjects above 16 years did not show evidence of partial union. Complete union was demonstrated as early as at 14 years (17/51; 33%), with highest incidence at 16 years (47/59; 80%), while all subjects above 16 years showed complete union.

Conclusions:
This study has proposed standard figures for age estimation of adolescent Kuwaiti males. Such figures are different from those published for other populations. Further studies are required for the ages of epiphyseal ossification of other skeletal bones.

Key Words: Age estimation; Epiphyseal union; Forensic anthropology
Funding Agency: NONE

Genetics
Category: Basic Sciences

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Comparative evaluation of oligonucleotides synthesized by ABI 3400 and Mermade 12 DNA synthesizers

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Introduction:
DNA synthesis requires oligonucleotides (primers), which are short nucleic acid polymers typically with 50 or fewer bases. The ABI 3400 DNA synthesizer can synthesize 4 oligonucleotides, whereas Mermade 12 can synthesize 12 oligonucleotides at a time. In ABI 3400 System, the cleavage of the synthesized oligonucleotides from the solid support occurs automatically; whereas, in Mermade 12, the cleavage is done manually. The aim of this study was to compare the yield, purity and performance of the oligonucleotides synthesized by the above two machines in functional assays.

Methods:
Two sets of oligos were synthesized for the amplification of two Brucella-specific genes employing the solid phase DNA synthesis (phosphoramidite method) according to standard procedures. The first set (Forward: 5'AGTTTGATCCTGGCTCAG-3' and Reverse: 5' ACCTTGTTACGACTT 3') and the second set (Forward: 5' CATGCGCTATGTCTGGTTAC 3'and Reverse: 5'AGTGTTTCGGCTCAGAATAAT 3') of primers were synthesized using the ABI 3400 and Mermade12, respectively. The concentration and purity of the synthesized oligos were measured using BIOTEK Spectrophotometer at OD 260/280nm. The primers were tested in PCR amplification of Brucella DNA using standard procedures and analyzed by agarose gel electrophoresis. Furthermore, sequencing of the amplified products was performed using the ABI 3130 Genetic Analyzer.

Results:
The primers synthesized by both the instruments were of desired purity (OD 260/280 = 1.1 to 1.7), and good yield (200 to 500 pmoles). In PCR, clear DNA bands were observed for both primer sets on agarose gels. In addition, DNA sequences of the PCR products obtained with both primer sets were of good quality.

Conclusions:
High quality oligonucleotides are synthesized by both the MERMADE 12 and ABI 3400 DNA synthesizers, but MERMADE 12 is more efficient, as compared to ABI3400, because the former can synthesize 12 oligos while the later can synthesize only 4 oligos at a time.

Key Words: Oligonucleotide; ABI 3400; Mermade 12
Funding Agency: Research Sector grant SRUL 02/13

Medical Education
Category: Undergraduate

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How future doctors define professionalism in the Arab world?

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Introduction:
Professionalism is a core competency in medicine. Numerous studies investigated how this competency taught and learned. However, few studies reported on the students' definition of professionalism especially in the Arab world. The aim of this study was to explore how do medical students in their final year of medical school in Kuwait define Medical Professionalism.

Methods:
Eighty-five final-year medical students in Kuwait were surveyed. They were asked to list up qualities defining professionalism. The responses were analyzed using Miles and Huberman method. They were categorized into three themes according to the CanMED roles defining professionalism namely demonstrating commitment through ethical practice; participation in profession-led regulation; and demonstrating commitment to physician health and sustainable practice.

Results:
A total of 265 competencies were listed and 93.2% of them were categorized under the theme describing professionalism as commitment through ethical practice. The three most commonly listed competencies were punctuality, respect, and well-attired. Only two competencies were listed under the themes describing professionalism as participation in profession-led regulation; and commitment to physician health and sustainable practice, namely obligation to rules and team work respectively.

Conclusions:
Medical Students in Kuwait have an incomplete view of professionalism that has to be addressed by reviewing the medical curriculum. Medical curricula should be designed to address a holistic and cultural definition of professionalism.

Key Words: Professionalism; Curriculum; Education
Funding Agency: None

Medical Education
Category: Graduate (Resident)

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Medical and surgical ward rounds in teaching hospitals of Kuwait University: Students' perceptions

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Introduction:
Teaching sessions during ward rounds are essential component of bedside teaching that provide medical students with the opportunity to see the patients as actual people and observe their physical conditions directly allowing for better understanding of illnesses. We aim to explore medical students' perception regarding medical and surgical ward rounds in the Faculty of Medicine of Kuwait University aiming to evaluate if this teaching activity is meeting the expectation of the learners.

Methods:
A pre-tested questionnaire was used to collect data from 124 medical students during the academic year 2012/2013. They were asked to provide current and expected rate (scale from 1 = lowest to 5 = highest) about competencies that were supposed to be gained during ward rounds. Mean scores were calculated, and student t-test was used to compare the results ($p < 0.05$ was the cut-off level of statistical significance).

Results:
Only 17 (12.1%) students declined to participate in the study. The current teaching status of all competencies in both disciplines was significantly less than expected by the students (p-value <0.001). The best taught competency was bedside examination in both medical (mean score 3.45/5.00) and surgical (mean score 3.05/5.00) rounds. However, medical ward rounds were better than the surgical ones in covering some competencies especially the teaching professional attitude and approach towards patients (p-value <0.001).

Conclusions:
Both medical and surgical ward rounds were deficient in meeting the students' expectations. Medical educators should utilize the available literature to improve the bedside teaching experience of their students.

Key Words: Ward rounds; Bedside teaching; Medical students
Funding Agency: None

Medicine
Category: Clinical

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Clinical applications of adiponectin measurements in type 2 diabetes mellitus – Screening, diagnosis and marker of diabetes Control

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Introduction:
Adipose tissue-derived adiponectin has pleiotropic protective effects with suppression of inflammatory and metabolic derangements that may result in insulin resistance, metabolic syndrome, Type-2 diabetes (T2DM) and cardiovascular disease. The aim of this study was to evaluate adiponectin as a screening tool and diagnostic marker of T2DM and diabetic control.

Methods:
Fasting adiponectin, insulin and glucose and HbA1c were determined in 575 subjects with undiagnosed diabetes but with family history of T2DM. To evaluate adiponectin as a marker of DM control, we studied 376 patients with known T2DM duration of 12.4±8.1 years. Clinical and anthropometric data were recorded and subjects were classified on the basis of the degree of adiposity, insulin resistance (IR) using the homeostasis model assessment, target HbA1c levels < 53mmol/mol. Using standard cut off values for glucose and HbA1c, receiver operating characteristic curve (ROC) analysis was used to examine the diagnostic performance characteristics for undiagnosed DM.

Results:
In undiagnosed subjects, adiponectin was significantly lower in subjects with IR (7.0 vs 8.5 µg/mL) and diabetic subjects (7.4 vs 8.6 µg/mL) compared with those without. 73 of 575 subjects were found to have T2DM. Binary logistic regression showed that the odds ratio of T2DM as predicted by adiponectin was 0.88 [95% confidence interval 0.80-0.96; p = 0.007]. At cut-off points of 7.5 µg/mL, the diagnostic sensitivity and specificity of adiponectin for T2DM were 64% and 52% respectively. In known T2DM subjects, those with good control (HbA1c < 53mmol/mol) had significantly higher adiponectin (8.5 vs7.1 µg/mL) compared to subjects with poor control.

Conclusions:
Adiponectin levels are associated with better glycemic control and could be a useful adjunct for screening for IR and T2DM. Therapeutic measures that increase adiponectin levels might be valuable targets for improving diabetes control and decreasing complications.

Key Words: Adiponectin; Type 2 Diabetes Mellitus; Diabetes Control
Funding Agency: KFAS grant 2004-1302-03

Medicine
Category: Clinical

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Pattern of dyslipidemia in young adults with type 1 diabetes

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Introduction:
Although dyslipidemia is the major preventable risk factor for coronary heart disease and the main cause of premature death in individuals with type 1 diabetes, studies have shown that it is largely underdiagnosed and undertreated. This study aims to assess the pattern of dyslipidemia in young adults with type 1 diabetes in Kuwait.

Methods:
In a cross-sectional study, data for young adults (12-30 years) with type 1 diabetes who attended the diabetes OPD clinic at Al-Sabah hospital were collected. Age, gender, smoking status, diabetes duration, body mass index (BMI), HbA1c, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, and presence of diabetic retinopathy and nephropathy were recorded. Presence of dyslipidemia was defined as LDL-C (>2.6 mmol/l), HDL-C (<1.0 for men and <1.3 mmol/l for women), and triglycerides (>1.7 mmol/l).

Results:
Lipid profile was available for 61 adults with type 1 diabetes. Mean age and duration of diabetes was 19.4+3.9, and 7.1 years respectively. More than half of the patients (53%) were male, and the majority (61%) were Kuwaiti citizens. Obesity (BMI>30) was present in 15.1% of the patients, and 4.9% of the patients were hypertensive and current smoker. Mean HbA1c was 9.9+1.9%, and only 3.9% achieved the target (<7%). Mean levels of LDL-C, HDL-C and, triglycerides were 2.9+0.86, 1.32+0.35, 1.18+0.80 respectively. Dyslipidemia was present in 59.0%, 32.8% and 18.0% of the patients for LDL-C, HDL-C and, triglycerides respectively. Albuminuria and any retinopathy were present in 20.5% and 13.5% of the patients respectively. Higher total cholesterol, LDL-C and triglyceride levels were positively correlated with higher HbA1c levels.

Conclusions:
Young individuals with type 1 diabetes have high prevalence of dyslipidemia. Achieving good glycemic control and treatment of dyslipidemia are important steps to prevent future cardiovascular events.

Key Words: Diabetes; Dyslipidemia; Type 1
Funding Agency: None

Medicine
Category: Graduate MSc (Basic Science)

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Spectrum of changes in body composition of normal Kuwaiti female subjects

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Introduction:
Data on changes of components of body composition in normal Kuwaiti female subjects were not reported before or unavailable.

Methods:
Body composition was studied in healthy Kuwaiti females aged between 20-69 years. Subjects were included into the study if they were not taking any medication and were not known to have previous illnesses for at least 12 months. Subjects were stratified into 5 groups based on their age decades. Their body composition was assessed by different methods. Initially, weight, height, waist and hip circumferences were measured for each subject. Then, total bone mineral density (BMD) was measured using dual-energy X-ray absorptiometry (DXA) machine. From the total BMD, we then calculated % body fat, % lean body mass and % bone mineral content.

Results:
140 Healthy Kuwaiti females, of age range 20-69 years, were included in this study. Their (mean±SEM) age and BMI were 44±1 years and 28.8±0.5 kg/m2. They were stratified based on age-decades into 5 groups (group 1, n=29, aged 20-29 years; group 2, n=19, aged 30-39; group 3, n=42, aged 40-49; group 4, n=35, aged 50-59; and group 5, n=15, aged 60-69). As age advances from group 1 to group 5, body weight (p=0.0012), body mass index (BMI) (p=0.0001), waist (p=0.0001) and % body fat (p=0.0008) demonstrated significant positive trend, whereas height (p=0.0117), % lean body mass (p=0.0052), and % bone mineral content (p=0.0001) demonstrated significant negative trend. Age demonstrated significant positive correlation with body weight (r=0.25, p=0.008), BMI (r=0.38, p=0.0001), waist (r=0.52, p=0.0001), and % body fat (r=0.34, p=0.0001), but it demonstrated significant negative association with height (r= - 0.24, p=0.0049), % lean body mass (r= - 0.29, p=0.0007), and % bone mineral content (r= - 0.48, p=0.0001).

Conclusions:
This study shows that trend for adiposity with reduction in bone mineral content is a hallmark of advanced age in normal Kuwaiti female subjects.

Key Words: Body composition; Kuwaiti; Females
Funding Agency: None

Medicine
Category: Clinical

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Post-kidney transplantation anemia: Epidemiology, risk factors, and outcome

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Introduction:
Post-renal transplant anemia and its influence on transplant outcomes have not yet been reported from the Middle East in the era of erythropoietin. We aimed to evaluate post-transplantat anemia in renal recipients.

Methods:
Out of 2000 renal transplant recipients who were transplanted at HAMED AL-ESSA ORGAN TRANSPLANT CENTER of Kuwait, 183 of them (9.15%) were maintained on erythropoietin. Six months post-transplant, patients who did not achieve target hemoglobin (HB>12 grams/dl) comprised group 1(n=36), while those who had Hb less than 12 grams/dl will comprised group2 (n=147). We evaluated these cases for possible causes of resistant anemia.

Results:
The majority of patients in both groups were females (67.3 vs. 69% respectively; p=0.86) with mean age of 42.7±16.3 vs. 37.2±15.6 years (p=0.11). In the studied groups, the prevalence of anemia was 88.8%vs. 78.3 %(p=0.18) in both groups with an overall prevalence (83.5%) at the time of discharge following transplantation and it decreased to 79.1% 6 months post-transplantation. In analyzing anemia degree in these groups, our calculations revealed an almost equal distribution, with mild anemia in 26.4% of the cases, moderate in 36.4%, and severe in 33.6% after 6 months of transplantation. Serum iron was significantly lower in anemia group (p=0.01).Most of the anemic patients had received grafts predominantly from cadaveric or unrelated donors, whereas most of non-anemic group had received theirs from related donors. We observed that patient age correlated negatively with serum iron(r=0.215, p=0.048); serum ferritin correlated negatively with Hb 6 months post-transplantation (r=-0.328; p=0.004). There was no significant difference in patient or graft outcome among different groups (p>0.05).

Conclusions:
Iron use remains suboptimal in renal transplant recipients. Live related donors and exogenous EPO are protective of anemia. Post-transplant anemia at 6 months did not influence graft or patient outcome.

Key Words: Anemia; Renal transplant; Outcome
Funding Agency: None

Medicine
Category: Clinical

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Reduced adiponectin level in untreated hyperthyroidism

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Introduction:
Adiponectin and resistin are some of the recently discovered adipocytokines that participate in the regulation of intermediate metabolism. The aim of this study was to evaluate circulating levels of adiponectin and resistin in patients with thyroid hyperfunction and compare their levels with controls

Methods:
Twenty nine untreated hyperthyroid patients and 34 normal controls were studied. Patients and controls were matched for age, sex and body mass index. The subjects were assessed after an overnight fast and their blood was collected for measurement of adiponectin, resistin, glucose, insulin, intact proinsulin and thyroid function.

Results:
Adiponectin level was significantly lower in untreated hyperthyroid patients than normal subjects (patients versus controls, mean±SEM, 2.04±0.27 vs. 2.73±0.39, p=0.049) whereas resistin level was similar in patients and controls. Fasting glucose (p=0.01), insulin (p=0.007), and intact proinsulin (p=0.02) were significantly higher in the patients than controls. Within the patients, adiponectin demonstrated a trend of negative correlation with free T3 (r = -0.35, p=0.08) and free T4 (r = -3.2, p=0.09). However, neither adiponectin nor resistin were associated with TSH, age, BMI, fasting glucose, insulin or intact proinsulin.

Conclusions:
Untreated hyperthyroidism is associated with reduction in adiponectin levels which demonstrated a trend of inverse relation with thyroid status. It would be possible that inadequate secretion of adiponectin may have a role in the adverse metabolic changes associated with hyperthyroidism.

Key Words: Adiponection; Resistin; Hyperthyroidism
Funding Agency: None

Medicine
Category: Clinical

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Prevalence of blood borne viruses in the dialysis unit, Mubarak Al-Kabeer Hospital, Kuwait

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Introduction:
Transmission of hepatitis B virus (HBV), hepatitis C virus (HCV) and human immune deficiency virus (HIV) does take place in dialysis units worldwide at different rates. The aim of this study was to identify the prevalence rates of HBV, HCV and HIV in the dialysis unit, Mubarak Al-Kabeer Hospital, Kuwait.

Methods:
Design:
Retrospective study
Settings:
Dialysis Unit and Virology Unit, Mubarak Al-Kabeer Hospital, Kuwait
Subjects:
In 2012, a total of 1,369 samples from adult patients on dialysis at Mubarak AL-Kabeer Hospital were screened.
Intervention:
HBV, HCV and HIV were screened for HBV surface antigen (HBsAg) by ARCHITECT HBsAg Qualitative II 2011 (Abbott), HCV antibodies (Anti-HCV) by ARCHITECT Reagent Kit 2011 (Abbott) and HIV antigen and antibody (HIV Ag/Ab) by ARCHITECT HIV Ag/Ab Combo Reagent Kit 2011 (Abbott), respectively

Main Outcome Measures:
Prevalence rates of HBV, HCV and HIV in the dialysis unit, Mubarak Al-Kabeer Hospital, Kuwait.

Results:
HBV, HCV and HIV prevalence among dialyzed patients in the Mubarak Al-Kabeer Hospital dialysis unit was 1.2%, 6.3% and 0.1% respectively.

Conclusions:
This study, to our knowledge, is the only study providing recent data on blood borne viruses (BBVs) among patients in a dialysis unit in Kuwait. A multi center study is recommended to determine the national prevalence of BBVs in all the dialysis unit of Kuwait.

Key Words: Dialysis; Blood borne viruses; Kuwait
Funding Agency: None

Medicine
Category: Clinical

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Early vs. late acute antibody mediated rejection among renal transplant recipients in terms of its response to rituximab therapy.

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Introduction:
No comparable trials concerning the use of rituximab among renal transplant recipients with acute antibody mediated rejection.
Aim of the study:
We aimed to compare early and late acute AMR in terms of its response to rituximab therapy.

Methods:
Out of 1200 kidney transplant recipients performed in Hamed Al-Essa Organ Transplant Center of Kuwait, 103 developed acute AAMR and were subcategorized into 3 groups according to the onset of rejection. All patients received the standard management of AAMR according to our protocol (PP and IVIG). We added rituximab to the management of cases of group 1 (n=27, with early AAMR) and group 2(n=38, with late AAMR) while group 3(n=38) represented non-rituximab group. We compared the 3 groups regarding the outcome regarding graft and patient.

Results:
All patients were comparable regarding demographic data (patient age, sex, pre-transplant type of dialysis viral profile, type of induction, donor criteria, and pretransplant co-morbidities).we observed that delayed and slow graft function were significantly higher in groups 2,3($p=0.02$), however we found no significant difference in the 3 groups regarding NODAT,BK viral infection or malignancy. Despite significantly higher serum creatinine at 6 months in group 1($p=0.038$), graft outcome was significantly better in that group compared to the other groups ($p=0.011$). Patient outcome was comparable in the 3 groups ($p>0.05$).

Conclusions:
Early AAMR in renal transplant recipients had significantly better outcome when rituximab was added to the standard management.

Key Words: Rituximab; Renal transplant; AAMR
Funding Agency: none

Medicine
Category: Basic Sciences

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Adipocyte Enhancer-Binding Protein-1 over-expression promotes and ablation attenuates atherosclerosis in ApoE-/- and LDLR-/- mice

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Introduction:
Atherogenesis is a long-term process involving inflammatory response and metabolic dysfunction. Adipocyte enhancer-binding protein-1 (AEBP1) impedes macrophage cholesterol efflux, promoting foam cell formation, via PPARg1 and LXRa down-regulation. The objective of this study is to assess the role of macrophage AEBP1 in atherogenesis and evaluate the effect of its over-expression and ablation on atherosclerotic lesion formation in mice.

Methods:
Atherogenesis and macrophage infiltration were assessed using AEBP1-/-/LDLR-/- double-knockout mice, en face analysis, bone marrow (BM) transplantation, and immunohistochemistry of aortic cryosections. mRNA and protein levels were assessed by real-time PCR and immunoblotting, respectively.

Results:
AEBP1-transgenic mice (AEBP1TG) with macrophage-specific AEBP1 over-expression exhibit hyperlipidemia and develop atherosclerosis. Consistently, ablation of AEBP1 results in significant attenuation of atherosclerosis in the AEBP1-/-/LDLR-/- double-knockout mice. BM transplantation experiments reveal that LDLR-/- mice reconstituted with AEBP1-/-/LDLR-/- BM cells (LDLR-/-/KO-BM chimera) display significant reduction of atherosclerosis lesions compared to control mice reconstituted with AEBP1+/+/LDLR-/- BM cells (LDLR-/-/WT-BM chimera). Furthermore, transplantation of AEBP1TG BM cells with normal ApoE gene into ApoE-/- mice (ApoE-/-/TG-BM chimera) leads to significant atherogenesis despite the restoration of ApoE expression. Macrophages from ApoE-/-/TG-BM chimeric mice express reduced levels of PPARg1, LXRa, ABCA1 and ABCG1 and increased levels of the inflammatory mediators IL-6 and TNFa compared to macrophages of control chimeric mice (ApoE-/-/NT-BM) that received AEBP1-non-transgenic (AEBP1NT) BM cells.

Conclusions:
Our in vivo experimental data strongly suggest that macrophage AEBP1 plays critical regulatory roles in atherogenesis. We anticipate that AEBP1 may serve as a potential therapeutic target for the treatment.

Key Words: Macrophages; Atherosclerosis; Bone marrow transplantation
Funding Agency: none

Medicine
Category: Clinical

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Finger position alters the median nerve properties within the carpal tunnel: A pre-post MRI comparison study

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Introduction:
Purpose: The purpose of this study was to compare the properties of the median nerve and the flexor retinaculum within the carpal tunnel with Magnetic Resonance Imaging (MRI) under two conditions: (a) fingers extended, and (b) fingers in an isometric squeeze grip.

Methods:
Thirty-Four volunteers participated in this experimental study. The flexor retinaculum and median nerve characteristics were measured during both conditions using MRI.

Results:
The isometric squeeze grip condition resulted in significant palmar bowing of the flexor retinaculum ($t = 7.67$, $p < .001$), a significant flattening-ratio of the median nerve ($t = 4.308$, $p < .001$), and no significant decrease in the cross-sectional area of the median nerve ($t = 2.508$, $p = 0.017$).

Conclusions:
The isometric squeeze grip condition resulted in anatomical deformations within the carpal tunnel, possibly explained by the lumbrical muscles incursion into the carpal tunnel during finger flexion.

Key Words: Musculoskeletal disorder; Lumbricals; Carpal Tunnel Syndrome
Funding Agency: Kuwait University Research Priority Grant # RN-02-09.

Medicine
Category: Clinical

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Zinc deficiency

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Introduction:
Zinc is an essential mineral that is required for every system in our body during different stages of life. Although, deficiency of zinc usually manifested by delayed healing of wounds, growth and mental retardation, taste abnormalities and others, loss of hair constitutes the main complain especially among females that enforce physicians to request Zinc test. Seeking medical advice for this problem would be by identifying reasons for this deficiency before direct diagnosis of zinc deficiency using Zinc tests. Therefore, other tests such as thyroid function test, iron, or fluorides should be ordered.

Methods:
Retrospectively, we revised zinc results and other tests "if ordered" using our system of manual recording during the period of 2004-2009.

Results:
105 zinc requests were found in our records that include 10 males and 95 females. Median Zinc level 12.9 nmol/l (IQR 11.200-16.000) calculated with positively skewed curve; p 0.001. Mann-Whitney test showed significant difference in the medians between females (median 12.48 nmol/l; IQR 10.95-13.45) and males (median 18.13 nmol/l; IQR 13.64-20.95). However, none of the patients in this study have other tests done for them.

Conclusions:
Requesting single test for Zinc a lone is of little help for clinical decision making.

Key Words: Zinc; Loss of Hair; Thyroid Function
Funding Agency: None

Medicine
Category: Clinical

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Prospective evaluation of the effect of short term oral vitamin D supplementation on peripheral neuropathy in type 2 diabetes mellitus

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Introduction:
Vitamin D [25(OH)D] deficiency is an independent risk factor for diabetic peripheral neuropathy (DPN). Our objective was to assess effectiveness of short term oral vitamin D supplementation on peripheral neuropathy in Type 2 diabetes.

Methods:
A prospective, placebo-controlled trial including 83 Type 2 diabetic patients with DPN and vitamin D deficiency. Patients were assigned sequentially into treatment and placebo groups. DPN was assessed using neuropathy symptom score (NSS), neuropathy disability score (NDS) and nerve conduction study (NCS). Vitamin D status was determined by measuring serum total 25(OH)D. Patients received either oral vitamin D3 capsules or starch capsules once weekly for eight weeks. Primary outcomes were changes in NSS and NDS from baseline. The secondary outcome was changes in NCS result.

Results:
There were 52 (62.7%) patients in treatment group and 31 (37.3%) patients in placebo group. Serum 25(OH)D concentrations significantly improved after oral vitamin D supplementation in treatment group compared to placebo group (33.6 ± 26.1 vs. 1.9 ± 3.6, $p < 0.0001$). Similarly, the improvement in NSS values was significantly more in treatment group compared to placebo group (-1.3 ± 1.5 vs. -0.4 ± 1.0, $p=0.018$). No improvement was observed for NDS and NCS between the two groups after treatment.

Conclusions:
Correction of vitamin D status with oral vitamin D3 supplementation in the short term improved symptoms of neuropathy in Type 2 diabetes.

Key Words: Peripheral Neuropathy; Type2 Diabetes; Vitamin D
Funding Agency: None

Medicine
Category: Clinical

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Recurrent urinary tract infection among renal transplant recipients: risk factors and long term outcome

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Introduction:
Urinary tract infection (UTI) is the most common type of bacterial infection contracted by recipients of renal allografts and may have an adverse impact on graft and patient's survival. We aimed to evaluate the risk factors of recurrent UTI in renal transplant recipients, and its impact on patient and graft survival.

Methods:
An eighty six per cent of1019 patients (who were transplanted between 2000 to 2010 in Hamed Al-Essa organ transplant center of Kuwait) developed at least one episode of UTI however; only 6.2% patients had recurrent UTI. We compared the patients who had recurrent UTI (group 1) and those who had no or non-recurrent UTI (group 2) against their risk factors.

Results:
Patients of group 1 were significantly younger than those of group 2 (34.9 ± 23vs. 42.8 ± 16 year, $p<0.001$ respectively), with female preponderance ($p<0.001$).The percentages of thymoglobulin induction(21.5%) were significantly higher in group 1.Patients with pretransplant urological problems experienced significantly more recurrent UTI ($p<0.0001$). Hepatitis C patients were significantly more prevalent among group 1(10.8% vs. 3.8%, $p=0.008$).Long term graft outcome (functioning, failed and lost follow up)were78.5%, 21.5 and 0% vs. 84.5, 13.9 and 1.2% respectively (P = o.18). The patient outcome (live, dead and lost follow up) were73, 1.6 and 25.6% vs. 62.1, 0.3 and 33.6% respectively (P = 0.187).

Conclusions:
Adult age, female sex, thymoglobulin induction, pretransplant urological problems and hepatitis C infection were considered risk factors of recurrent UTI among our renal transplant recipients. However, recurrent UTI did not adversely impact graft or patient survival.

Key Words: Recurrent UTI; Kidney transplant; Outcome
Funding Agency: None

Microbiology, Virology and Immunology
Category: Basic Sciences

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Microbial biodiversity and viral contaminants of drinking water in Kuwait

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Introduction:
Outbreaks of infectious diseases attributable to drinking water may not be common in resource-rich countries, but they still occur and can lead to serious acute, chronic, or sometimes fatal health consequences. In this study, drinking water samples from different regions of Kuwait were explored for possible microbial diversity and viral contamination.

Methods:
Drinking tap water samples were collected from the six different Kuwaiti governorates, with three different sampling points for each governorate (18 samples). All samples were analyzed by confocal microscopy for the detection of bacteria. The samples were cultured in vitro to detect culturable organisms. High quality DNA was isolated from the growing cultures and the identity of the organisms was determined by sequencing the bacterial 16S ribosomal RNA (rRNA) genes. RNA was extracted from water samples and analyzed for the detection of viruses (Astrovirus, Enterovirus, Norovirus, Rotavirus, and Hepatitis A) using commercial kits in one step real-time RT-PCR.

Results:
Confocal microscopy showed the presence of bacteria in the water samples. The 16S ribosomal RNA (rRNA) gene sequencing, followed by BLAST search, identified several bacterial species. Of these species, the only bacterium with known health effects was Acinetobacter baumanii, which often causes opportunistic infections in immunocompromised people. As for the viruses examined in this study, RNA for none of the studied viruses could be detected in the drinking water samples analyzed.

Conclusions:
The preliminary results of this study indicate that the drinking water samples analyzed from various locations in Kuwait are relatively safe for drinking and do not contain many harmful pathogens.

Key Words: Microbial Biodiversity; Viral Contaminants; Drinking Water in Kuwait
Funding Agency: Research Sector Project No. SRUL02/13, Kuwait University

Microbiology, Virology and Immunology
Category: Basic Sciences

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Simple, low-cost molecular screening for TR34/L98H mutations in cyp51A gene for rapid detection of triazole-resistant *Aspergillus fumigatus* isolates

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Introduction:
Objective: Invasive aspergillosis (IA) is a life-threatening infection in immunocompromised patients. Triazoles are effective drugs; however, triazole-resistant Aspergillus fumigatus strains have been isolated from clinical specimens and environmental sources. The dominant resistance mechanism involves TR34/L98H mutations in cyp51A. This study developed low-cost PCR and PCR-RFLP assays targeting the promoter and codon 98 regions for rapid detection of triazole-resistant A. fumigatus isolates carrying TR34/L98H mutations.

Methods:
Reference A. fumigatus strains carrying wild-type and mutant sequences in promoter region and codon 98 in cyp51A (cyp51A98) and 40 itraconazole-susceptible and 35 itraconazole-resistant isolates were used. Drug susceptibility to triazoles was determined by Etest. PCR assay of promoter region and PCR amplification of cyp51A98 region followed by AluI restriction digestion yielded different patterns in agarose gels. Results were confirmed by direct DNA sequencing of respective gene fragments.

Results:
Reference strains yielded expected results for promoter and codon 98 regions. PCR-RFLP from all itraconazole-susceptible isolates yielded three fragments showing wild-type sequence at cyp51A98. PCR-RFLP assay from 32 itraconazole-resistant isolates yielded two fragments indicating L98H mutation while 3 isolates yielded wild-type pattern at cyp51A98. The latter 3 isolates contained other cyp51A mutations. All 32 itraconazole-resistant isolates with L98H mutation yielded 139 bp amplicons (TR34 present) while remaining 3 itraconazole-resistant and all itraconazole-susceptible isolates yielded 105 bp amplicons indicating wild-type promoter region. DNA sequencing confirmed the results from selected isolates.

Conclusions:
Simple, low-cost methods have been developed for molecular detection of triazole-resistant A. fumigatus isolates carrying TR34/L98H mutations and will help in proper management of patients with IA in resource-poor settings.
Key Words: Triazole-resistant A. fumigatus; TR34/L98H cyp51A mutations; Rapid molecular detection
Funding Agency: KURS grant MI 01/09

Microbiology, Virology and Immunology
Category: Graduate MSc (Basic Science)

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Distribution of virulence genes in *Helicobacter pylori* cultured from native arab Kuwaiti patients with dyspepsia

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Introduction:
H. pylori, the causative agent of several upper gastrointestinal diseases, possesses a number of virulence genes. The objective of the study is to determine the relationship between a set of virulence genes and the histopathology of gastric mucosa. We have completed the study of virulence genes of the isolates which is presented here.

Methods:
Three biopsies from the stomach (2 from antrum and 1 from corpus) were obtained from 141 consecutive, adult, native, Arab Kuwaiti patients with dyspepsia seen at Al-Amiri Hospital or Mubarak Al-Kabir Hospital, Kuwait, during Nov 2012-Feb 2013. Biopsies were cultured on selective agar microaerobically. Chromosomal DNA originating from a single colony was used as the template in PCR assay for the detection of virulence genes encoding the following factors: cag A and its C-terminal motif (EPIYA) subtypes, vacA and its various subtypes, OipA, and iceA and its alleles.

Results:
H. pylori was cultured from 50 out of 141 patients studied. The distribution of virulence genes in the 50 H. pylori isolates are as follows: cagA,36 (72%) with EPIYA motif detected in 24 (48%) with B type (15 isolates), A type (4 isolates), A and B type (3 isolates), B and C type (1 isolate) and C type (1 isolate); vacA 50(100%) with its subtypes, vacAm1, 3 (6%), vacAm2, 36 (72%), vacAs1, 16 (32%), vacAs2, 23 (46%), vacAs1a, 29 (58%), vacAs1b, 24 (48%), vacAs2, 35 (70%), vacAi1, 13 (26%), vacAi2, 39 (78%), vacAd1, 10 (20%), and vacAd2, 33 (66%); oipA, 41 (82%); and iceA1, 10 (20%) and iceA2, 13 (26%).

Conclusions:
This study has demonstrated that H. pylori infecting the native, Kuwaiti patients possess a number of virulence genes. In other studies, presence of some of these genes was correlated with the development of gastritis, gastric ulcer or gastric cancer. When the histopathologic study on the biopsies of these patients is complete, it will be possible to correlate the presence of these virulence factors with the disease outcome.

Key Words: H. pylori; Virulence genes; Gastric pathology
Funding Agency: Enrolled for MSc at Arabian Gulf University, Bahrain, partly funded by the University

Microbiology, Virology and Immunology
Category: Clinical

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Epidemiology of candiduria in a general hospital in Kuwait

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Introduction:
There has been important changes to the epidemiology of Candida urinary tract infection (CUTI) over the past decades. Candiduria may represent infection, colonization or even contamination. The majority of cases are asymptomatic. Candida species other than Candida albicans have emerged as an important causes of infection. Species such as Candida glabrata and Candida tropicalis are far more common than previously thought. Furthermore, with the wide spread use of azoles antifungal agents. The emergence of resistance must be viewed with concern. The aim of this study is to investigate species distribution and antifungal susceptibility profile of Candida causing candiduria in Farwania hospital, Kuwait.

Methods:
During a 10 months period, a total of 13691 urine culture were received in our laboratory. 85 considered as CUTI and were processed in Farwania hospital Laboratory. Organisms were identified by conventional methods and the use of ViteK 2 automation system (Biomerieux, France). Susceptibilities of the isolates to amphotericin B, voriconazole, fluconazole and caspofungin were determined by E-test. Patients risk factors were also assessed and analyzed.

Results:
Of the 13691 urine culture received in our laboratory for processing, 2550 were regarded as positive urinary tract infections. Of these, 85 were identified as CUTI with an incidence of 3.3% (85/2550). The ratio of female to male was 2:1. The average age of the patients was 54. The most common isolate was C. albicans (54% %). The major predisposing factors associated with candiduria were urinary catheterization (72%) and antibiotic therapy (54%).

Conclusions:
C. albicans remains the commonest species causing CUTI . The changing trends in the epidemiology of candiduria, especially with risk factors, should be closely monitored. Species identification and antifungal susceptibility testing may have therapeutic implications.

Key Words: Candida albicans; Candiduria; Risk factors
Funding Agency: None

Microbiology, Virology and Immunology
Category: Graduate PhD (Basic Science)

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Non-endemic genotypes of *Candida albicans* cause candidemia cases in Kuwait as revealed by multilocus sequence typing

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Introduction:
C. albicans and C. dubliniensis are closely-related species causing candidemia in susceptible patients. C. albicans show greater diversity than C. dubliniensis isolates in fingerprinting studies. Endemic genotypes of C. albicans causing candidemia cases are reported from some centers. This study performed fingerprinting of clinical C. albicans and C. dubliniensis isolates by highly discriminatory MLST for determining source of infection among candidemia patients in Kuwait.

Methods:
Clinical C. albicans (n=65) and C. dubliniensis (n=71) isolates identified by phenotypic and species-specific PCR assays were used. MLST were performed by PCR-sequencing of housekeeping genes and data were used for assigning diploid sequence type (DST). Evolutionary relatedness was determined by UPGMA. Combined sequence data was also used to generate NJ tree with maximum likelihood option and bootstrap analysis with 1000 replicates.

Results:
All isolates were correctly identified by PCR and/or DNA sequencing of ITS region of rDNA. Among 71 C. dubliniensis isolates, only 11 different DSTs were identified including 3 new DSTs. Interestingly, all 5-flucytosine-resistant isolates (n=15) belonging to ITS sequence-based genotype 4 belonged to DST 14 by MLST. On the contrary, 43 different DSTs (including 22 new DSTs) were identified among 65 C. albicans isolates. Only one large cluster contained 9 isolates (DST 656). However, they were recovered over a 2-year period at different hospitals and no epidemiological link was apparent.

Conclusions:
Consistent with world reports, population structure of C. dubliniensis in Kuwait is also clonal with all 5-FC resistant isolates belonging to DST14. However, C. albicans strains were heterogeneous. Unlike some centers, no endemic C. albicans genotypes were identified suggesting endogenous source of candidemia in most patients in Kuwait. This is the first report on MLST analyses of C. albicans and C. dubliniensis isolate from the Arab world.

Key Words: Candida albicans; Candida dubliniensis; Multilocus sequence typing
Funding Agency: Research Sector grant YM 10/11, Research Core Facility grant GM 01/05 SRUL 00/13

Microbiology, Virology and Immunology
Category: Clinical

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Prevalence and oOutcome of bacteremia cause by ESKAPE pathogens in a neonatal unit in Kuwait

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Introduction:
Infection due to ESKAPE pathogens has been recently identified as a serious emerging problem worldwide. ESKAPE pathogens are of increasing clinical significance in all age groups and effectively "escape" the effects of antibacterial drugs. However, information on bacteremia caused by these 6 organisms in neonates is lacking. We aimed to determine the frequency and outcome of bacteremia in neonates.

Methods:
All episodes of bacteremia prospectively documented in neonates from January, 2011-to-December, 2013 were analyzed.

Results:
Of 1117 episodes of bacteremia, 250 (22.4%) were caused by ESKAPE pathogens. However, out of 353 Gram-negative neonatal bacteremia, 202(57.2%) were caused by ESKAPE organisms. While only 7% (48/682) of Gram-positive bacteremia episodes were caused by ESKAPE pathogens. Seventy one (28.4%) were due to rESKAPE strains (vancomycin-resistant Enterococcus faecium 0, methicillin-resistant Staphylococcus aureus 8, extended –spectrum beta-lactamase (ESBL)-producing Klebsiella pneumoniae 26, carbepenem-resistant Acinetobacter baumanii 0, carbapenem and quinolone-resistant Pseudomonas aeruginosa 1 and derepression chromosome β-lactam and ESBL-producing Enterobacter Spp 36). 96% were late onset neonatal bacteremia and overall fatality rate was 10.8%.

Conclusions:
Neonatal bacteremia due to rESKAPE pathogens is frequent and causes significant morbidity and mortality. rESKAPE should be considered when selecting empirical therapy for late-onset neonatal bacteremia.-

Key Words: ESKAPE; Bacteremia; Neonate
Funding Agency: None

Microbiology, Virology and Immunology
Category: Graduate PhD (Basic Science)

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Genetic diversity of detected human metapneumovirus in Kuwait

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Introduction:
Human metapneumovirus (hMPV) infection accounts for 5% of respiratory tract infections (RTIs) among hospitalized patients in Kuwait, as reported in our previous studies. It was mostly detected among infants and elderly. In order to assess the disease burden of different hMPV genotypes and subtypes, the genetic diversity of detected hMPV was evaluated by a phylogenetic analysis based on sequences of G gene that encodes glycosylated attachment protein.

Methods:
A total of 31 hMPV-positive respiratory specimens that were identified during the years 2009-2011, were subjected to nested reverse transcription polymerase chain reaction (RT-PCR) for the G gene amplification. The nested PCR products were purified and directly sequenced to identify the circulated hMPV genotypes. Phylogenetic analysis was conducted using MEGA version 5, according to the neighbor-joining clustering method.

Results:
Out of 31 hMPV-positive specimens, only 21 gave good quality sequences for analysis. The hMPV identity percentage was ranging from 81% to 99%. The phylogenetic analysis of the G gene showed that the hMPV sequences clustered into five main clades (A1, A2a, A2b, B1, and B2). Of the 21 strains, 13 (62%) were grouped in the A2b lineage, 7 (33%) in the B2 lineage, and 1 (5%) in the B lineage.

Conclusions:
Different hMPV subgroups based on G gene analysis were detected among our hMPV-positive respiratory specimens, and genotype A2b of hMPV appears to predominate during the study period. This is the first report on the genetic diversity of G gene of hMPV strains isolated from hospitalized patients with respiratory tract infections in Kuwait.

Key Words: Human Metapneumovirus (hMPV); Genetic Diversity; G Gene
Funding Agency: Supported by College of Graduate Studies and Research Administration, Grant # YM 05/09, Kuwait University, and the Research Unit for Genomics, Proteomics and Cellomics Sciences (OMICS), Kuwait University, with the Research Project No. SRUL02/13.

Microbiology, Virology and Immunology
Category: Graduate PhD (Basic Science)

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Characterization of methicillin-resistant *Staphylococcus aureus* in Kuwait hospitals: 1992-2010

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Introduction:
Methicillin-resistant Staphylococcus aureus (MRSA) have been isolated in Kuwait hospitals since 1992. However, there have been no comprehensive study of their genotypes. The aim of this study was to investigate the distribution of MRSA clones obtained from patients in Kuwait hospitals from 1992 to 2010.

Methods:
Four hundred MRSA isolates representing prevailing PFGE types obtained from 13 hospitals in Kuwait were characterized using SCCmec typing, spa typing and multi locus sequence typing.

Results:
In total, 57 spa types and 27 sequence types were detected among isolates studied. The dominant genotypes were ST239-III-t421 (86; 21.5%), ST241-III-t037 (43; 10.7%), ST239-III-t945 (28; 7.0%), ST239-III-t037 (26; 6.5%), ST239-III-t860 (18; 4.5%), ST22-IV-t223/t852/t032 (33.0;8.2%), ST80-IV-t044/t045/t376 (27;6.7%), ST30-IV-t019/t318/t345 (14;3.5%), ST5-II-t003/t688 (20; 5.0%), ST6-IV-t304 (9;2.5%) and ST36-IV-t018/t605 (8; 2.0%). Other genotypes occurred less frequently. The number of MRSA genotypes increased from one (ST239-III-t037) in 1992 to four in 1996, eight in 1999, six in 2001, 11 in 2005 and 23 in 2010. While the ST239-III-t037 genotype was detected in 1992, 1996 and 2005, the ST239-III-t421 was detected from 1992 to 2010. ST241-III-t037 genotype was detected from 1997 to 2002. The ST30-IV-t019 was first detected in 1996 while ST80-IV-t044 first appeared in 1997. Among the ST22 isolates, the ST22-IV-t032 was detected in 2005 while ST22-IV-t223 was detected in 2005 and 2010. Novel genotypes detected in 2010 included ST772-V-t657, ST8-IV-t008, and ST88-IV-t690.

Conclusions:
The study revealed changes in the numbers and diversity of MRSA clones in Kuwait hospitals overtime. Although a diversity of new MRSA clones were observed in 2005 and 2010, the ST239-III-t421 genotype remained the dominant MRSA clone in Kuwait hospitals.

Key Words: MRSA; Spa typing; Multi locus sequence typing
Funding Agency: Research Administration, grant no. YM 02/12

Microbiology, Virology and Immunology
Category: Clinical

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Evaluation of chromogenic medium and direct latex agglutination test for detection of group B *Streptococcus* in vaginal specimens from pregnant women in Lebanon and Kuwait

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Introduction:
This study was undertaken to evaluate chromogenic medium and direct latex agglutination test (DLA) for detection of Group B Streptococcus (GBS) in the vaginal specimens of pregnant women, and to ascertain the prevalence of GBS in this population in Kuwait and Lebanon.

Methods:
Vaginal swabs, collected from women at 35-37 weeks, were cultured on 5% sheep blood agar (SBA), colistin nalidixic acid agar (CNA), Strept B Select chromogenic agar (SBS) as well as Lim enrichment broth in 168 cases in Lebanon while only SBA was used for 1391 samples in Kuwait. In addition, vaginal samples from 102 GBS-positive and 20 GBS-negative women near the time of delivery, were collected in Kuwait for evaluation of DLA test.

Results:
During the study period the prevalence of GBS colonization was determined to be 20.7% (288/1391) in Kuwait while 18.4% of 168 pregnant women in Lebanon had vaginal cultures positive for GBS. By direct plating of vaginal swabs on the three media used, the isolation rates of GBS was 51.6%, 64.5%, and 77.4% on SBA, CNA, and SBS, respectively, which increased to 90.35, 93.1%, and 96.8%, respectively, following subculture of Lim broth after 18 h of incubation. The sensitivity of DLA test was found to be dependent on the density of GBS colonization, resulting in 100% sensitivity and 100% specificity for heavy (> 102 CFU/swab) and moderately heavy (50-100 CFU/swab) growth of GBS. However, for vaginal specimens yielding < 50 CFU/swab, the sensitivity, specificity, positive and negative predictive values of DLA were 100%, 55.5%, 63.6%, 100%, respectively.

Conclusions:
A chromogenic agar, such as, SBS and DLA test can be used for rapid detection of GBS in pregnant women. DLA test, in particular, can prove to be a useful tool for immediate detection of GBS in women near delivery so that intrapartum antibiotic prophylaxis can be initiated.

Key Words: Group B Streptococcus (GBS),; Chromogenic medium; Direct latex agglutination test
Funding Agency: None

Microbiology, Virology and Immunology
Category: Clinical

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Primary cervical screening of women for human papillomavirus (HPV) by HPV-DNA testing in Kuwait

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Introduction:
The number of women infected with human papillomavirus (HPV) and distribution of HPV genotypes vary across populations and with age. High-risk HPV types are detected in 99% of cervical cancers. In this study, we present data of cervical screening for HPV obtained from native Kuwaiti (K) and non-Kuwaiti (NK) female populations of different age groups.

Methods:
From Jan. 2009 through Dec. 2013, women between the ages of 20 - >50 years, who sought gynecological consult at different centers from all over Kuwait, were tested for genital HPV infection. The study population included ethnic K and NK (expatriate) females. Cervical samples were tested for HPV-DNA as per manufacturer's instructions by using Digene hybrid capture 2 (hc2) technique, which involves nucleic acid hybridization assay.

Results:
A total of 6205 women were enrolled in the study, comprising 4671 K and 1533 NK females. The test was positive for HPV-DNA in 486 (10.4%) and 239 (15.5%) of K and NK women, respectively. However, the overall positivity rates were 7.83% and 3.83% for K and NK women, respectively. Of the total positive samples, highest positivity was observed in 26-35 years age group among K women (14.8%) as compared to 18.4% in 31-35 year age group among NK women. Overall highest positive rates were found in 16% of women in 31-35 year age group in Kuwait. Including mixed infections, 76.8% of women were positive for HR HPV genotypes whereas 42% were infected with LR types.

Conclusions:
The overall prevalence of HPV among females in Kuwait is lower than reported from other countries. Our data indicate that the burden of HPV infection is highest among those aged 31-35 years. Knowledge about HPV types prevalent in Kuwait would be useful in devising optimum strategy for cervical cancer prevention.

Key Words: Human papillomavirus; Cervical testing; Molecular technique
Funding Agency: None

Microbiology, Virology and Immunology
Category: Clinical

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Antibiotic resistance of *Escherichia coli* isolated from community patients with urinary tract infections

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Introduction:
Escherichia coli E.coli) are the most common microorganisms causing urinary tract infections (UTIs). Uropathogenic E.coli (UPEC) strains possess several virulence determinants that allow them to colonize the urinary tract, avoid host defences, and cause damage to the uroepithelium. In addition, E.coli exhibit changing susceptibility patterns.Therefore this study was undertaken to determine and to compare the in vitro antibiotic resistance of E.coli isolates during 2010-2012 in community-acquired UTIs in London Hospital, Kuwait.

Methods:
During 1/1/2010-31/12/2012, a total of 224 E.coli isolates caused community-acquired UTIs (71 E.coli isolates during 2010, 83 during 2011 and 88 during 2012). Isolation was performed by standart method. The identification and the susceptibility test to the antimicrobial agents were performed by the mini API system (Biomerieux).

Results:
The resistance of E.coli isolates to antibiotics for 2010, 2011 and 2012 respectively was: Amoxicillin/Clavulanic acid 47,1%/44,4%/53,4%, Cefuroxime 26,8%/11,0%/8,1%, Ceftriaxone 5,6%/8,5%/7,0%, Gentamicin 8,7%/8,7%/8,7%, Nitrofurantoin 2,9%/1,2%/3,4%, Trimethoprim/Sulfamethoxazole(TMP/SMZ) 47,8%/34,7%/45,8%, Nalidix acid 37,8%/3,2%/52,2%, Ciprofloxacin 12,5%/7,9%/25,3%, Meropenem 0%/0%/2,8%. The presence of ESBL producing strains E.coli has been determined in 10 cases (4,5%) from 224 analysed.

Conclusions:
We noticed a rapidly increase in resistance rates in E.coli isolates to TMP/SMZ and Nalidix acid. Resistance rates to cephalosporines and quinolones were significant raised.Resistance to Meropenem, Nitrofurantoin and aminoglycosides remained almost stable. These data provide the information on the level of antimicrobial resistance amongst the uropathogenic E.coli nisolates. The susceptibility pattern of E.coli strains isolated from patients with UTIs will serve as a guide in the proper management of UTIs.

Key Words: Urinary Tract Infections (UTIs); Uropathogen; Antibiotic resistance
Funding Agency: None

Microbiology, Virology and Immunology
Category: Clinical

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Detection of viral co-infections in hospitalized patients with respiratory tract infection in Kuwait.

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Introduction:
Improvement in molecular technologies in the past ten years allows us to discover new viruses. The simultaneous detection of a broad spectrum of viruses allows for the identification of viral co-infection in respiratory infections. In this study, we aim to detect viral co-infection among hospitalized patients with respiratory tract infections in Kuwait.

Methods:
The aim of this study is to investigate the role of viral co-infection in patients with respiratory tract infection by using real time-PCR techniques.

Results:
In total, 934 hospitalized patients aged between 3 days and 80 years were screened over three years, from September 2010 to September 2013. Among the 351 patients diagnosed with viral infections, human rhinovirus was detected in 42.8%, influenza A virus in 16.5% and respiratory syncytial virus in 14.7%. Viral co-infection was detected in 49 (13.96%) patients with human rhinovirus being the most common virus associated with co-infection (26 patients or 53.1%), followed by adenovirus (14 patients or 28.6%) and human coronavirus-OC43 (12 patients or 24.5%). It is interesting to note that three patients had three viral co-infections.

Conclusions:
Simultaneous testing of respiratory viruses by real-time PCR is a suitable tool for the detection and evaluation of the role of viral co-infections in respiratory tract infections.

Key Words: Respiratory viruses; Co-infection; PCR
Funding Agency: Research No. (MI 03/08) by the Research Sector, Kuwait University.

Microbiology, Virology and Immunology
Category: Basic Sciences

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Chlorhexidine induced post-antifungal effect and phospholipase production of oral *Candida albicans* isolates

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Introduction:
Candida albicans is the major aetiological agent of oral candidosis. An important pathogenic attribute of C. albicans is the production of extracellular phospholipases. Post-antifungal effect (PAFE) is the suppression of fungal growth following brief exposure to antifungal agents. It is another determinant of candidal pathogenicity. Chlorhexidine gluconate (CG) is an antimicrobial mouth wash with antifungal properties. Its concentration in the mouth reaches sub-therapeutic levels during dosage intervals due to the diluent and cleansing effect of saliva. Therefore Candida undergoes only a brief exposure to CG during treatment, similar to that of the PAFE phenomenon. Hence the objective was to determine the PAFE and phospholipase production of oral C. albicans isolates following brief exposure to sub-therapeutic concentrations of CG.

Methods:
Fifty oral C. albicans isolates were exposed to three sub-therapeutic concentrations of CG (0.005%, 0.0025% and 0.00125%) for one hour. Thereafter the antiseptic was removed by dilution and the PAFE and phospholipase production was determined by a turbidometric method and a plate assay using egg yolk-agar medium, respectively.

Results:
Mean in vitro PAFE ± SEM (hours) of oral C. albicans isolates following 1 hour exposure to 0.005%, 0.0025% and 0.00125% CG was 6.97 ± 0.77, 1.85 ± 0.58 and 0.62 ± 0.01, respectively. Compared to the controls, the phospholipase production of these isolates was significantly suppressed with a percentage reduction (± SEM) of 21.68 ± 1.11%, 18.20 ± 1.08% and 14.04 ± 0.52% following exposure to 0.005%, 0.0025% and 0.00125% CG, respectively.

Conclusions:
Brief exposure of C. albicans isolates to CG would continue to have an antifungal effect by suppressing candidal growth as well as phospholipase production, thereby reducing candidal pathogenicity and exemplifying additional pharmacodynamics of CG. Acknowledgements: Work was partially supported by KU Research Grant No DB 01/13.

Key Words: Chlorhexidine; Candida albicans; Post-antifungal effect
Funding Agency: Research Grant No. DB 01/13.

Microbiology, Virology and Immunology
Category: Basic Sciences

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Confocal laser microscopy: A comparative study of applications for two confocal machines

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Introduction:
Confocal laser scanning microscopy (CLSM) is a valuable tool for obtaining high resolution images and 3-D reconstructions of cells and tissues. The purpose of this work is to compare the performance of two confocal machines (LSM 510 Meta and LSM 700) for imaging of live and fixed cell lines.

Methods:
Three cell lines were stained using dapi (4',6-diamidino-2-phenylindole, dihydrochloride) and Phalloidin for nuclear and actin filament staining, respectively. Cells were grown, treated, fixed and stained directly in chamber slides. After mounting, the specimens were viewed under the two confocal microscopes. By default, live cell imaging was done in whole-mounts and required no specific processing, other than staining. Optimizations for concentration and incubation conditions of fluorescent probes for different cell lines were performed. The appropriate negative controls were included to establish background fluorescence and nonspecific staining of the cells with the fluorescent dyes.

Results:
Although, the optimal conditions varied for the two microscopes, both of the confocal microscopes yielded high resolution images for fixed specimens stained with dapi. However, only LSM 510 Meta provided high quality images with live cells using actin filament staining dye Phalloidin.

Conclusions:
The Confocal laser scanning microscopy is a highly valuable tool, capable of collecting high quality multispectral images across the visible range. While confocal microscopes are effective and very useful instruments, it is extremely important to excite samples with the appropriate excitation wavelength and to carefully consider which confocal imaging is the proper approach for a particular biological application.

Key Words: Confocal microscopy; Cell lines; Staining
Funding Agency: Kuwait University Research Sector Grant SRUL02/13

Microbiology, Virology and Immunology
Category: Clinical

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Prevalence of group B *Streptococcus* in pregnant women in Kuwait and Lebanon: Risk Factors, evaluation of vaginal flora and antimicrobial susceptibility

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Introduction:
Guidelines recommend universal screening of all pregnant women at 35 - 37 weeks of gestation for group B streptococcus (GBS) colonization & reserve a risk-factor-based approach for women who have no prenatal cultures. This study determines prevalence of GBS among pregnant women in Kuwait and Lebanon and assesses association between risk factors and vaginal flora in this patient population.

Methods:
Two vaginal samples each from 168 women between 35 - 37 weeks of gestation were obtained in Lebanon. One sample was cultured on blood agar (BA), Strep B Select agar, CNA agar and Lim's broth and the other was evaluated for vaginal flora on Gram's stained smears. Colonies suggestive of GBS were identified by catalase test and agglutination in group B antisera. Antimicrobial susceptibility to different antibiotics was tested on BA. Socio-demographic and obstetric data were obtained by designed form.

Results:
The prevalence of GBS colonization was 20.7% and 18.4% in Kuwait & Lebanon, respectively. Evaluation of Gram stained vaginal smears revealed inverse relationship between lactobacilli presence and GBS colonization. Resistance of GBS to erythromycin (E) was found in 18.8% & 25.8% & to clindamycin (CL) in 20.2% & 12.9% of strains in Kuwait & Lebanon, respectively. The range of MIC for penicillin was 0.0.16-0.094 mg/L in strains from Lebanon. Demographic analysis did not reveal any statistically significant differences in GBS colonization rates between various age groups (p=0.498) or levels of education (p=0.696) among Lebanese women.

Conclusions:
Prevalence of GBS remains high in this region with no identifiable risk factors for its acquisition. Furthermore, increase in penicillin MIC and resistance to E & CL should prompt susceptibility testing for all GBS isolates. The resistance profile of these strains represents an emerging public health concern that needs further surveillance.

Key Words: GBS; Risk factors; Vaginal flora
Funding Agency: None

Microbiology, Virology and Immunology
Category: Undergraduate

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Microbiological contamination of stethoscopes and disinfection practices among clinicians in public emergency and medical intensive care units in Kuwait

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Introduction:
The aim of this study was to determine the prevalence of microbiological contamination of stethoscopes in emergency departments (EDs) and intensive care units (ICUs) in all secondary care hospitals in Kuwait; and to evaluate the stethoscope hygiene practices of clinicians in these two settings.

Methods:
This is a cross-sectional study that collected samples for culture from all personal and shared stethoscopes in all EDs and ICUs. Two specimens were taken from each stethoscope, one from bell and the other from diaphragm. Microbiological identification was done using standard laboratory methods by a senior microbiologist. Data on stethoscope hygiene practices were collected by self-administered questionnaire. All clinicians in EDs and ICUs in all shifts were approached; while clinicians with no personal stethoscopes were excluded.

Results:
Out of the 235 personal and shared stethoscopes, 223(95%) were colonized. Despite one personal stethoscope, all of the 132 personal stethoscopes were colonized. Coagulase negative Staphylococcus was the predominant organism and was isolated in 91% of bells and 83% of diaphragms; followed by Micrococcus (60% of bells, 49% of diaphragms). Methicillin-resistant Staphylococcus aureus (MRSA) was identified in 1.4% of bells and 0.5% of diaphragms; while Gram-negative bacteria were isolated from 6% of bells and 4% of diaphragms. Approximately 80% of the clinicians reported that they ever cleaned their stethoscopes, most of whom cleaned their stethoscopes weekly.

Conclusions:
The prevalence of stethoscope contamination is extremely high in EDs and ICUs in secondary care hospitals in Kuwait. Although some of the isolated organisms can be considered non-pathogenic, various reports have described their potential harm among patients in ICUs. Isolation of MRSA from stethoscopes is of great concern and call for efforts to consider guidelines for stethoscope hygiene which is currently under intense debate in other settings.

Key Words: Contamination; Stethoscopes; Intensive Care Units
Funding Agency: None

Microbiology, Virology and Immunology
Category: Basic Sciences

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Determination of bacterial cell number and viability using colony forming unit method and flow cytometry

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Introduction:
The classical method of colony forming unit (CFU) for the determination of bacterial number and viability relies on the ability of cells to actively grow and form visible colonies on solid media. This method takes long time, and under some circumstances, the number of viable organisms may be severely underrepresented, e.g. in case of sub-lethally damaged organisms. Flowcytometry, by using the dye exclusion, is a fast method for cell counting and differentiation between viable and dead cells. Propidium iodide (PI) is a membrane impermeant dye that is generally excluded from viable cells. It labels only the membrane-compromised bacteria. Cells with compromised membranes exhibit red-fluorescent nucleic acid staining; whereas the live cells are non-fluorescent. The aim of this study was to determine the number of viable bacteria using CFU and flowcytometry methods and compare the results.

Methods:
A single colony of Escherichia coli strain BL21 was grown overnight at 37^0C in Luria Broth (LB) medium. The culture was left at room temperature for up to 30 days. Aliquots were sub-cultured, at different time intervals, on LB agar, incubated overnight at 37^0C and the number of CFUs were counted. For flow cytometry, 10 µlitre Propidium Iodide (10 µgram/ml PBS) was added to 1 ml bacterial suspension and incubated in the dark for 1 min. The PI fluorescence was determined with the Beckman Coulter FC 500 flow cytometer.

Results:
Both the CFU results as well as the flow cytometry analyses showed that the viability of E. coli decreased gradually upon incubation of the bacterial culture at room temperature. However, this decrease was more pronounced with CFU method than flow cytometry.

Conclusions:
Although, both CFU and flowcytometry provided similar results, the flow cytometry is a rapid alternative to quantify viable bacterial cells.

Key Words: Bacterial viability; Colony forming unit; Flow cytometry
Funding Agency: Kuwait University Research Sector grant SRUL02/13

Microbiology, Virology and Immunology
Category: Clinical

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A relatively high number of pregnant women in Kuwait remain susceptible to Rubella: A need for an alternative vaccination policy

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Introduction:
Rubella and hepatitis B are frequently causative agents of prenatal infections. These infections can lead to important complications in pregnancy for maternal and fetal health. Despite the existence of effective vaccine, infection due to rubella virus is not eradicated. Nevertheless, preventive measures are still the best approaches to control and spread of hepatitis B virus. This study aimed to measure the prevalence of anti-rubella IgG and hepatitis B surface antigen (HBs Ag) among pregnant women in Kuwait in order to assess the effectiveness of the current vaccination programs.

Methods:
This retrospective study involved 4062 pregnant women evaluated in health centers in Hawalli province of Kuwait. They were screened for anti-rubella IgG and HBs Ag, using commercially available assays.

Results:
The mean age of the pregnant women was 29.2± 5.26 years (range 17-49 years). Rubella IgG prevalence among pregnant women was 88.4% (n=3589), 276 (6.8%) of pregnant women had no antibody to rubella and 197 (4.8%) had rubella antibody level of ≤ 10 IU/ml. Therefore, 473 (11.6%) of pregnant women were susceptible to rubella. The proportion of susceptible women increased with increasing in age (from 3.4% to 10.3% and from 3.4% to 6.7%, among the <20 years and the ≥40 years age group, respectively) (p=0.016). The prevalence of HBs Ag was 0.3%, and did not vary with age.

Conclusions:
The prevalence of both anti-rubella IgG and HBs antigen among pregnant women in Kuwait were relatively high. However, about 11.6% of pregnant women in Kuwait remain susceptible to rubella infection and hence congenital infection and fetal malformation.

Key Words: Rubella; Hepatitis B; Pregnant women
Funding Agency: None

Microbiology, Virology and Immunology
Category: Basic Sciences

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Aerial prevalence, animal pathogenicity and antifungal drug susceptibility of multidrug-resistant *Aspergillus calidoustus* isolated in Kuwait

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Introduction:
Objective: Aspergillus calidoustus belongs to the Aspergillus section "Usti," along with A. ustus, A. granulosus, A. puniceus, and A. pseudodeflectus and is an emerging cause of invasive aspergillosis (IA) in transplant recipients. We studied the environmental prevalence of this species in outdoor and hospital environment in Kuwait and determined its pathogenicity in BALB/c mice.

Methods:
Air sampling was done at ground level and at ~50 feet above the ground level inside and outside Mubarak Al-Kabeer hospital by exposing malt extract agar plates supplemented with chloramphenicol (50 mg/L) for 15 min. A. calidoustus colonies were identified by phenotypic characteristics and multilocus sequencing. Antifungal drug susceptibility testing was determined by Etest. Conidia (1 x 106) were injected into tail vein of control (n=12) and immunosuppressed (n=12) mice, 3 mice from each group were sacrificed on 10, 15, 20 and 25 days postinfection and internal organs were removed for direct microscopic examination and culture.

Results:
Of 330 colonies of Aspergillus spp. obtained from indoor hospital air, 6 (1.8%) were A. calidoustus. One (out of 156) isolate originated from outdoor air. One isolate came from BAL specimen of a patient with pneumonia. All isolates showed reduced susceptibility to voriconazole, posaconazole and itraconazole with clinical isolate exhibiting complete resistance. The MICs for amphotericin B ranged between 0.25-2 µg/ml. None of mice died and no gross lesions were observed, however, scanty fungal elements were seen in KOH-calcoflour mounts. Culture positivity of internal organs was higher in immunosuppressed mice.

Conclusions:
A. calidoustus with reduced susceptibility to triazoles is present in hospital environment in Kuwait and was also isolated from a patient with pneumonia. Preliminary data suggest that A. calidoustus can persist in host tissues warranting further studies for virulence and invasiveness of this emerging human pathogen.

Key Words: Triazole-resistant A. calidoustus; Environmental prevalence; Pathogenicity
Funding Agency: Supported by KURS grant MI 01/09

Microbiology, Virology and Immunology
Category: Clinical

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Performance comparison of automated BACTEC MGIT 960 system with the radiometric BACTEC 460TB system for testing susceptibility of *Mycobacterium tuberculosis* isolates to first-line drugs in a low TB incidence country

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Introduction:
The reliability of nonradiometric, fully automated BACTEC MGIT 960 system for drug susceptibility testing (DST) of Mycobacterium tuberculosis to first-line drugs isoniazid (INH), rifampin (RIF), streptomycin (SM) and ethambutol (EMB) was compared to that of radiometric BACTEC 460TB system. Detection of resistance conferring mutations in appropriate regions of M. tuberculosis genome by DNA sequencing was used to resolve discrepant results.

Methods:
A total of 55 M. tuberculosis isolates recovered from pulmonary and extra-pulmonary specimens were tested for their susceptibility to first-line drugs. The DST by BACTEC 460TB and MGIT 960 systems were performed (Becton Dickinson). DNA sequencing of three (hot-spot, N-terminal and cluster II) regions of rpoB, katG codon 315,inhA regulatory region, embB codons 306, 406 and 497, rpsLcodons 43 and 88 and 500 and 900 regions of rrs gene was performed to resolve discrepant results. False resistance and false susceptibility results were defined as major errors (ME) and very major errors (VME), respectively.

Results:
Overall level of agreement between BACTEC 460TB results and those of BACTEC MGIT 960 method was 93.6%. All isolates yielded identical results by both methods for INH and SM. Rifampin results agreed for 53isolates (96.4% agreement) while EMB results agreed for 42 isolates (78.1% agreement). Fourteen M. tuberculosisisolates yielded discrepant results of which 12 and 2 isolates were resistant to EMB and RIF, respectively, by BACTEC 460TB but susceptible by MGIT 960 system. DNA sequencing data resolved all discrepant results in favor of BACTEC 460TB system.

Conclusions:
Our data demonstrate that MGIT 960 system is an accurate method for DST of M. tuberculosis against INH and SM while two VME for RIF were caused due to a very rare (I572F) rpoB mutation. However, 12 VME associated with DST to EMB by MGIT 960 system are in accordance with previous reports showing EMB with least concordant results.

Key Words: Mycobacterium tuberculosis; Drug susceptibility testing; MGIT 960 system,
Funding Agency: None

Microbiology, Virology and Immunology
Category: Clinical

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Evaluation of the comparative performance of Verigene blood culture nucleic acid system to conventional techniques in a tertiary-care hospital in Kuwait

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Introduction:
The diagnosis of bacteremia and sepsis is a priority in a Clinical Microbiology . A key predictor of mortality rates in patients with severe blood stream infection is the time to identification of the causative pathogen and initiation of targeted therapy.
Objectives:
To evaluate the performance of Verigene (BC-GP and BC-GN) nucleic acid test for the direct identification of Gram-positive and Gram-negative bacteria from positive blood culture bottles with their resistant markers in comparison with the conventional culture technique.

Methods:
All blood culture bottles showing Gram-positive cocci or Gram-negative bacilli by Gram stain were processed in Verigene for BC-GP and BC-GN in comparison with conventional methods using Vitek II, and Vitek MS.

Results:
In 63 patients with positive blood culture for Gram-positive cocci, Verigene correctly identified all Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus fecalis, Enterococcus fecium and Streptococcus mitis. Verigene correctly detected MecA gene in all coagulase-negative staphylococci, but failed to detect it in two isolates of S. aureus. It correctly identified two S. aureus isolates as MRSA.Verigene failed to detect VAN A and VAN B in two of the four Enterococcus faecium isolates. In 63 patients with positive blood culture for Gram-positive cocci, Verigene identified correctly all Enterobacteriace, Pseudomonas aeruginosa and Acinitobacter baumanii. However it failed to detect three Stenotrophomonas maltophilia as the bacteria is not in the database. Verigene correctly detected all ESBL-producing Enterobacteriacae but failed to detect resistance markers of the three MDR-Psuedomonas aeruginosa and 5 of the 6 Acinitobacter baumanii isolates.

Conclusions:
Verigene BC can be used for the direct and rapid identification of Gram-positive and Gram negative bacteria and their resistance markers directly from a blood culture bottles with a turn around time of 4 hours.
Key Words: Verigiene; Blood culture; Direct detection
Funding Agency: none

Microbiology, Virology and Immunology
Category: Graduate PhD (Basic Science)

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Human leukocyte antigens and gender compatibility in renal transplant in Kuwaiti patients

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Introduction:
Renal transplantation is the preferred, definitive treatment for end stage renal disease (ESRD). However, graft rejection remains a major cause of morbidity and mortality of patients after transplantation. The role of HLA matching in kidney transplantation has been a hotly debated issue. Many argue that current immunosuppression regimens obviate the benefits of HLA matching altogether, raising the question of whether HLA matching should be used or not before renal transplantation. The Objective was to evaluate the possible effect of HLA-A, B and DR compatibility and gender matching between patients and their donors on the development of rejection after renal transplantation in Kuwaiti population.

Methods:
HLA-A, -B, and –DR typing was performed by complement-dependent cytotoxicity (CDC) method for 181 renal transplant patients and 181donors.

Results:
No statistical significant differences were found between patients with rejection and those without for the frequencies of HLA antigens except for HLA-DR17 (OR=2.6, P=0.003, Pc=0.045). HLA incompatibility between patients and their donors was more associated with renal transplant when compared to HLA compatibility (P= 0.003). Also, gender mismatch was more frequent in patients suffering from rejection than patients without rejection (P=0.005) especially if a female patient received kidney from a male donor (P=0.008).

Conclusions:
It can be concluded that HLA-DR17 antigen, HLA incompatibility and gender mismatch between patients and their donors especially when a female receive kidney from a male may be risk factors for the development of graft rejection after renal transplantation in Kuwaiti population.

Key Words: Immunology; Tissue typing; Transplantation
Funding Agency: None

Microbiology, Virology and Immunology
Category: Basic Sciences

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Anti-Lyme IgM and IgG antibodies in sera of human subjects residing in Kuwait

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Introduction:
Lyme disease caused by Borrelia burgdorferi is uncommon in Kuwait, but people visiting endemic countries may get infected and develop symptoms when they come back to Kuwait. The aim of this study was to determine the serological evidence of infection in people who returned back from endemic countries and were clinically suspected of Lyme disease.

Methods:
A total of 80 sera, obtained from patients attending five major hospitals in Kuwait, during 2009 to 2013, were tested for anti-Borrelia burgdorferi IgM and IgG antibodies using enzyme immunoassay (EIA). The samples were tested using a commercial assay (Serion Classic, Germany). The test employs a positive control, a negative control and a cut off serum. To achieve a high level of sensitivity, a combination of a European strain of the genus Borrelia garini along with Borrelia afzelli PKo was used. The antigen cocktail had the antigen OspC and VisE, which are particularly important for the diagnosis of early stage Borrelia disease, in addition to the late stage critical protein P100. In order to further increase the sensitivity, a recombinant VisE was added to the coating antigen complex. Specificity was optimized by the addition of a lysate of Treponema phagedenis to the dilution buffer which selectively absorbs any cross reacting Treponema antibodies which may be present.

Results:
A total of 32/80 (40%) sera were positive for anti- Borrelia burgdorferi antibodies. Out of these, 20 were positive for IgM only, 6 for IgG only and 6 for both IgM and IgG.

Conclusions:
ELISA could be useful for serological evidence of infection with Borrelia burgdorferi due to its immunoglobulin specific analysis of the immune response.

Key Words: Lyme disease; Antibodies; Kuwait
Funding Agency: None

Microbiology, Virology and Immunology
Category: Undergraduate

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Molecular characterization of *Brucella* isolates infecting humans in Kuwait

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Introduction:
Brucellosis, caused by the organisms of genus Brucella, is endemic in Kuwait. Human brucellosis, often a chronic and relapsing disease, may be caused by four species and various biovars of Brucella. It is not possible to differentiate between relapse and reinfection because of difficulties in identifying Brucella species/biovar using classical methods. The newly discovered molecular methods are considered accurate, reliable and fast for bacterial species/biovar identification. In this study, for the first time in Kuwait, we have used molecular methods [real-time PCR (RT-PCR) and 16s rRNA gene sequencing] for the identification of Brucella species and biovars isolated from human specimens in Kuwait.

Methods:
A total of 93 Brucella isolates were obtained from human specimens. A loopful of bacterial colonies from individual culture plates were suspended in saline in a tube and heated at 95°C for 10 minutes. DNA was purified from the heated specimens using the Qiagen DNA mini kit, according to the manufacturer's instructions. The species were identified by Brucella-specific primers in RT-PCR using Roche LightCycler. The MicroSeq® 500 16S rDNA bacterial identification kit (Applied Biosystems) was used for DNA sequencing, according to the methods recommended by the kit supplier. The sequences were assembled and the Brucella species/biovar were identified using the MicroSeq® Bacterial Identification Software, NCBI BLAST and SeqMatch.

Results:
The RT-PCR results suggested that all of the 93 isolates were Brucella mellitensis. The 16s rRNA gene sequencing confirmed their identity as B. mellitensis. Furthermore, the later technology identified the biovars of B. mellitensis.

Conclusions:
This work demonstrates that RT-PCR MicroSeq® 16S rRNA gene sequencing can provide rapid confirmatory identification of Brucella isolates at species level and also identify the biovars.

Key Words: DNA Sequencing; RT-PCR; Brucella
Funding Agency: Supported by Kuwait University Research Sector grant SRUL02/13

Microbiology, Virology and Immunology
Category: Clinical

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Caparison between BD TBc ID Test and Gen-probe Accuprobe assay for identification of *M. tuberculosis* complex

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Introduction:
One third of the world population is infected with Mycobacterium tuberculosis (MTbc). The slow growth of MTbc delays clinical diagnosis and treatment, additional delay happens for identification and differentiation between MTbc and Non Tuberculosis Mycobactria (NTM).
Objectives: To evaluate BD MGIT TBc Identification Test(TBc ID, BECTON & DICKINSON, USA) for the rapid identification of mycobacteria from BD MGIT tubes.

Methods:
A total of 100 isolates corresponding to 100 patients were processed by BD TBc ID and compared with GEN-PROBE Accuprbe Assay USA according to the manufacturer recommendation. Ten control strains (7MTB and 3NTM) were also evaluated.

Results:
Eighty five isolates, 7 of them MTB controls, were identified as Mycobacterium tuberculosis by both BD TBc ID and GEN-PROBE Accuprbe with 100% sensitivity. Thirteen of the isolates, 3 of them NTM controls were negative by the 2 methods. Two of the isolates were positive by BD TBc ID but negative by GEN-PROBE Accuprbe. Both the isolates were from patients with active TB and the result was confirmed with GeneXpert MTB/RIF (cephide, USA). Thus, the corrected specificity of BD TBc ID is 100%.

Conclusions:
In the absence of gold standard test for the identification of MTB, BD TBc ID is a rapid and accurate method for the identification of MTB.

Key Words: BD TBc ID Test; Gen-probe Accuprobe; Mycobacterium
Funding Agency: None

Microbiology, Virology and Immunology
Category: Clinical

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Impact of malaria infection on hematological parameters

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Introduction:
Malaria is caused by parasites of the genus Plasmodium that affect humans in tropical countries. 216 million cases of malaria in 106 countries with 655,000 deaths were reported in the world in 2010 (WHO). Eighty six per cent of these deaths were among children under 5 years of age mostly in African sub-Sahara. The aim of the present study was to analyze the haematological parameters which can give initial hint for malarial infection.

Methods:
All the suspected patients were checked with Giemsa stained thick and thin blood films in Infectious Diseases Hospital Laboratory. The speciation and density of the parasite were also counted from each patient. The full blood count was also performed using a Coulter Counter.

Results:
We conducted a retrospective analysis of hematologic changes in 72 patients with imported malaria (6 cases of P. falciparum; 15 cases of P. vivax and 51 cases of mixed infection of P. falciparum and P. vivax) in Infectious Diseases Hospital, Kuwait. Twenty four (33%) patients were found anemic and 57 (79%) had thrombocytopenia. There was a significant inverse relationship between parasitemia and platelet count. The platelet count was reduced to 34 x 109/L at 48,000 parasites/ µl of blood, whereas, hemoglobin was found 89 g/L at higher density of the parasites.
The parasitemia ranged from 73 – 48,000/ µl of blood. Anemia was defined as a hemoglobin level, 12 g/dL for men and ,10 g/dL for women. Using these criteria, 24 (33%) were anemic, 57 (79%) patients were thrombocytopenic. The MPV (>8 fl) was found higher in severe cases of thrombocytopenic patients. The white blood cells, monocytes, and neutrophils counts were also increased, whereas, the red blood cells, lymphocytes and eosinophils counts were reduced but not significant.

Conclusions:
Thrombocytopenia (<150x109/l), low leukocyte count (<4x109/l) and anemia (<12 g/dL in males and <10 g/dL in females) may be used as probable indicator for malaria in endemic countries.

Key Words: Malaria; Anemia; Thrombocytopenia
Funding Agency: none

Microbiology, Virology and Immunology
Category: Basic Sciences

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Proteomics analysis of *Escherichia coli* BL21 using the Proteome™ Lab PF 2D Platform

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Introduction:
The ProteomeLab™ PF2D protein fractionation system is a fully automated, two-dimensional system that resolves and collects proteins by isoelectric point in the first dimension and hydrophobicity in the second dimension. The system visualizes the complex pattern with a 2-dimensional protein map that is easy to interpret and the system's differential display allows to highlight differences in protein pattern expression. The aim of this study was to generate a proteome map of the gram negative bacterium Escherichia coli BL21.

Methods:
E. coli BL21 was cultured in Luria Broth (LB) agar at 370C for 48 h. The cells were suspended in saline and centrifuged to obtain the cell pellet. The cell pellet (0.5 mg/ml) was lysed according to the protocol provided with the ProteomeLab PF2D chemistry kit. The cell lysate (2 ml aliquot at 4.5 mg protein/ml) was injected into the system and separated by PF2D. The 1st and 2nd dimension runs were carried out as per the optimized ProteomeLab PF2D method. The proteins were detected with UV light at the wave lengths 280 and 214 nm, and the data were collected and analyzed using the ProteoVue software package.

Results:
In the first dimension, the absorbance of pH profiles were recorded at 280 nm using the high performance chromatofocusing chromatography and a total of 46 fractions were collected. Of these, 18 fractions were separated in the second dimension using high performance reversed phase chromatography and 467 different protein peaks were generated.

Conclusions:
The proteomic analysis of bacterial samples with the ProteomeLab PF2D allows rapid and high sensitivity resolution of proteins, thereby facilitating the identification of differential protein expression

Key Words: Proteomics analysis; Escherichia coli; PF 2D Platform
Funding Agency: Supported by Kuwait University Research Sector grant SRUL 02/13

Microbiology, Virology and Immunology
Category: Basic Sciences

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Genotyping of nethicillin-resistant *Staphylococcus aureus* in the Sultan Qaboos University Hospital, Oman reveals the dominance of PVL-negative ST6-IV/t304 clone

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Introduction:
Objectives: The epidemiology of Methicillin-resistant Staphylococcus aureus (MRSA) is constantly evolving epidemiology worldwide. However, there are no data on the clonal composition of MRSA at the Sultan Qaboos University hospital in the Sultanate of Oman. The objective of this study was to determine the prevalence and distribution of MRSA genotypes circulating at a tertiary hospital in the Sultanate of Oman.

Methods:
A total of 79 MRSA were obtained from different clinical samples and investigated using antibiogram, pulsed-field gel electrophoresis (PFGE), Staphylococcal chromosome cassette mec (SCCmec), Spa typing and multi locus sequence typing (MLST).

Results:
The isolates were susceptible to linezolid, vancomycin, teicoplanin, tigecycline and mupirocin but were resistant to tetracycline (30.4%), erythromycin (26.6%), clindamycin (24.1%), trimethoprim (19.0%), ciprofloxacin (17.7%), fusidic acid (15.2%), and gentamicin (12.7%). Molecular typing revealed 19 PFGE patterns, 26 Spa types and 21 sequence types. SCCmec - IV (86.0%) and SCCmec -V (10.1%) were the dominant SCCmec types. The ST6-IV/t304 (N=31), ST1295-IV/t690 (N=12) were the dominant genotypes followed by ST772-V/t657 (N=5), ST30-IV/t019/t021 (N=5), ST22-IV/t852 (N=4), ST80-IV/t044 (N=3) and 18 genotypes that were isolated sporadically. On the basis of SCCmec typing and MLST, 91.2% of the isolates were classified as community-associated MRSA (CA-MRSA) and 8.8 % consisting of four ST22-IV/t852, one ST239-III/t632, one ST5-III/t311 and one ST5-II/t003 were healthcare-associated MRSA (HA-MRSA).

Conclusions:
Conclusions: The study revealed the dominance of a PVL-negative CA-MRSA ST6-IV/t304 clone and provided insights into the prevalence and distribution of different MRSA genotypes at the tertiary hospital in Oman. It highlighted the importance of surveillance in detecting the emergence of new MRSA clones in a healthcare facility.

Key Words: MRSA; MLST; Antibiotic resistance
Funding Agency: Kuwait University MI 01/11

Microbiology, Virology and Immunology
Category: Basic Sciences

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Diversity of healthcare-associated MRSA genotypes in Kuwait hospitals

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Introduction:
The epidemiology of methicillin-resistant Staphylococcus aureus (MRSA) is changing globally. Consequently it is important to determine the prevailing MRSA clones in a healthcare facility for better management of infections. This study characterized MRSA isolated in 13 public hospitals in Kuwait to ascertain their clonal composition and the carriage of genes encoding Panton valentine Leukocidin (PVL).

Methods:
In total 205 non-repeat MRSA isolates obtained between 1 January and 31 December 2010 were characterized using antibiogram, Staphylococcal cassette chromosome mec (SCCmec), Spa typing and multi locus sequence typing.

Results:
The MRSA isolates were obtained from skin and soft tissue (30.0%), Nasal samples (27.3%) Respiratory samples (13.2%). Groin (5.3%) Vaginal swabs (2.4%), catheter tips (2.0%), Axilla (6; 2.9%), Eye (2.0%), Ear (1.4%), and fluid (0.5%). The isolates were resistant to gentamicin (47.3%), kanamycin (60.0%), erythromycin (77.6%), tetracycline (52.7%), fusidic acid (40.9%), ciprofloxacin (60.0%), trimethoprim (27.8%) and high-level mupirocin (5.4%). Thirty six (17.5%) of the isolates were positive for PVL genes. Molecular typing revealed 47 spa and 23 sequence types. The majority (49.7%) of the isolates belonged to established healthcare-associated MRSA genotypes ST239-SCCmec-III (34.6%) and ST22-SCCmec IV (15.1%). Other common genotypes were ST80-SCCmec-IV (6.8%), ST6-SCCmec-IV (3.9%), ST30-SCCmec-IV (2.9%), ST772-SCCmec-V (2.0%) and ST913-SCCmec-IV (2.0%). Spa typing subdivided the ST239-SCCmec-III isolates into seven spa types; t860 (N=18), t421 (N=15), t945 (N=13), t030 (N=12), t037 (N=11), t605 (N=1) and t314 (N=1). Similarly the ST22-SCCmec-IV isolates belonged to nine spa types; t223 (N=17), t852 (N=5), t790 (N=3) and one each of t032, t309, t3107, t5708, t5903 and t3935.

Conclusions:
The study revealed the diversification of healthcare-associated MRSA clones ST239-SCCmec-III and ST22-SCCmec-IV in Kuwait hospitals.

Key Words: MRSA; Molecular typing; Healthcare-Associated infection
Funding Agency: Kuwait University Grant YM 02/12

Neurology
Category: Clinical

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Targeted intra-arterial milrinone for symptomatic cerebral vasospasm

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Introduction:
Targeted endovascular treatment of symptomatic cerebral vasospasm associated with aneurysmal subarachnoid hemorrhage remains with worrisome side-effects. Milrinone, a selective phosphodiesterase III inhibitor has shown limited but promising results as an effective cerebral vasodilator with inotropic properties.

Methods:
A review of all patients with symptomatic and angiographically-proven vasospasm who received intra-arterial milrinone between January 2012 and January 2013 at a single neurological center was undertaken. Quantitative grading of angiographic vasospasm, evaluation of angiographic response following targeted treatment and any possible complications were assessed by a blinded reviewer. Immediate clinical neurological response was noted and 6 - 12 month follow-up using modified Rankin scale was performed.

Results:
Five patients (3 males and 2 females) with a mean age of 53 years were identified. On initial presentation of symptomatic vasospasm, all patients were treated with high dose continuous intravenous infusion of milrinone, blood pressure augmentation and maintenance of euvolemia. Due to recurrence of symptomatic vasospasm or no response to initial medical management, all patients required endovascular treatment. Intra-arterial milrinone resulted in (mean 9± 8%) increase in arterial diameter. Four patients (80%) neurologically improved within 1 hour post targeted treatment. No adverse neurological events were associated with intra-arterial milrinone. Duration of continuous intravenous milrinone was 12.4±3.6 days. Two patients remained intubated for >5 days and 1 patient died in ICU. All other patients (80%) had a good neurological outcome (modified Rankin scale ≤ 3) at the 6 - 12 months follow-up.

Conclusions:
Despite modest angiographic response to targeted intra-arterial milrinone on a background of high dose continuous intravenous infusion, neurological improvement in symptomatic cerebral vasospasm was attained.

Key Words: Aneurysmal subarachnoid hemorrhage; Targeted Intra-arterial Milrinone; Cerebral vasospasm
Funding Agency: None

Neurology
Category: Clinical

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Demographics and clinical characteristics of multiple sclerosis in Kuwait: An analysis of the national multiple sclerosis registry

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Introduction:
Kuwait is recently considered a high-risk geo¬graphical area for MS. The incidence of MS is increasing in both genders throughout the last decade. We aimed to study the demographics and clinical characteristics of multiple sclerosis (MS) patients in Kuwait.

Methods:
This cross-sectional study evaluated MS patients diagnosed according to the revised 2010 McDonald criteria. Demographics and clinical characteristics (age at onset, disease duration, symptoms presentation at onset, disease course, relapse rate and disability measures) were collected using the national MS registry.

Results:
Records of 736 MS patients were analyzed (64.8% were women). Mean age at onset and mean disease duration were 26.87 and 7.71 years respectively. 47.9% of patients had a disease duration ≤5 years while only 5.6% had MS for > 20 years. Supratentorial and cerebellar/brainstem, spinal and optic pathway symptoms were the presenting symptoms in 30.8%, 29.5%, 27.4%, and 23.9% of patients respectively. 77.7% of patients had relapsing remitting course while clinically isolated syndrome group constituted 9.5%. 52.2% of patients had <1 relapse per year. 72.8% of patients had EDSS score ≤3, whereas only 14.1% were found to have EDSS of ≥ 6.

Conclusions:
Demographics and clinical characteristics of MS in Kuwait were comparable to regional and international figures. However, the annual relapse rates and EDSS scores were relatively lower despite more prevalent brainstem/cerebellar and spinal manifestations at onset.

Key Words: Multiple sclerosis; Demography; Clinical characters
Funding Agency: None

Neurology
Category: Clinical

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Prevalence of migraine among medical students in Kuwait University.

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Introduction:
The prevalence of migraine among medical students is of particular interest as they are subjected to lots of tests and stresses that may precipitate migraine attacks. We aimed to determine the prevalence of migraine among medical students in Kuwait university.

Methods:
This cross-sectional and descriptive study, which included students registered to Medical Faculty at Kuwait University in the academic year of 2012-2013. Out of 808 registrants, 621 students accepted to participate in the study. Participants who had two or more headaches in the last 3 months were subjected to two preliminary questions and participants with at least one positive response were asked to perform the validated ID-Migraine™ test. Frequency of headache per month and severity of headache by Numeric Rating Scale (NRS) were reported.

Results:
Migraine headache was detected in 173 subjects (27.9%) based on the ID-Migraine™ test. The mean age of the migraine students was 20.17± 2.29 (16- 25 years). Thirty-seven were male (21.4%) and 136 were female (78.6%). Migraine was significantly more frequent in the last 2 grades (35.5 % and 44% respectively, $p<0.000$)¬. The frequency and the severity of headache were significantly increased during last 2 grades(5.55+1.34 and 7.23+1.27, $p<0.000$) (6.00+0.76 and 6.68+1.25, $p<0.000$) respectively. Stress 43 (24.9%), irregular sleep 36(20.8%), and much reading 32 (18.5%) were the most common triggering factors.

Conclusions:
There is a high prevalence of migraine among medical students in Kuwait university. Frequency and severity of headache increase with years of educations.

Key Words: Migraine; Medical Students; Prevalence
Funding Agency: None

Neurology
Category: Clinical

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Efficacy of Botulinum toxin-A treatment in chronic migraine – first Middle East experience

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Introduction:
BoNT-A is approved for prophylactic treatment of CM. We aimed to assess the efficacy and safety of Botulinum toxin-A (BoNT-A) in the treatment of chronic migraine (CM).

Methods:
This open-label prospective study included 40 CM patients. Each patient received 100 units of BoNT-A following fixed site fixed dose protocol. Patient's headache was assessed by their headache diary and recording Headache Impact test (HIT-6) at baseline and 4 th, 8 th and 12 th weeks following BoNT-A injection. Adverse events (AEs) were monitored to assess the efficacy of BoNT-A. For willing patients, BoNT-A injection was given and they were assessed at 3 months interval.

Results:
After BoNT-A treatment, there were reduction in all parameters (headache frequency and severity, analgesic consumption and HIT-6 score) by 35-40% at 4th week, 41-45% at 8th weeks and 39-42% at 12 th week post treatment. At 4th week, 62.5% of patients achieved good response while, 37.5% indicated no alteration in their headache frequency and severity. At 8th week and 12th week post treatment 30%, 25% respectively were found to have no response to treatment. Five patients (12.5%) experienced mild and short lasting AEs. There was 60-70% improvement of variables after repeated injections at 3 months interval.

Conclusions:
BoNT-A is effective and well tolerated therapy in the prophylaxis of CM.

Key Words: Chronic Migraine; Botulinum Toxin-A; Kuwait
Funding Agency: None

Neurology
Category: Clinical

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Cognition and its association with handedness among school children in Kuwait

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Introduction:
Many studies have explored the cognitive variation between left and right handed individuals. However, the differences, if any, remain poorly understood. The aim of this study was to assess the association between handedness and cognitive abilities.

Methods:
We tested 220 students aged between 6 and 10 from 12 randomly selected public schools. All identified left handed students were chosen and matched with right handed students by random selection. Handedness was assessed using traditional writing hand approach as well as the Wathand Box Test and the Grooved Pegboard Test, and cognition was measured using Cambridge University's CANTABeclipse cognitive battery.

Results:
Right handed children had superior visuospatial abilities (p= 0.011, r= 0.253), visual memory (p= 0.034, r= 0.205) and better scores in reaction time tests which incorporated elements of pattern recognition (p= 0.004, r= -0.271). Left handed children proved to have better simple reaction times (p= 0.036, r= 0.201). In terms of confounders, reaction time was significantly associated with the duration of breast feeding (p= 0.013, r= -0.239), playing videogames (p= 0.016, r= -0.233), and eating fast food (p= 0.005, r= -0.267). Visual memory was also significantly associated with playing video games (p= 0.045, r= 0.193) and eating fast food (p= 0.011, r= 0.242). Factors not significantly associated with cognition include gender and parental marital status and educational level.

Conclusions:
To our knowledge, this is the first study to employ the CANTAB tool in assessing handedness and cognition in healthy children. There are some statistically significant though small differences in cognitive abilities between right and left handed individuals. Larger prospective studies are required to fully analyze the relationship between handedness and cognition in order to improve prognostication and management of patients with neurological deficits.

Key Words: Cognition; Handedness; Kuwait
Funding Agency: Novartis International AG

Neurology
Category: Clinical

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Increasing prevalence and incidence rates of multiple sclerosis in Kuwait

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Introduction:
Kuwait was considered as low to intermediate risk area for MS. We aimed to determine the prevalence and incidence rates of MS among Kuwaiti nationals based on 2011 population census.

Methods:
This cross-sectional study was conducted between October 2010 and April 2013 using the newly developed national MS registry in Kuwait. Patients with a diagnosis of MS according to 2010 revised McDonald criteria were identi¬fied. Population data, based on the census carried out in 2011 was obtained from Kuwait Bureau of Statistics to determine the number of people at risk. The crude, age- and sex-specific prevalence and incidence rates were calculated. Prevalence was defined as the total number of patients with a diagnosis of MS per 100,000 inhabitants at the prevalence day of 31th December 2011, while an incident case was defined as any individual who first diagnosed MS between 1st January and 31th December, (in 2003, 2004, 2005 and 2011) expressed for every 100,000 inhabitants. We compared between the incidence in 2003 and 2011.

Results:
1176 MS patients were identified of which 927 (78.8%) were Kuwaitis and 249 (21.2%) were expatriates. Among Kuwaiti patients, female to male ratio was 1.8:1 with a mean age of 35.40± 10.99 years. The prevalence rate of MS was 85.05 per 100,000 persons (95% CI: 82.80 – 87.04). There was a peak in prevalence among patients aged 30–39 years. The incidence of MS was 6.88 per 100,000 persons (95% CI 5.52–8.55). Between 2003 and 2011, the incidence increased 3.22 and 2.54 times in women and men respectively.

Conclusions:
Kuwait is considered a high-risk area for MS. The significant increase in prevalence and incidence rates may represent a true increase despite the improvement in case ascertainment and case definition.

Key Words: Multiple sclerosis; Prevalence and incidence; Kuwait
Funding Agency: None

Neurology
Category: Clinical

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Efficacy of fingolimod treatment in relapsing multiple sclerosis patients in clinical practice: A multicenter experience.

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Introduction:
Fingolimod is the first oral disease modifying therapy (DMT) approved for the treatment of Multiple Sclerosis (MS). Post-marketing studies are important to confirm what were established in clinical trials. We aimed to evaluate efficacy of fingolimod in a cohort of relapsing MS patients treated with fingolimod in a real clinical practice setting.

Methods:
We identified patients who had been prescribed fingolimod using the MS registry in 3 MS clinics in Kuwait. Patients with EDSS ≤ 6 and at least 6 months follow-up were included. Patients with progressive MS were excluded. Primary endpoint was the proportion of relapse free patients at 6 months. Secondary endpoints included mean change in EDSS and proportion of MRI activity (new T2 or Gadolinium-enhancing lesions).

Results:
Out of 101 eligible patients, 61 were women and 40 men. Mean age and mean disease duration were 33.97 ±9.70 years and 7.32 ±6.03 years respectively. 78.2% patients received prior DMTs. Mean duration of fingolimod exposure was 16.04 ±5.36 months. The proportion of relapse free patients increased significantly (10.9% versus 78.2%; P < 0.0001) at 6 months. Mean EDSS score at baseline was 1.82 ± 0.73, which decreased significantly to 2.08 ±1.25. At 6 months, 19.8% of patients were free from MRI activity compared to 86.1% at baseline (p <0.0001). No serious adverse events were reported.

Conclusions:
In clinical practice, fingolimod is effective in reducing disease activity and progression of disability over the observational period. The extent of efficacy and safety were more pronounced than what reported in the pivotal trials.

Key Words: Fingolimod; Multiple Sclerosis; Kuwait
Funding Agency: None

Neurology
Category: Basic Sciences

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A role for the Immune System Released Activating Agent in the growth and differentiation of mouse brain cells

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Introduction:
The Immune System-Released Activating Agent (ISRAA) was recently described as a nervous system induced factor inducing immune responses in the spleen. The aim of this study was to examine the effect of ISRAA on growth regulation of embryonic brain cells in form of proliferation and differentiation of neurons and astrocytes.

Methods:
A standard procedure for primary culture preparation was employed from E15 balb/c mice embryonic brains. Cells were grown and treated with 50pg and 5 µg of ISRAA or left without treatment. MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5- diphenyltetrazolium bromide) and TUNEL (Terminal dUTP nick-end labeling assay) assays were respectively used to examine the proliferative and apoptotic effects of ISRAA. The morphological differentiation was examined by immunocytofluorece and confocal microscopy.

Results:
Results showed significantly higher proliferation when cells were treated with 50pg ISRAA compared to untreated cells ($p<0.0001$) with no detectable apoptosis. On the contrary, treatment with 5 µg ISRAA depicted decreased proliferation with positive apoptosis. Furthermore, treatment with 50pg induced profound differentiation of astrocytes, but not neurons compared to unstimulated cells.

Conclusions:
Thus, ISRAA may play a role in the development of the brain cells via its proliferative effects and differentiation of astrocytes representing a cytokine activity for ISRAA since it was previously shown to act as an immune modulator and herein as a growth regulator.

Key Words: ISRAA; Proliferation; Differentiation
Funding Agency: This investigation received financial support from the Arabian Gulf University – Bahrain and from Kuwait Foundation for the Advancement of Sciences (KFAS) project code 2011-1302-02.

Nuclear Medicine and Radiology
Category: Basic Sciences

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Antitumor effects of asiaticoside on MCF-7 breast cancer cells and nude mouse xenografts

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Introduction:
Test the antitumour effects of asiaticoside treatment in vitro and in nude mouse xenografts.

Methods:
Nude mice (n=20) and MCF-7 cells were used in this study. Viability assays of MCF-7 cells were performed after 48-h treatments with different concentrations of asiaticoside. Flow cytometry was used to quantify caspase 3, tumour necrosis factor-alpha, and interleukin-1 levels. Nude mice were divided into five groups. Group I served as a control. Group II included tumour-bearing nude mice in which MCF-7 cells (2x107 cells /0.1 ml /site) were inoculated in the 3rd week. Group III nude mice were subjected to pre- and post- treatment with asiaticoside (200 µg/animal) at weeks 1-2 and 4-7; MCF-7 cells were injected in the 3rd week. Group IV nude mice were treated with a similar dose of asiaticoside beginning at week 6, and MCF-7 cells were injected in the 3rd week. Group V nude mice were treated with asiaticoside alone (drug control).

Results:
The IC50 of asiaticoside in MCF-7 cells was 40 microM. Asiaticoside was cytotoxic to MCF-7 cells, as caspase-3 activity was detected after 48 h and increased with increasing asiaticoside doses. The expression of the cytokine TNF-α and IL-1β significantly decreased in vitro and in vivo after asiaticoside administration. Nude mice from each group were healthy, and after the 7th week of the experiment, tumours in groups II, III and IV showed 5.8, 6.2, and 5.2% lower weight, respectively, compared to group I.

Conclusions:
Asiaticoside is effective in vitro and in vivo at inducing tumour cell apoptosis and anti-inflammatory effects.

Key Words: Asiaticoside; MCF-7 cells; Nude mice
Funding Agency: Research Grant MN01/09 , Kuwait University Research Sector and support through Grant SRUL02/13 funding the Research Core Facility Project.

Nuclear Medicine and Radiology
Category: Clinical

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Changes in diameter and valve closure time of leg veins across the menstrual cycle

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Introduction:
Objectives. To determine the changes (if any) in vein diameter (D) and valve closure time (VCT) of the lower limb veins in healthy young nulliparous females at different phases of the menstrual cycle.

Methods:
Fifty-three young nulliparous females were asked to undergo clinical evaluation and duplex ultrasound examination of both lower limb veins to monitor changes in vein D and VCT at different phases of their menstrual cycle. The vein D by B-mode imaging and VCT by pulsed Doppler trace were calculated at days 1-4, 14-16, 25-28 of the subject's menstrual cycle. Freidman and related-samples Wilcoxon signed rank tests were used to determine time related changes in venous function.

Results:
The volunteers age was 20.60±1.90 years (Mean±SD) and their body mass index was 23.90±4.90 (Mean±SD, kg/m^2). There was a gradual increase in the vein D and VCT at specified phases of menstrual cycle. Friedman and related-samples Wilcoxon signed rank tests for venous segment D and VCT changes between the different phases of the menstrual cycle were performed and showed statistical significance for each venous segment within each limb (p= 0.003-0.025). Also when adjusted for BMI, statistical significance exists for the same venous segment in the same limbs (p=0.001-0.049). There was no statistical significance for the same venous segment at the same phase of menstrual cycle between limbs (related-samples Wilcoxon signed rank test, p=0.079-0.97).

Conclusions:
During the menstrual cycle, the lower limb veins show increase in vein D and in VCT. These changes are probably mediated by the female sex hormones.

Key Words: Female sex hormones; Leg veins; duplex ultrasound
Funding Agency: None

Obstetrics and Gynecology
Category: Clinical

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Comparison of hysterosalpingography and hysteroscopy in evaluating the uterine cavity in infertile women

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Introduction:
To investigate the diagnostic value of hysterosalpingography (HSG) for intracavitary and structural uterine pathologies in comparison with hysteroscopy (HS) in women with infertility.

Methods:
This was an observational study of 280 women undergoing infertility investigation. The main outcome measures were sensitivity, specificity, positive and negative predictive values of HSG relative to hysteroscopy in diagnosing the following uterine pathologies: intrauterine synechiae, intrauterine fibroids/polyps, a mullerian anomalies.

Results:
HSG had a sensitivity of 75% in detecting intrauterine synechiae, specificity of 86.5%, positive predictive value of 63% and negative predictive value of 91.8%. For fibroids or polyps, the corresponding values were 82.3%, 40.9%, 56.4% and 71.4%. Lastly, for mullerian anomalies, of the corresponding values were 86.6%, 76.3%, 48.1% and 95.7%.

Conclusions:
HSG remains a useful screening test in evaluating the uterine cavity of infertile women if office sonohysterography or hysteroscopy is not available, particularly in the absence of tubal pathology.

Key Words: Hysterosalpingography (HSG); Hysteroscopy (HS); Infertility
Funding Agency: none

Obstetrics and Gynecology
Category: Basic Sciences

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Effects of glucocorticoid on the cytokine network during pregnancy in the rat: Consequences for pregnancy outcome

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Introduction:
Imbalances in the intrauterine cytokine milieu around the time of implantation and invasion may play a causative role in disorders associated with early pregnancy failure, and are also associated with the abnormal trophoblast development.

Objective of study: To evaluate the effect of glucocorticoid on the placenta level of cytokines of the Interleukin system and correlate this with the pregnancy and placenta outcome.

Methods:
Dexamethasone acetate was administered via drinking water with 1 g/ml to induce intrauterine growth restriction in the female SD rats. Sham control rats were injected twice daily with 0.1 ml of 4% ethanol in saline. Whole placenta frozen in liguid nitrogen and stored at -80^{o} C were thawed and homogenized and the supernatant used for ELISA to evaluate content of Rat placental TNFα, IL-1α, IL-1β, IL-2, IL-4, IL-6 and IL-10.

Results:
Dexamethasone is associated with significant reduction of mean maternal, fetal, placental, basal zone placenta and labyrinthine placental weight compared to control rats. There is a significant increase in TNF, in the experimental group a 16 and 19 day gestation (P<0-05) but decrease at 21 dg compared with control. IL-1a levels were higher in the experimental group compared to control (P<0.05) and at 19 dg with IL-1b (P<0.05) but decreased at 21 dg (P<0.05). With IL-2, the levels increased at 19 dg (p<0.01). IL-4 levels decreased at 19 dg and 21 dg. IL-4 are lower at 16, 19 and 21 dg in the experimental group (P<0.05) and significant decrease in IL-6 and IL-10 throughout gestation (P<0.01). Th1/Th2 ratios w in the experimental group compared to control (P<0.01)

Conclusions:
Dexamethasone-induced intrauterine growth restriction (IUGR) is associated with altered expression T helper Cytokine with predominance of T helper 1 proinflammatory cytokines.

Key Words: Intrauterine growth restriction,; Glucocorticoids; T helper cytokines.
Funding Agency: Kuwait University Research Sector Project #MY02/08

Obstetrics and Gynecology
Category: Clinical

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Symptom relief after oral pentosan sulfate or intra-vesicle chondroitin sulfate treatment in patients with interstitial cystitis

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Introduction:
Chronic Pelvic Pain (CPP) and recurrent cystitis are common conditions that present to the gynecologist's office. It is becoming recognized that CPP in women associated with lower urinary tract symptoms (LUTS), may be related to Interstitial Cystitis (IC). Common treatments are oral tablets of pentosan sulfate (Elmiron) and intra-vesicle bladder instillation of chondroitin sulfate (Uracyst). Both treatments reported to be effective over placebo but both are very different in their method of administration. Objective: To compare treatment response in terms of symptoms and to measure improvement in quality of life.

Methods:
Retrospective cohort study. 248 patients who had bladder hydrodistention (HD) for LUTS were reviewed;168 patients were excluded. Two groups were compared; 51used Elmiron and 29 received Uracyst. Pelvic Pain Urgency and Frequency (PUF) scores were collected prospectively prior to and at 6 weeks following HD; then at 3 and 6 months after initiating the treatment course. Symptom, bother and total score calculated. Symptom score included day and night time frequency, dyspareunia, severity and type of pelvic pain, severity and type of urinary urgency. Bother score included the degree of bothersome symptoms with nighttime frequency, dyspareunia, pelvic pain and urinary urgency. Total score included the combination of symptom and bother scores

Results:
Of 80 patients, 51 patients had Elmiron treatment and 29 patients received Uracyst for 6 months. All study patients had history of LUTS and completed the PUF score before undergoing HD for diagnostic and therapeutic value, 6 weeks after the HD, 3 and 6 months after initiating specific IC treatment. The PUF results were analyzed as symptom, bother and total scores in each treatment group. Both Elmiron and Uracyst treatments significantly improved the symptom, bother and total PUF score compared to baseline scores before and 6 month after treatment. We found that the symptom, bother and total scores were significantly improved after 3 months with the use of Elmiron treatment in comparison to Uracyst treatment. No differences were found after 6 months of treatment between the two-treatment groups.

Conclusions:
The treatment of interstitial cystitis with either oral pentosan sufalte or intra-vesicle chondroitin sulfate improves the symptom score, bother score and total PUF score
Oral pentosan sulfalte treatment had an earlier effects at 3 months compared to intra-vesicle chondroitin sulfate, there were no differences between the two treatment groups after 6 months.

Key Words: Interstitial Cystitis (IC); Chronic pelvic pain (CPP); Irritative lower urinary tract symptoms (LUTS)
Funding Agency: None

Obstetrics and Gynecology
Category: Clinical

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Role of the neurometer as adjunct to screening for sacral neuromodulation therapy

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Introduction:
Sacral Neuromodulatiom (SNM) is offered to patients to correct their voiding dysfunction. Part of the SNM therapy is a screening test Percutaneous nerve evaluation (PNE) to predict the patient response to the therapy. PNE is minimally invasive screening test with the predictive value of 30%. Neurometer is a simple non invasive instrument to assess objectively the Pain Tolerance Threshold (PTT) of the Patients selective dermatome. Objective: To assess the role of neurometer in improving the selection of patients with voiding dysfunction for the Sacral Neuromodulation.

Methods:
The current is a pilot study designed to test the feasibility of neurometer as an adjunctive to the screening test. Twenty seven patients candidates for PNE had the test with the neurometer (PTT) for the sacral 3-5 dermatome bilaterally done . Both PNE and PTT tests are done by different investigators who were blinded for the result of the other test. The results of PNE & PTT readings were collected for all patients. The arbitrary result of PTT 90 was used as the cut off point for assessment of the response of the neurometer test.• Study data were analyzed using SPSS database. Chi-square and Fisher exact test analysis were used to detect statistical differences. All tests were considered significant at $P < 0.05$.

Results:
Total of 27 patients were included in the pilot study, median age of 45y, 24 female, 3 males. The indications for PNE were in 22 patients with refractory overactive bladder (OAB), 2 patients with urinary retention and 3 patients with frequency urgency syndrome. A total of 17 patients showed a +ve PNE.
The PTT reading did not show correlation with the type of underlying diagnosis of the voiding dysfunction, patient age nor gender. Fifteen patients who showed PTT < 90 had a positive response to the PNE screening test. PTT reading correlated with the outcome of the PNE for the patients. P=0.037

Conclusions:
The neurometer is a simple and predictable test to help improving the selection of patients for SNM.
Key Words: Sacral nerve modulation (SNM); Percutaneous nerve evaluation (PNE); Pain tolerance threashold (PTT)
Funding Agency: None

Obstetrics and Gynecology
Category: Clinical

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Evaluation of venous thromboembolism risk and adequacy of prophylaxis in high risk pregnancy in Arabian gulf states (EVE-RISK study)

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Introduction:
Venous thromboembolism (VTE) is one of the leading causes of maternal mortality and morbidity during pregnancy and post-partum period. There is no published data on VTE prophylaxis in high-risk pregnancies in Arabian Gulf States. The objective of this study is to estimate the prevalence of pregnant women at risk of VTE, as well as, the proportion of those at risk of VTE who received the recommended VTE prophylaxis according to the American College of Chest Physicians (ACCP) 2008 published guidelines in every day clinical practice in the antenatal clinics in Arabian Gulf States.

Methods:
EVE-Risk study is a non-interventional, cross-sectional, multi-national (United Arab Emirates, Kuwait, Bahrain, Qatar, and Oman) survey of all eligible pregnant women (≥18 years) screened during antenatal clinics at 7 centers in Arabian Gulf States. Patients were recruited during a 3-month period between September 2012 and December 2012. Analysis was performed using descriptive statistics.

Results:
Of 4,131 screened pregnant women, the proportion of pregnancies at higher risk of VTE was 32.4% (n=1,337). Common VTE risk factors were: obesity (75.8%), multiparity (33%), recurrent miscarriages (9%), varicose veins (7%), thrombophilia (2.5%), immobilization (2%), previous VTE (1.6%) and sickle cell disease (2.8%). Only 8.3% (n=111) high-risk patients received the recommended VTE prophylaxis. Enoxaparin was used in 80% (n=89) of cases followed by tinzaparin (4%; n=4). Antiplatelets were prescribed in 11% (n=149) of pregnant women, 59% of those were on VTE prophylaxis. Side effects (mainly local bruising at injection site) were reported in 12% (n=13) cases.

Conclusions:
A large proportion of pregnant women in the Arabian Gulf are at risk of VTE. However, only a small proportion of them received the recommended VTE prophylaxis.

Key Words: Thromboembolism; Pregnancy; Arabian Gulf
Funding Agency: This study is an invistigator sponsored trial that was financially sponsored by Sanofi Gulf Countries without any interference at all study times

Obstetrics and Gynecology
Category: Clinical

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Induction of labor in grand multiparous women with previous cesarean delivery: How safe is this?

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Introduction:
To compare the outcome of induced and spontaneous labor in grand multiparous women with one previous lower segment cesarean section, so that the safety of labor induction could be assessed.

Methods:
In 102 women (study group) labor was induced and the outcome was compared with 280 women (control group) who went into spontaneous labor. All 382 women were grand multiparous and had one previous cesarean section.

Results:
There were no significant differences in oxytocin augmentation, cesarean sections scar dehiscence, fetal birth weight, or Apgar score between groups. There was 1 neonatal death, 2 still births, 1 early neonatal death, and 1 congenital malformation in the study group and this was not significant. There was no significant difference in vaginal birth in the study (80.9%), and the control group (65.8%).

Conclusions:
As there were no significant differences in outcome measures between the 2 groups, induction of labor may be a safe option in grand multiparous women with one previous cesarean section, unless contraindicated.

Key Words: Grand multipara; Previous cesarean section; Prostaglandin
Funding Agency: None

Obstetrics and Gynecology
Category: Clinical

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Is membrane sweeping beneficial at the initiation of labor induction?

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Introduction:
To determine the effect of cervical membrane sweeping at the initiation of labor induction in comparison to no sweeping.

Methods:
Randomized trial outcomes of labor after induction in pregnant women at term were compared. Women were assigned to "sweep" or "no sweep" groups at the initiation of labor induction. Outcome measures induced duration of labor, maximum dose of oxytocin used, induction-labor interval and mode of delivery.

Results:
We recruited 300 nullipara (group A) [150 "sweep", 150 "no sweep"] and 300 multiparas (group B), (150 "sweep" and 150 "no sweep"]. Among group A those who received intravaginal prostaglandin (PG) E2 and oxytocin, simultaneous sweeping had significantly shorter mean induction-labor interval (12.9±1.1 versus 16.1±1.1 hours, P = 0.046), lower mean dose of oxytocin (6.2±0.6 versus 10.21±1.2mU/minute, P=0.01), and increased normal delivery rates (vaginal delivery 81.3% versus 56.2%, P=0.01). Sweeping also had a favorable effect on nulliparas who received oxytocin alone (mean induction-labor interval 5.9±2.9 versus 10.9¯2.6 hours P=0.04, mean maximum dose 9.8±1.1 versus 15.2±1.1 mU/min P=0.01). These results were restricted to women with unfavorable cervix in group A. There were no differences in any outcome measures in multiparous women.

Conclusions:
Membrane sweeping at the initiation of labor induction, had a beneficial effect on labor and delivery, which was limited to nulliparas with unfavorable cervix requiring priming with PGE2
Key words: Membrane sweeping, Multipara, Nullipara, Outcome measures

Key Words: Membrane sweeping; Multipara, Nullipara; Outcome measures
Funding Agency: None

Obstetrics and Gynecology
Category: Clinical

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The significance of the second caesarean section in the reduction of institutional caesarean section rate

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Introduction:
The caesarean section rate has increased worldwide and in Kuwait, with rates of 30-40% been reported. This increasing rate has contributed to rising incidence of maternal morbidity in many Institutions. The aim of our study was to assess the events associated with the second caesarean section in our institution.

Methods:
All the patients undergoing caesarean section[c/s] at Maternity Hospital, Kuwait, from Jan 1st to December 31st, 2013 were identified. The patients having their first [groupA] and second [group B] c/s were identified and a comparative study of both groups undertaken. The social and clinical bio-data of these patients were extracted from our records and the antenatal, intrapartum and postpartum course of pregnancies were established and the outcome documented.

Results:
During the study period, 10,586 deliveries were recorded at Maternity Hospital, including 3,676 caesarean sections, a c/s rate of 34.7%. 840 of the caesarean patients were having their first procedure [groupA] and 607, their second [group B]; 484 patients from group A and 341[group B] with complete records were further analyzed and constitute the basis of this study.The mean age and parity in group B was significantly higher, 30.89±4.932 vs 29.94±5.558 [P=0.008] and 1.49±1.224 vs 0.98±1.598 [P<0.0001]. The mean gestational age at delivery, 38.12±2.614 vs 37.66±3.106] and fetal birth weight, 3211.60±691.507 vs 2829.73±863.259 were also significantly higher for group B, P=0.02 and P<0.0001 respectively. The most frequent indications for c/s were failure to progress, 27.1% vs 19.1%, non-reassuring fetal status [fetal distress], 23.6% vs 9.5% and breech presentation, 13.8% vs 5.5% were more significantly recorded in group A. 53.2% of the group B patients demanded for repeat c/s. The maternal morbidity, 0.12%, was low.

Conclusions:
The incidence of repeat caesarean section in group B was quite high and its reduction will contribute to the reduction of c/s rate.

Key Words: Second; Caesarean Section; Reduction Institution Rate
Funding Agency: None

Obstetrics and Gynecology
Category: Basic Sciences

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Maternal-fetal transport kinetics of manganese in perfused human placental lobule in late gestation: An in vitro study

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Introduction:
This study was undertaken to explore for the first time, maternal-fetal transport kinetics of an essential trace element, manganese in human placenta in vitro

Methods:
Human placentae from normal uncomplicated pregnancies were collected post-partum. Manganese in nitric acid (Sigma Chem Co,USA) at 100 times the physiological concentration of 0.5-1mg/L,along with antipyrine (Sigma Chem Co, USA) as internal reference marker were then injected as a single bolus (100ul) into the maternal arterial circulation of perfused placental lobules and perfusate samples collected from maternal and fetal circulations over a period of 5 minutes. National Culture and Tissue Collection medium, diluted with Earle's buffered salt solution was used as the perfusate. Concentration of manganese in perfusate samples was assessed by atomic absorption spectrophotometry (Varian, FRG)while that of antipyrine was assessed by spectrophotometry (Shimadzu Co, Japan). Transport kinetics of substances studied were computed using established permeation parameters.

Results:
Differential transport rates of manganese and antipyrine in 8 perfusions differed significantly ($p<0.05$) for all efflux fractions investigated. Transport Fraction(TF) of manganese averaged 54% of bolus dose in 8 perfusions, representing 89.0% of reference marker TF. The difference observed in TF values of manganese and antipyrine was statistically significant ($p<0.05$) Pharmacokinetic parameters such as area under the curve, absorption rate, elimination rate of manganese compared to reference marker were significantly different ($p<0.05$) between the two groups. Absorption rate: elimination rate indices of manganese differed significantly compared to antipyrine index as well ($p<0.05$)

Conclusions:
Our studies elaborate for the first time in literature, maternal-fetal transport kinetics of manganese in human placentae in vitro and the possibility of active transport of manganese in human placenta cannot be excluded.

Key Words: Manganese; Maternal-Fetal Exchange; Human Placenta
Funding Agency: KFAS Research Grant# 2010130203

Obstetrics and Gynecology
Category: Clinical

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Antimullerian hormone is a marker of spermatogenesis but not sperm quality

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Introduction:
Anti-Müllerian hormone (AMH) is a glycoprotein secreted in the male by the Sertoli cells and responsible in male embryos for Müllerian duct regression. In the adult it is a proven biomarker of ovarian reserve. Its role in male infertility is still controversial.
Objective of study: To evaluate the association between Anti-Mullerian Hormone (AMH) and Sperm parameters, hormone profile and histopathological abnormalities of the testis.

Methods:
Eighty-six men with infertility of at least one year, form the subject of this study. Clinical evaluation and semen analysis were done according to WHO guidelines (2010). Seminal AMH was estimated by Enzyme-linked sorbent-assay (ELISA), while Hormone profile-FSH, LH,prolactin and testosterone were estimated with Radio-immuno-assay. Only those with Azoospermia had Fine needle testicular aspiration.

Results:
The mean serum AMH was 3.66±2.45 and was lowest in patients with Azoospermia 0.045mg/L compared to 2.90 with Oligozoospermia ($P<0.01$) and Normozoospermia 3.86 ($p<0.001$), showing increasing trend with sperm concentration. Evaluation of the effect of smoking revealed; non smoking azooospermic men was 0.052±0.040 mg/L versus 0.039±0.009 in smokers ($p<0.05$), among oligospermic men, non-smoking 3.62±2.42 versus 0.65±0.44 for smokers ($p<0.001$) and in men with normozoospermia ; non-smokers 5.25±3.84 versus 3.11±2.64 in smokers ($p<0.01$). AMH was lower with diabetes mellitus 0.063±0.025 versus 0.028±0.006 for non-diabetic azoospermic men ($p<0.05$). The trend was the same in diabetic men with oligozoospermia and normozoospermia. There was positive correlation between AMH and Testosterone ($r=.48$, $p<0.05$).

Conclusions:
AMH was significantly associated with sperm concentration and Testosterone and not with sperm motility, teratozoospermia and leukocytospermia. AMH may serve as a reverse for spermatogenesis but not for other sperm parameters.

Key Words: Antimullerian Hormone; Spermatogenesis; Smoking, Diabetes Mellitus
Funding Agency: Kuwait University Research Sector Project #MY02/08

Obstetrics and Gynecology
Category: Basic Sciences

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The role of oxidative stress in intrauterine growth restriction induced by glucocorticoids

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Introduction:
Although the placenta is very vulnerable to oxidative stress, the role of Oxidative Stress in the mechanisms in the inhibitory effects of dexamethasone on placental growth to induce intrauterine growth restriction (IUGR) are not fully understood.
The aim of study is to evaluate the relationship between Oxidative Stress and Glucocorticoids in the induction of IUGR

Methods:
Sprague-Dawley (SD) rats used were maintained on a cycle of 12 h light and 12 h darkness at 22ºC. Female rats were mated with male rats and when sperms were detected in the vaginal smears this was designated as day 0 of pregnancy. IUGR induction in the SD rats was with Dexamethasone. Oxidants–Tumour Necrosis Factor alpha (TNF-α), malondialdehyde (MDA), antioxidant superoxide dismutase (SOD), Catalase (CAT), glutathione peroxidase (GPX) and total antioxidant capacity (TAC) were determined by commercial kits and cytokines by ELISA. Cell apoptosis of the placenta was assessed by TUNEL staining.

Results:
There was increased in oxidant MDA and TNF-α in the experimental rats compared to controls ($p<0.05$), and decreased TAC, SOD, CAT and GPX in serum and placenta. There was predominance of Th1 proinflammatory cytokines. Analysis of markers of placental cell apoptosis showed increased in Bax and Caspase 3 and decrease in Bcl-2 expression in the placenta in dexamethasone –induced intrauterine growth restriction compared to control rats.

Conclusions:
Glucocorticoids induced oxidative stress causes oxidative damage and accelerated apoptosis which results in IUGR and neonatal morbidity and mortality and later adult problems.

Key Words: Glucocorticoids,; Oxidative stress, Apoptosis, .; Intrauterine growth restriction
Funding Agency: Kuwait University Research Sector Project #MY02/08

Oncology
Category: Basic Sciences

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BRCA1 gene status in breast cancer patients from Kuwait: the involvement of D693N and E1038G variants

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Introduction:
The status of BRCA1 gene to breast cancer in Arab women has not yet been explored. The aim of this study was to analyze the spectrum of BRCA1 mutations in breast cancer patients from Kuwait and to identify possible Kuwaiti founder mutations.

Methods:
We analyzed the entire coding regions of the BRCA1 gene for 106 unselected Kuwaiti breast cancer patients and 114 healthy controls. A family history was obtained from each patient and blood sample was processed for DNA analysis. We used denaturing high-performance liquid chromatography (DHLPC) to screen all exons for possible variants. DHPLC variants were confirmed by direct sequencing.

Results:
The frequency of D693N, P871L, E1038G, M1083V and S1040N mutations in healthy controls was 7%, 32.45%, 34.2%, 0% and 0.87%, respectively. The prevalence of these five mutations in breast cancer patients was 18.9%, 24.5%, 41.5%, 0.94% and 2.83% . The mean age of onset in patients with E1038G, D693N and combined mutation D693N and E1038G was 53.4, 47.0 and 46.2 respectively ($p<0.05$). The frequency of the 2201 C>T polymorphism was 55.6% CC, 38.3% CT and 6.1% TT in controls and 46.3 CC, 43.5% CT and 10.2% TT in cases. The frequency of the 2430 T>C polymorphism was 53.6% TT, 39.3% TC and 7.1% CC in controls and 46.1% TT, 41.2% TC and 12.7% CC in cases.

Conclusions:
Our data shows for the first time the spectrum of BRCA1 mutations in breast cancer patients from an Arab population. We show here that the spectrum of BRCA1 mutations in Kuwait is different from all studied populations. We observed that Kuwaiti women with combined D693N and E1038G variants have increased risk for developing breast cancer ($p<0.05$).

Key Words: BRCA1; Breast Cancer; Kuwait
Funding Agency: Kuwait University Grant # MB04/07

Oncology
Category: Undergraduate

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Anti-proliferative activity of 5-triazolylmethyl- and 5-acetamido-oxazolidinone derivatives

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Introduction:
In the face of increasing resistance to existing antibiotics, oxazolidinones, exemplified by linezolid, have been developed as promising agents. In this study we investigated several 5-triazolylmethyl- and 5-acetamido-morpholino and N-substituted-piperazino oxazolidinone derivatives for any antiproliferative activity against breast cancer and normal cells.

Methods:
MTT assay, validated by cell counting, was used to assess the effect of 12 derivatives (concentrations from 100nM to 10microM) on the proliferation of MCF7 breast cancer cells. The three most active compounds were then tested on MDA231 breast cancer cells and HBL100 normal breast cells. Cytotoxicity of those selected was determined by assessing the extent of apoptosis by flowcytometry. The anti-metastatic potential of these compounds was assessed on MDA231 by the wound healing and agarose invasion assay.

Results:
The 5-triazolylmethyl piperazino-oxazolidinone derivatives containing 4-N-(2-chlorocinnamoyl), 4-N-(4-nitrobenzoyl) and 4-N-methylsulfonyl moieties showed the most potent cytostatic activity against the cancer and normal cells, inhibiting proliferation by up to 70%, in the same order of their reported antibacterial activity against S. aureus, but at much higher concentrations. Unexpectedly, there was a significant stimulation of proliferation at 100nM, well below their antibacterial MIC. The compounds also retarded motility and invasion of MDA231 cells.

Conclusions:
Nine of the derivatives tested showed no effect on any of the eukaryotic cell lines, which also shows their preferential activity against bacteria. Three compounds however exhibited potent cytostatic activity against both normal and cancer cells. Their bi-phasic response suggests multiple targets on eukaryotic cells. Used solely to treat bacterial infection they may encounter unwanted side effects. However at >10 microM these may be further studied as anti-cancer agents because of their anti-metastatic properties.

Key Words: Oxazolidinones; Anticancer; Breast cancer
Funding Agency: None

Pathology
Category: Graduate (Resident)

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Study of patatin-like phospholipase-3/adiponutrin I148M polymorphism and biochemical markers in nonalcoholic fatty liver disease

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Introduction:
Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease. Some of gene polymorphisms have been reported to be associated with NAFLD. We hypothesize that the single-nucleotide polymorphism rs738409 C>G at position 148 in the patatin-like phospholipase-3 gene (PNPLA3) will increase the susceptibility of NAFLD. This study aims to examine the association of PNPLA3 polymorphism with the prevalence and severity of NAFLD among Kuwaiti lipid clinic patients and to study the association of NAFLD with markers of liver damage including alanine aminotransferase, alkaline phosphatase, gamma glutamyl transferase, total bilirubin, and tissue inhibitor of metalloproteinases-1.

Methods:
78 Kuwaiti lipid clinic patients were enrolled. Their anthropometric parameters, chemistry profile, TIMP-1, PNPLA3 gene and abdominal ultrasound were analyzed. Statistical analyses were performed with SPSS 20.0. Mean values were compared by analysis of variance. Binary logistic regression analysis was used to ascertain the association of variables with the NAFLD and metabolic syndrome. A P-value < 0.05 was considered as statistically significant.

Results:
The I148M variant of PNPLA3 gene and markers of liver damage were not associated with NAFLD. Moderate-to-severe hepatic steatosis was significantly associated with low high-density lipoprotein-cholesterol (P= 0.007), high alanine aminotransferase (P= 0.034) and G allele (P= 0.009). Patients carrying the CG and GG genotypes had significantly higher levels of total bilirubin (P= 0.011) and more severe degrees of hepatic steatosis (P= 0.042) compared to those carrying the CC genotype.

Conclusions:
The I148M variant of PNPLA3 gene and biochemical markers of liver damage are not associated with NAFLD in Kuwaiti lipid clinic patients. The mutant G allele is a risk factor for severe grades of hepatic steatosis in patients with NAFLD.

Key Words: NAFLD; PNPLA3; Kuwait
Funding Agency: None

Pediatrics
Category: Clinical

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Postmortem diagnosis in sudden cardiac deaths in Kuwait in the year 2013

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Introduction:
Sudden cardiac death is commonly defined as an unexpected natural death due to cardiac cause within a short time period (usually within one hour) with or without onset of symptoms and without any prior conditions that would appear fatal. The objective of the present study is to determine the prevalence and patterns of sudden cardiac death in Kuwait during the year 2013.

Methods:
A retrospective Cohort study was done of 197 sudden cardiac death cases. The study was carried out at the General Department of Criminal Evidence (GDCE), Forensic Medicine Department, Kuwait. Evaluation of related cardiac death cases were retrieved from GDCE after performing a detailed autopsy including external and internal postmortem examination, toxicological, pathological investigations. Most of the cases revealed no previous medical history.

Results:
The study revealed that the majority of the received sudden cardiac death cases died of coronary heart disease (60%), (15%) of the cases were hypertrophic cardiomyopathy cases, the rest of the cases included ; congenital heart disease (4%) myocarditis (5%), mitral valvopathy (6%), vascular and small vessel disease related to hypertension, DM and immunological etiology (7%) and right ventricular dysplasia (3%).

Conclusions:
The present study conducted in Kuwait for the first time, revealed that the majority of the received sudden cardiac death cases died from coronary heart disease (60%), with atherosclerotic coronary changes and narrowing. Thorough and fulfilled postmortem examination is mandatory to ascertain the cause of sudden cardiac death.

Key Words: Sudden cardiac death; Cardiomyopathy; Congenital heart disease
Funding Agency: None

Pathology
Category: Graduate PhD (Basic Science)

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Associations of common TERC single nucleotide polymorphisms with telomere length, human telomerase reverse transcriptase and obesity related factors

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Introduction:
Studies have mapped putative loci that may probably be involved in regulating leukocyte telomere length [LTL]. The strongest associations with LTL were reported for SNP rs12696304 and rs16847897 near TERC on 3q26. It is unclear though whether this locus identified in Europeans exerts a similar effect on LTL in other populations. The present study was performed to: study the influence of TERC polymorphisms on LTL, [hTERT], indices of obesity and explore the potential associations with type 2 diabetes mellitus [T2DM].

Methods:
In a study on 225 T2DM patients and 245 age and sex matched controls, we used Allelic Discrimination (AD) genotyping to determine TERC SNPs (rs12696304 and rs16847897). hTERT, adiponectin, Insulin, Homeostasis Model Assessment[HOMA], and LTL were measured. Body Mass Index (BMI),waist circumference (WC) were recorded.

Results:
[C/C] genotype of rs16847897 was significantly associated with telomere shortening [OR=1.6,p=0.004] and lower levels of hTERT[OR=0.4,p=0.006]. Nevertheless, [C/C] was significantly associated with higher BMI[OR=2.2, p=0.006], WC[OR=23.4,p=0.007]. However,[C/C] genotype of SNP rs16847897 was associated with hypo-adiponectemia [OR=0.6, p=0.006]. [G/G] of SNP rs12696304 was significantly associated with shorter telomeres[OR=1.5, p=0.004],lower hTERT[OR=0.7,p=0.006],hypo-adiponectemia[OR=0.5, p=0.008]. However,[G/G] genotype of SNP rs12696304 was associated with higher anthropometric measures such as BMI [OR=1.2,p=0.006],WC[OR=5.3,p=0.004]. Using binary logistic regression; [C/C] genotype of SNP rs16847897 and [G/G] genotype of SNP rs12696304 were significantly associated with higher risk T2DM[OR=1.7,p=0.004].

Conclusions:
We provide insights into genetic determination of a structure that is critically involved in genomic stability. Given the central role of telomere length in determining telomere function; our findings could have broad relevance for both normal and pathological age associated processes.

Key Words: SNPs; Telomeres; Telomerase
Funding Agency: Research Sector and College of Graduate Studies Project Number YM06/11

Pathology
Category: Basic Sciences

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HCV genotypes, IL28B and PNPLA3 polymorphisms in hepatitis C patients from Kuwait

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Introduction:
Kuwait is part of a geographical area of high hepatitis C virus (HCV) incidence. Our objectives were to establish a rapid and sensitive diagnostic method for HCV genotyping and mixed genotype identification, and to determine whether degree of HCV fibrosis is dependent on HCV genotype(s), host immunity, or liver metabolic deficiency.

Methods:
Frozen blood from 53 HCV infected patients were processed for HCV RNA and genomic DNA extraction, followed by genotyping assays. HCV genotyping was performed by nested-PCR for specific identification of HCV genotypes/subtypes. Restriction fragment length polymorphism (RFLP) was used to determine interleukin 28B (IL28B) rs8099917, rs12979860, and patatin-like phospholipase domain-containing 3 (PNPLA3) rs738409 genotypes. HCV infected histological liver sections were analyzed for fibrosis grade.

Results:
In our cohort the most prevalent HCV genotype as a single infection was genotype 1 (46.6%), as well as in mixed genotype infections (83.3%). Genotypes of SNPs relevant to IL28B did not associate with any assayed parameters, while PNPLA3 rs738409 G allele associated with severe fibrosis stages ($p = 0.025$).

Conclusions:
The most symptomatically prevalent HCV genotype in Kuwait is genotype 1. Incidence of mixed genotypes is relatively high in Kuwait. Degree of fibrosis is dependent on liver metabolic efficiency.

Key Words: Hepatitis C virus; HCV genotyping; Patatin-like phospholipase domain containing 3
Funding Agency: None

Pathology
Category: Clinical

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Aspergillus fungal arteritis causing vascular anastomotic rupture and loss of commercially transplanted kidney

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Introduction:
Invasive filamentous fungal infections resulting from exposure to contaminated sources, infected donors or breaches in aseptic techniques during organ procurement, transport or implantation have been identified as a major complication of commercial or transplant tourism. Such infections frequently originate at the graft site and are associated with high rates of graft loss.

Methods:
Herein we report a case of a 45 year old female who underwent a live unrelated renal transplant in Pakistan.

Results:
The patient developed Aspergillus fungal arteritis leading to arterial anastomotic rupture resulting in the loss of commercially transplanted renal allograft.

Conclusions:
Fungal arteritis is a rare entity that affects graft arteries which can lead to fatal aneurysmal dilatation and rupture

Key Words: Allograft; Aspergillus; Vasculitis
Funding Agency: None

Pathology
Category: Clinical

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Mubarak AL Kabeer Hospital - experience with the New Bethesda System for reporting thyroid aspirates : cytohistologic correlation

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Introduction:
FNAC is increasingly being used to manage patients with enlarged thyroid in order to to determine which patients will benefit from surgical intervention. In 2007, the Bethesda system (TBS) for reporting thyroid cytopathology was proposed. The aim of our study was to assess TBS reporting in our hospital and to evaluate its specificity based on cyto histologic correlation.

Methods:
A total of 7809 thyroid aspirates were examined at MAKH from 2004 to 2012. A histological diagnosis was available in 322 cases. The archival aspirates with cytohistological correlation were classified into unsatisfactory, benign, follicular lesions of undetermined significance(FLUS), follicular lesions rich in Hurthle cells(FLUS HCR), follicular neoplasm (FN), suspicious for malignancy and positive for malignancy.

Results:
Of the 322 cases with cytohistological correlation 7(2.1%) were unsatisfactory, 94 (29.2%) benign, 47(14.6%) FLUS, 11 (3.4%) FLUS HCR, 15(4.7%), FN/SFN, 81(25.2%) suspicious for malignancy and 67 (20.8 %) malignant of which 64 (95.5 %) were papillary carcinoma. The sensitivity, specificity, negative predictive value and positive predictive value was 71.5, 78.7, 54, and 88.8% respectively.

Conclusions:
Our experience demonstrates that the new TBS reporting proposed is excellent for reporting thyroid aspirates. Each diagnostic category conveys specific risks of malignancy which offers guidance for patient management.

Key Words: Thyroid Bethesda System; Fine needle aspirates
Funding Agency: Ministry Staff

Pathology
Category: Clinical

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The value of touch imprint cytology of prostate core needle biopsy specimens – Mubarak Al Kabeer experience.

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Introduction:
The aim of this study was to determine the diagnostic value and accuracy of touch imprint cytology (TIC) of prostate core needle biopsy (CNB) specimens in predicting the final benign or malignant histology in patients with suspected prostate carcinoma.

Methods:
TIC was prepared from 354 CNB performed under transrectal ultrasound guidance on 59 patients with suspected prostate cancer as shown by high PSA or abnormal findings in the prostate on rectal examination. Two touch imprints were prepared from each CNB. TIC results were correlated with histology of the CNB.

Results:
Of the 336 (94.9%) satisfactory TIC from 354 CNB analysed the cytological diagnosis rendered was 40 (11.9%) malignant; 2 (0.6%) suspicious; 45 (13.4%) atypical and 249 (74.1%) benign. TIC accurately predicted the final histology in 336 biopsies with a sensitivity of 84% and a specificity of 90.8%. A strong agreement was seen between TIC and CNB ($p<0.001$).

Conclusions:
The routine use of TIC complements CNB reports and helps provide an immediate and reliable cytological diagnosis of prostate lesions.

Key Words: Touch imprint cytology,; Core needle biopsy,; Prostate carcinoma
Funding Agency: None

Pathology
Category: Clinical

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Gender differences in the interactions between adipokines and the insulin-like growth factor-I system in a metabolically high risk population.

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Introduction:
Despite potential mechanisms that link obesity and insulin resistance (IR) with the insulin-like growth factor (IGF)/IGF-binding protein (IGFBP) system, the interactions between adipose tissue derived adipokines and the IGF-I system remain unknown. This study evaluates if gender differences could account for the conflicting published reports.

Methods:
Fasting adiponectin, resistin, leptin, leptin receptor (sOB-R), insulin, glucose, total IGF-I, IGFBP-3 and lipid profile were determined in 590 (238M and 352F) first-degree relatives of Type 2 Diabetes patients. Sex hormone binding globulin (SHBG), oestradiol (E2), testosterone (T), were measured. Free androgen index (FAI), free leptin index (FLI), bioavailable IGF-1 (BIGF1), insulin sensitivity (%S) and IR (HOMA) were calculated.

Results:
There are significant differences in mean (SEM) BIGF1 between males (87.6 (9.1)) and females (67.7 (4.6)). There were also significant gender differences in adiponectin, leptin, sOB-R, FLI, %S and IR. There were no gender differences in resistin and IGFBP3. Significant gender differences were found in the correlations of BIGF1. The following showed significant correlations with BIGF1 in females but not in males: adiponectin, sOB-R, FLI, SHBG, glucose, insulin, %S, IR, waist circumference, BMI, Apo B, total cholesterol, triglycerides and LDL-cholesterol. Males and females showed similar correlations of all other variables with BIGF1. Correlations with sex hormones (E2, T, SHBG, FAI) were not significant in males and females. Multivariate linear regression analysis showed that age, BMI, WC, adiponectin, FLI were significant determinants of BIGF1 in females but not in males. Age was the only significant determinant of BIGF1 in males.

Conclusions:
There are significant gender differences in the metabolic interaction between adipokines and the IGF-1 system. Despite the putative links with obesity, sex steroids do not play a role in the gender differences.

Key Words: Adipokines; Insulin-Like Growth Factor-I System; Gender
Funding Agency: KFAS grant 2004-1302-03

Pediatrics
Category: Clinical

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Pattern of beverage intake and milk and dairy product sufficiency among high school students in Kuwait

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Introduction:
Objectives: This study was thus designed to explore the pattern of beverage intake among high school students in Kuwait and its effect on the milk and dairy product sufficiency and its relation to their body mass index (BMI).

Methods:
The present study was performed on 98 girls and 92 boys aged 16 to 18 years, enrolled from governmental high schools in Al-Ahmadi governorate, Kuwait. A reliable dietary questionnaire on nutritional knowledge, food choices, and eating behavior together with food frequency sheet regarding milk and dairy products intake were completed by the students. All included students had their weight, height measured, and BMI calculated.

Results:
The present study revealed significant insufficiency in daily milk intake among sweetened carbonated beverage drinkers especially in males with a noticeable increase in packed fruit juice drinkers as well as among the heavy tea and coffee drinkers especially in female students. Dairy intake was similarly affected but with less statistical significance. There was no significant difference in BMI among the studied students with respect to milk or dairy intake, drinking carbonated beverage, packed fruit juice or tea and coffee. More students with sufficient milk intake reported proper practice and more males who had insufficient milk and dairy intake reported improper practice with more obese and overweight students displaying improper practice too.

Conclusions:
The intake of sweetened carbonated beverages and less likely packed fruit juices are affecting the sufficiency of milk and dairy intake among high school students in Kuwait. Though BMI was not related to milk and dairy insufficiency, more overweight and obese students displayed improper practice which makes it prudent to highlight the importance of improving this practice aiming at promoting their health and achieving one suggested goal in prevention of the global obesity epidemic from prevailing in Kuwait.

Key Words: Beverages; Dairy; School students
Funding Agency: None

Pediatrics
Category: Clinical

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Non-transfusion dependent thalassemia among children in Kuwait

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Introduction:
Non-transfusion-dependent thalassemia (NTDT) is a distinct diagnostic entity because of its inherent peculiar complications. It is a group of diseases characterized by mild –to-moderate anemia that may require blood transfusion occasionally. The 3 main classes are Hb H disease, beta thalassemia intermedia (BTI) and HbE-beta thalassemia (EBT).

Methods:
This is a chart review of the NTDT cases being currently followed in the pediatric hematology clinics of Mubarak, Amiri and Adan Hospitals, Kuwait to document the demographic, hematological and clinical characteristics of the patients.

Results:
There are 29 patients of whom there were 15 BTI, 12 HbH and 2 EBT with a mean age of 10.9±5.5 years. Most (78.6%) were Kuwaitis. Each patient had been transfused on 0 to 7 occasions. One BTI patient was the only one who had been splenectomized. The mean Hb in the BTI and HbH patients were 9.8 ± 1.1 g/dl and 9.5±1.2 respectively. One of the 2 EBT patients is a 4-year-old Kuwait boy who has never been transfused and maintains a Hb of 8 – 9 g/dl and the other is a 3-year-old Indian girl who has been transfused once and maintains her Hb at 7–8 g/dl. Fourteen (48.3%) patients had enlarged spleens of between 2 and 10 cm below the costal margin. The serum ferritin ranged from 14 to 593 and a mean of 133.5±64.9 ng/ml. One 16 year-old female Jordanian BTI patient developed focal seizure and dysarthria and turned out to have middle and cerebral artery stenosis and Moyamoya. Otherwise none of the other patients have any co-morbidities or complications.

Conclusions:
NTDT is not uncommon in Kuwait. The 2 common conditions are HbH and BTI. The phenotype is generally mild. The BTI patients need to be monitored for thrombotic phenomena. Liver iron concentration should be assessed (using MRI) in the older patients since serum ferritin may not reflect the true body iron burden.

Key Words: Beta Thalassemia; HbH; E-Beta thal
Funding Agency: None

Pediatrics
Category: Clinical

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Neurocognitive status of Kuwaiti pediatric sickle cell disease patients

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Introduction:
Sickle cell disease (SCD) is characterized by neurocognitive deterioration especially in patients who have had overt stroke or silent brain infarcts. However, these complications are uncommon in Kuwaiti pediatric patients and there is no previous study investigating cognitive function in our patients.

Methods:
This was a cross-sectional study of SCD patients (48; 30 males and 18 females) in Kuwait. Instruments designed to test different domains of cognitive function were administered by a child psychologist to all the patients and a control group (40; 20 males and 20 females) made up of their non-SCD siblings. Magnetic resonance imaging (MRI), transcranial Doppler (TCD) and single photon emission computed tomography (SPECT) were done to identify SCD patients with brain infarcts, cerebral arterial stenosis or blood flow deficits.

Results:
The mean age of the patients and controls were 10.34 ± 3.64 and 10.58 ± 2.68 years respectively. The mean Wechsler Intelligence Scale for Children IQ scale scores (%) were, respectively, for patients and controls: (i) verbal: 84.7±7.7 vs. 84.8±8.9; (ii) performance: 85.9±.9 vs. 87.1±9.4; and (iii) full scale: 84.9±7.3 vs. 86.3±7.9. There were no significant differences in any of the neurocognitive tests between the patients and sibling controls. However, the mean full scale IQ scores of the 5 patients with silent infarcts (79.5±7.4) were significantly lower ($P<0.05$) in comparison to patients without infarcts (85.5±7.1) and the controls especially the full scale intelligence, comprehension – verbal and the Benton visual tests. None of the patients had abnormal TCD values or cerebral blood flow deficits on SPECT.

Conclusions:
While Kuwaiti SCD pediatric patients are generally spared the CNS structural complications, their full scale IQ may be affected, especially for those with silent brain infarcts. There is a need to identify this group early for appropriate intervention.

Key Words: Sickle cell disease (SCD); Magnetic resonance imaging (MRI); Transcranial Doppler (TCD)
Funding Agency: Kuwait University Research Administration Grant MK01/08

Pediatrics
Category: Clinical

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Arabic translation and validation of the newest vital sign health literacy tool: A pilot project to test health literacy of care givers of children with type 1 diabetes in Kuwait

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Introduction:
Health literacy is a recognized concept in patient care. The Newest Vital Sign (NVS) is an instrument that tests health literacy using a nutrition label. Numerous studies in the west linked health literacy to outcomes of diabetes care. No studies looked into health literacy in the Arab world and no tool has been established to test health literacy in Arabic-speaking populations.
Objectives:
1- Translate and validate the NVS tool to Arabic.
2- Test the Arabic version of the NVS tool on a pilot of Arabic-speaking care givers of children with type 1 diabetes.

Methods:
The development of the Arabic of NVS:
Phase 1 (Production of the Arabic version)
Phase 2 (Translation Validation)
Phase 3 (Pilot Project): the Arabic version of NVS is used to measure health literacy among a pilot of caregivers of pediatric patients of type 1 diabetes.

Results:
•After production of the Arabic version of the NVS tool, the mean comparability and similarity scores were accepted for each item on the tool (<2.5) except for three items. These three items represented the product information in the food label (score > 2.5). These three items were not reviewed and accepted as is as it is the official presentation of product information on food labels in Kuwait. With this the version was accepted for use.
•Caregivers with adequate health literacy scores, their children did not have poor glycemic control (HbA1C ≥ 9%). And those with likely limited health literacy, their children did not have well (HbA1C ≤7.5%) or moderate (HbA1C 7.6-8.9%) glycemic control.

Conclusions:
•The Arabic version of the NVS tool seems to be an accepted tool. However, it was hoped to validate the Arabic tool against a gold- standard Arabic literacy test, but due to lack of such test, the tool is accepted. •Limited health literacy of caregivers seems to be linked to inadequate glycemic control of their children. •Further link should be studies on a larger sample.

Key Words: Literacy; Diabetes; Outcome
Funding Agency: None

Pediatrics
Category: Clinical

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The use of botulinum toxin in children with obstetrical brachial plexus palsy

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Introduction:
Evaluation the efficacy of Botulinum toxin (BoNT in children with obstetrical brachial plexus palsy (OBPP).
Design: Retrospective study.

Methods:
9 children weighing more than 10 kilos, mean age 36 months (±39 SD), with OBPP and co-contractions between two muscles groups (Biceps/Triceps, Deltoid/Latissmus Dorsi).
Intervention: Assessment before and 6 months after injection. All were injected with Botox with a dose of 5 IU/Kg under ultrasound guidance (total dose 50-80 IU). Muscles injected: Triceps brachii (9); Latissmus dorsi (8); Subscapularis (6); Deltoid and Pectoralis major (1). The injections were preceded by pain killer, anxiolytics, and MEOPA gas. The rehabilitation program included three sessions/ week.
Outcome Measures: (1) Mallet scale; (2) Muscle power (MRC); (3) Range of motion.

Results:
9 children, mean age 36 months (± 39 SEM), 5 girls and 4 boys; 7 right OBPP and 2 left. The average birth weight 4.2 kg (± 0.47 SD). 3 received a second injection. Before treatment, 8 had co-contractions (Biceps/Triceps) and 5 have co-contraction (Deltoid/Latissimus Dorsi). After 6 months, 3 have co-contraction (Biceps/Triceps)(co-contractions disappeared in 62% of cases, $p = 0.007$); and 4 have co-contractions Deltoid/Latissimus Dorsi (co-contractions disappeared in 20% of cases, $p = 0.17$).Subjectively, 7 children (78%) had improvement noted by their parents. Mallet score improved in 6 patients (67%) ($p = 0.004$). 2 patients had initial score 2, 6 patients had score 3 and 1 patient had score 4. After 6 months, 3 patients had score 3 and 6 had score 4.

Conclusions:
Motor disturbances and loss of functional movements are common consequences of OBPP that compromise the quality of life of affected patients. The use of BoNT in the treatment of this problem shows interesting results, although the studies published to date are retrospective and often performed on small numbers. New prospective studies on larger samples are needed to confirm these results.

Key Words: Obstetrical brachial plexus palsy; Botulinum toxin; Rehabilitation
Funding Agency: none

Pediatrics
Category: Clinical

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Pediatric beta thalassemia major in Kuwait

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Introduction:
Beta-thalassemia major (TM) is an inherited chronic hemolytic anemia with significant morbidity and mortality. There have been significant recent advancements in its management. This is a review of pediatric TM patients followed in three hospitals in Kuwait. The study documents the pattern of the disease in affected patients - presentation, related complications and current management.

Methods:
This is a retrospective chart study of 41 TM patients attending Mubarak, Amiri and Adan hospitals' pediatric hematology clinics. The following were documented: age, gender, clinical presentation, height, weight, skull bossing, and associated co-morbidity along with blood transfusion pattern, serum ferritin, iron chelation and other management.

Results:
Of the 41 patients, 22 were Kuwaiti and 19 non-Kuwaiti with 29 (69.2%) males and 12 (29.7%) females. The age at presentation was < 1 year in 15(38.4%), between 1-2 years in 17 (43.5%) and between 2-4 years in 7(17.9%). All had regular blood transfusion to keep hemoglobin ≥10g/dl. Iron chelation was started when serum ferritin was more than 1000 ng/ml. All the patients had normal growth; only two had height <5th percentile. Endocrine assessments including thyroid function and growth hormone were within the normal range. The serum ferritin level ranged from 1000-4000 ng/ml with most between 1500-3000 ng/ml. Hepatosplenomegaly was found in 21 (50.2%) patients; splenectomy was done in 1 patient due to hypersplenism. Skull bossing ± maxillary prominence was found in 6 (15%) patients. Only 1 patient had hepatitis C infection after blood transfusion in his country.

Conclusions:
Our pediatric TM patients have generally satisfactory transfusion regimes and growth. However tissue iron status assessment especially with magnetic resonance imaging evaluation is still deficient and bone disease is under evaluated.

Key Words: Beta thalassemia major; Kuwait; Magnetic resonance imaging
Funding Agency: None

Pediatrics
Category: Clinical

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Palivizumab in preventing respiratory syncytial virus outbreaks in neonatal intensive care units.

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Introduction:
Respiratory syncytial virus (RSV) causes frequent nosocomial outbreaks in general pediatric wards but is less commonly reported in neonatal intensive care units. We investigated an outbreak of RSV infection in the neonatal unit at Maternity Hospital and a call to modify the guidelines of palivizumab prophylaxis is there

Methods:
Chart review was performed after an RSV outbreak which occurred in our unit in February 2012. A case of RSV was defined as an infant with a nasopharyngeal aspirate positive for RSV by PCR. Management of the infected infants and their outcome were also recorded.

Results:
During the outbreak, 12 preterm infants (beside the index case) turned RSV positive (mean age at infection, 38days; mean birth weight, 1457 g; and mean gestational age, 31 weeks). Clinical manifestations included cough, congestion, increased oxygen requirement, apnea and respiratory failure. Six infected infants became very sick and required intubation with IPPV mechanical ventilation. There was no significant difference in birth weight or gestational age between those who were intubated and the non-intubated infants. The RSV-positive patients were isolated, the ward closed to admissions and infection control measures were implemented. Palivizumab was administered to all patients and their contacts and no new cases were subsequently identified. All infants survived with five infants (including the index case) had residual chronic lung disease.

Conclusions:
The current guidelines which recommend palivizumab prophylaxis to preterm infants after discharge during winter season seem to be insufficient to prevent outbreaks in NCUs like ours. Palivizumab combined with infection control measures appears to prevent the spread of RSV during outbreaks in the NICUs. More studies are needed to investigate whether the use of palivizumab prophylaxis should start at NCUs in order to reduce RSV outbreaks.

Key Words: Neonatal Intensive Care Unit; Respiratory syncytial virus; Palivizumab
Funding Agency: None

Pediatrics
Category: Clinical

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Gulf Neonatal Infection Study (GNIS)

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Introduction:
Neonatal sepsis is set to increase globally because of the increased number of premature babies that are prone to infection particularly with use of life-support care. Gulf Cooperation Council (GCC) countries have introduced sophisticated tertiary care for newborns without sufficient attention to preventing infection. This study aims to investigate the incidence of neonatal sepsis and describe the main causative organisms and their anti-microbial resistance in GCC countries.

Methods:
A prospective study is currently conducted in Maternity Hospital in Kuwait, King Abdulaziz Hospital in Saudi Arabia; and Tawam Hospital and Dubai Hospital in United Arab Emirates using standard data collection form. Neonatal sepsis is defined as the growth of a single potentially pathogenic organism from blood or cerebrospinal fluid (CSF) in infants with clinical and laboratory findings consistent with infection. Early-Onset sepsis (EOS) was defined in the first two days of birth while Late-Onset sepsis (LOS) beyond two days of birth.

Results:
Over five-month period, 136(16 EO and 120 LO) infections were identified among 14,413 live births (overall incidence 9.4 per 1000 live births). The incidence of EOS and LOS was 1.1 and 8.3 per 1000 live births respectively. The most common causative organism for EOS was Group B Streptococcus (GBS) followed by E. coli while the most common organism for LOS was Coagulase-negative staphylococci followed by Klebsiella spp. There was only one infection due to MRSA; and of 44 infections caused by gram negative organisms,10(23%) and 7(16%) were resistant to third generation cephalosporin and gentamycin respectively.

Conclusions:
GBS seems to be a major contributor to EOS in GCC countries which highlights the importance of intrapartum antibiotic prophylaxis. Resistance of Gram-negative organisms to antibiotics in neonatal care units is lower than that reported in other developing countries but requires continuous surveillance

Key Words: Neonatal sepsis; GCC countries; Anti-microbial resistance
Funding Agency: Kuwait University, RX01/13

Pediatrics
Category: Clinical

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Medical student's perceptions and attitudes to pediatrics: Pre- & Post-pediatric clerkship

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Introduction:
Pediatric clerkship might have a major influence in directing medical student's decisions to pediatrics as a future career specialty. This study aims to investigate how the pediatric clerkship affects medical student's perceptions and attitudes towards pediatrics, and their interest in pursuing pediatrics as a future carrier.

Methods:
A questionnaire was administered to 6th year medical students at the beginning and end of the pediatric clerkship during the 2012-2013 year. The questionnaire had questions regarding 14 different perceptions and attitudes toward pediatrics, and the interest in pursuing pediatrics as a future career. The responses were reported on a 5-point Likert scale. The post-clerkship questionnaire included questions regarding the best and worst aspects of the pediatric clerkship.

Results:
A total of 75 students completed the pre- & post-clerkship questionnaires. There was a significant shift of interest to pediatrics as a future career following the pediatric clerkship ($p=0.001$). Additionally, there was a significant favorable change of medical student's perceptions and attitudes to pediatrics ($P <0.01$) in these areas: working with children is enjoyable, it is difficult to work with children, pediatricians are nice to work with, interaction with parents is uncomfortable, pediatrics offers many future specialties, it is difficult to diagnose children, pediatric conditions carry a good prognosis and pediatrics is less prestigious than other specialties. Students reported that working with a pediatric team was the best aspect of the clerkship (62.7%) The worst aspect of the clerkship was dealing with parents (53.3%).

Conclusions:
The pediatric clerkship has a significant positive effect on medical student's perceptions and attitudes to pediatrics and is significantly associated with a shift of interest to pediatrics as a future career.

Key Words: Clerkship; Pediatrics; Medical students
Funding Agency: None

Pediatrics
Category: Clinical

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Breast feeding practice in Kuwait: determinants of success and reasons for failure

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Introduction:
Objective: This study was performed to explore the possible determinants of the duration of breast feeding practice in Kuwait to help develop strategies for boosting this practice thus fulfilling the WHO set goals.

Methods:
Two hundred thirty four mothers from Al-Ahmadi district, Kuwait, completed a questionnaire concerning the feeding history of their youngest infant. It included three sections. The first one explored the sociodemographic data of the mother and details about her infant`s dietetic history. The second addressed the factors that might have contributed to her willingness to continue her breast feeding practice. A third section inquired about the factors leading to her decision to conclude breast feeding.

Results:
Only 26.5% of the enrolled women in the current study completed breast feeding for 6 months. Separate housing, higher maternal age, the late start of the first breast feeding session, working without feasibility of breast feeding the infant, breast feeding information given after rather than before birth, maternal and infant sickness were all significant contributors influencing early cessation of breast feeding as reported by mothers. On the other hand, father`s support to continue breast feeding was a significant factor that encouraged the practice.

Conclusions:
Preventive strategies are recommended for boosting breast feeding practice with special emphasis on the factors linked to early cessation aiming at full implementation of the WHO global public health recommendations for successful breast feeding in Kuwait.

Key Words: Breast Feeding; Determinants; Kuwait
Funding Agency: None

Pediatrics
Category: Undergraduate

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The experience of pediatrics allogeneic bone marrow transplant in Kuwait

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Introduction:
Pediatric Allogeneic Bone marrow transplant (BMT) is started in Shaikha Badria Stem transplant center in Kuwait since Nov,2011, for all the benign hematological cases . This study describes the outcome of the BMT of 12 patients.

Methods:
This is a retrospect study of 12 pediatric patients, age ranged from 3 to 17 years ,referred from Amiri ,Sabah ,NBK, Mubarak, Adan ,Farwaniya hospitals, with the diagnosis of Beta -Thalassemia major,severe aplastic anemia, pediatric myelodysplastic syndrome (MDS), and congenital dyserthropiotic anemia, who underwent hematopoietic stem cell transplantation (HSCT) from a human leukocyte antigen (HLA) identical sibling donor between November, 2011 to December 2013. Informed consent from parents was taken. All the Beta-Thalassemia major patients were conditioned with Busilvex ,Cyclophosphamide with thiotepa. Patients were followed up for a median of 19 months post-transplant.

Results:
There were 9 Beta-Thalassemia patients, 2 aplastic anemia, 1 MDS and 1 congenital dyserythropiotic anemia . The median age was 9 years. The Beta-Thalassemia major showed distribution of Pesaro risk II, and III categories as 6 and 3 patients, respectively. The median neutrophil, and platelet recovery were 19 and 25 days, respectively. None of the patients had graft failure. 11 out of the 12 patients were alive. One patient was lost due to development of severe acute GVHD skin, gut and liver, then interstitial pneumonitis. Six patients developed Gram-negative, 2 patients Gram-positive bacteremia, one patient developed lung aspergillosis, 4 patients had febrile neutropenia. Cytomegalovirus reactivation occurred in 5 patients. All alive patients are normal with normal quality of life, and the median follow-up was 19 months.

Conclusions:
Pediatric allogeneic BMT is successful in Kuwait for benign hematological diseases.

Key Words: Pediatrics Bone Marrow Transplant; Beta thalassemia Major; Pediatric myelodysplastic syndrome (MDS)
Funding Agency: None

Pharmacology and Toxicology
Category: Basic Sciences

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Differential signaling by the human incretin receptors

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Introduction:
Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) are incretin hormones that function primarily to enhance glucose stimulated-insulin secretion. In type 2 diabetes mellitus (T2DM) there is a loss of the insulinotropic effect of both peptides. Pharmacological levels of GLP-1 can however overcome this loss of response whereas this is not the case for GIP. GLP-1 and GIP exert their insulinotropic effects through their respective receptors expressed on pancreatic beta-cells. Both the GLP-1 receptor (GLP-1R) and the GIP receptor (GIPR) are members of the secretin family of G protein-coupled receptors (GPCRs) and couple positively to adenylate cyclase via Gs. We compared signaling properties of these two receptors in order to understand why GLP-1 but not GIP remains insulinotropic in T2DM.

Methods:
Signalling through Gs was investigated using a cAMP-responsive luciferase (cre-luc) reporter gene assay. Agonist stimulated arrestin recruitment to the two receptors was investigated using confocal microscopy and fluorescence resonance energy transfer (FRET).

Results:
GIPR displays significantly higher ($P<0.005$) ligand-independent activity than GLP-1R in a cre-luc assay when expressed at similar levels in HEK-293 cells. YFP-labelled arrestin3 displayed a robust translocation to agonist stimulated GLP-1R but not to GIPR. These results were quantified as loss of cytoplasmic fluorescence over time. At 15 minutes the loss of cytoplasmic fluorescence stimulated by GLP-1 was significantly greater ($P<0.005$) than with GIP. These observations were confirmed in FRET experiments where GLP-1 stimulated recruitment of both CFP-labelled GPCR kinase 2 (GRK2) and CFP-labelled arrestin3 to YFP-labelled GLP-1R. In contrast GIP did not stimulate recruitment of either GRK2 or arrestin3 to its receptor.

Conclusions:
GIPR displays higher basal activity than GLP-1R but does not recruit GRK2 or arrestin effectively.

Key Words: GLP-1; GIP; Arrestin
Funding Agency: MR02/12

Pharmacology and Toxicology
Category: Basic Sciences

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Role of cannabinoid CB1 receptors in the enhanced antinociception induced by coadministration of indomethacin and minocycline against paclitaxel-induced neuropathic pain

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Introduction:
In previous studies, we observed that coadministration of indomethacin and minocycline potentiates their antinociceptive activity against inflammatory pain. Both drugs can independently alter the endocannabinoid system, which might contribute to their antinociceptive activity. The objective of this study was to evaluate whether coadministration of these drugs has antinociceptive effects in rodents with paclitaxel-induced neuropathic pain (PINP) and if the cannabinoid CB1 receptor plays a role in the combination's effects.

Methods:
Paclitaxel was administered to BALB/c mice and Sprague Dawley rats to induce thermal hyperalgesia and mechanical allodynia, respectively. Mice with paclitaxel-induced thermal hyperalgesia were treated with indomethacin, minocycline, a CB1 receptor antagonist AM 251 alone or in combination or their vehicles (n = 8-17). Thermal nociception was measured using a hot plate. Rats with paclitaxel-induced mechanical allodynia were treated with indomethacin, minocycline alone or in combination or their vehicles (n = 8). Mechanical allodynia was measured using a dynamic plantar aesthesiometer.

Results:
Treatment of mice with indomethacin or minocycline alone had no effect on paclitaxel-induced thermal hyperalgesia ($P>0.05$), whereas coadministration of the two drugs attenuated it ($P<0.05$). The antihyperalgesic effects of indomethacin plus minocycline was blocked by the administration of AM 251. Treatment of rats with either indomethacin or minocycline alone increased withdrawal threshold but did not completely abrogate paclitaxel-induced mechanical allodynia, whereas coadministration of the two drugs completely abrogated it ($P<0.01$).

Conclusions:
The results indicate that coadministration of indomethacin and minocycline abrogates established PINP. The potentiation of the effects of this drug combination against neuropathic pain is possibly through modulation of the endocannabinoid system.

Key Words: Chemotherapy-induced neuropathic pain; Minocycline; Cannabinoid CB1 receptor
Funding Agency: Kuwait University Research Sector grant number PT01/08

Pharmacology and Toxicology
Category: Graduate PhD (Basic Science)

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C. elegans aging is modulated by hydrogen sulfide and the sulfhydrylase/cysteine synthase cysl-2

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Introduction:
Hydrogen sulfide has been reported to regulate cell cycle and survival in healthy cells suggesting that it may play a role in cell fate and hence the aging process. This study aims to unravel the biological response to hydrogen sulfide using the nematode Caenorhabditis elegans as an animal model. We explored the involvement of exogenous H2S (via the donor GYY4137) as a modulator of the aging process and protection against stress. We also characterized the phenotypic changes after knocking out the gene K10H10.2 (cysl-2) which was hypothesized to be implicated in endogenous hydrogen sulfide fate/response. Key results were validated in cell culture experiments utilizing bovine aortic endothelial cells (BAECs).

Methods:
Strains used were Bristol N2 (wild type) and cysl-2 (ok3516). Assays performed include: toxicity assessment (brood size, growth and lifespan), H2DCF-DA oxidative stress assay, stress resistance assay, Polymerase Chain Reaction (PCR), measurement of hydrogen sulfide synthesizing activity and CellTiter-Blue Cell viability test.

Results:
Chronic treatment with GYY4137 extended median survival by 17-23% and increased tolerance towards oxidative and endoplasmic reticulum stress. Also, cysl-2 was upregulated by GYY4137 treatment and the deletion of cysl-2 resulted in a significant reduction in lifespan which was partially recovered by GYY4137 treatment. GYY4137 was able to protect BAECs from oxidative stress and hydrogen peroxide-induced cell death.

Conclusions:
The disturbance of the endogenous hydrogen sulfide system in C. elegans is detrimental for survival, reproduction and growth. Exogenously applied hydrogen sulfide promotes growth and enhances survival. This might be due to antioxidation and ROS scavenging. An analogous protection was observed in BAECs. These findings highlight the role of endogenous hydrogen sulfide in aging and cellular response to stress and the potential of exogenous hydrogen sulfide donors to target ageing and stress.

Key Words: Hydrogen sulfide; Ageing; Stress
Funding Agency: None

Pharmacy
Category: Clinical

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Evaluating the cost-effectiveness of fidaxomicin and vancomycin in the treatment of *Clostridium difficile* infection from a hospital perspective

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Introduction:
This study compared the costs and effectiveness of fidaxomicin and vancomycin for the treatment of Clostridium difficile infection (CDI). This analysis was conducted from a hospital perspective to assist health-care providers in deciding whether to add fidaxomicin to their formularies.

Methods:
A decision analytic model examined whether fidaxomicin or vancomycin is more cost-effective for treating CDI. Outcomes data for this analysis were obtained from OPT-80-003 Clinical Study Group (fidaxomicin versus vancomycin) clinical trial. The main outcomes were clinical cure (resolution of symptoms), recurrence of CDI, and global cure (clinical cure with no recurrence). Cost data were calculated per CDI patient using the following estimates: hospitalization for 10 days ($17,196), fidaxomicin regimen for 10 days ($2,800), and vancomycin regimen for 10 days ($26.8).

Results:
The baseline cost-effectiveness analysis found that fidaxomicin was slightly more effective but more costly than vancomycin. A hospital would pay an extra $31,539 if fidaxomicin were chosen to treat each episode of CDI. The model is most sensitive to hospitalization costs, which is consistent with the literature. A one-way sensitivity analysis on drug cost found that fidaxomicin did not dominate whatever the cost was. A two-way sensitivity analysis on hospitalization cost and the clinical cure rate of fidaxomicin found that vancomycin was only dominated when fidaxomicin cure rates reached 97%, which is highly unlikely.

Conclusions:
Based upon this cost-effectiveness analysis, vancomycin is the recommended drug of choice for CDI treatment. The hospital would pay an extra $31,539 to treat each episode of CDI using fidaxomicin. Fidaxomicin would only be preferred if it had a higher clinical cure rate and a cheaper price according to the sensitivity analysis. As a conclusion, hospitals could consider fidaxomicin as second line treatment for cases in which patients have failed a course of treatment

Key Words: Outcomes Research; Pharmacoeconomics; Cost-effectiveness
Funding Agency: None

Pharmacy
Category: Undergraduate

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Identifying and quantifying the return unwanted medications during the take–back event at the Health Sciences Center in Kuwait

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Introduction:
Take-Back events are available in most countries to return Unwanted Medications (UMs) for safe disposal. An event was organized by the pharmacy students at the Health Science Center (HSC) which includes Faculty of Medicine (FOM), Faculty of Dentistry, Faculty of Pharmacy (FOP) and Faculty of Allied Health Sciences.
Objective: To identify and quantify the UMs returned from the HSC community.

Methods:
On September 11, 2013, a take-back event was held from 9-3pm at the HSC lobby to collect UMs from students, staff and their relatives. Official letters of permission for collection were obtained. The information regarding the medication's therapeutic class, source (private or public health sector), expiry date and the affiliation of the participants were collected by trained pharmacy students. The amount of UMs was measured in kilograms. The data were analyzed using SPSS.

Results:
Unwanted medications were received from 77 participants, of which 45 (58.4%) were from FOP and 19 (24.7%) were from FOM. The participants consisted of 50 (64.9%) students, 13 (16.9%) employees and 11 (14.3%) academic staff. The weight of the UMs was 75.5 kg. A total of 1452 items were received and sorted. The UMs consisted mainly of tablets 920 (63.4%) and 893 (61.5%) medications were expired. The UMs were mainly pain killers 272 (18.7%) and 181 (12.5%) drugs were for treating infections. The main source of the UMs was public health sector 519 (35.7%).

Conclusions:
The amount of medications returned shows that the participants have a positive willingness to dispose their UMs safely. Most of the UMs were returned by the pharmacy students because they received lectures on this topic. One third of the UMs were unexpired, which could be donated. The public health sector was the main source as most of the medications are provided free of cost in Kuwait.

Key Words: Unwanted medications; Kuwait; Pharmacy students
Funding Agency: None

Pharmacy
Category: Undergraduate

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Availability of general sales list medicines and the selling of paracetamol tablets in cooperative societies in Kuwait

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Introduction:
In Kuwait, medicines are available as prescription-only medicines, over-the-counter medicines and as general sales list (GSL) medicines. The public can buy the GSL medicines from the cooperative societies (co-ops). The sale of GSL medicines is regulated by ministerial degree (621), 1998, of Kuwait's Ministry of Health (MOH). This list includes paracetamol, to be sold as tablets only. Studies have shown that restricting the pack sizes of paracetamol, sold as GSL to the public, has reduced the number of deaths through intentional overdose and hepatotoxicity. Objectives: To investigate if the medicines sold in co-ops comply with the regulations of MOH and the dosage forms and pack sizes of paracetamol sold in co-ops.

Methods:
A cross-sectional survey was conducted during May and June, 2013. A random sample of 26 main co-ops are in each of the six governorates in Kuwait, was included in the survey. An inventory table, designed after a pilot study, was used to collect data on the name, dosage form, strength and pack size. The acquired data was compared with the MOH list for any discrepancies.

Results:
Out of the 26 co-ops surveyed, none of co-ops complied with the MOH GSL medicines list and 23 co-ops had stocked paracetamol as elixir and as combination products of paracetamol with other ingredients such as caffeine. The pack sizes of paracetamol stocked by the co-ops varied between 48 tablets and even 100 tablets. The public were able to buy any quantity of paracetamol formulations.

Conclusions:
There is an urgent need for revision and update on the GSL medicines that can be sold in the co-ops in Kuwait by MOH with regular inspections to all co-ops. Restrictions on the quantity of paracetamol tablets per pack that can be sold by the co-ops have to be stated in the revision of the GSL medicines list. .

Key Words: General sales list medicines; Kuwait; Paracetamol
Funding Agency: None

Pharmacy
Category: Basic Sciences

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Sodium alginate-based microspheres of salbutamol sulphate for nasal administration: Formulation and evaluation

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Introduction:
Salbutamol sulfate is a direct acting sympathomimetic; it is used for the treatment of acute and chronic asthma. Orally administered salbutamol or the swallowed portion of an inhaled dose undergoes first pass metabolism. Nasal delivery has a distinct advantage of protecting drug from hepatic first-pass metabolism.

Methods:
This aim of this project is to develop, characterize and evaluate mucoadhesive sodium alginate microspheres for salbutamol sulfate employing the effect of addition of other mucoadhesive polymers; carboxymethyl cellulose sodium, carbopol 934P and hydroxylpropyl methyl cellulose with sodium alginate on the swelling behavior, mucoadhesion property, in-vitro drug release, morphology and particle size of the formulated microspheres, DSC examination for any drug-polymer interaction. Furthermore, the nasal mucosal irritation after repeated administration of the formulated microspheres on rabbits was evaluated applying a non-invasive method.

Results:
An emulsion cross-linking method was successful in preparing alginate microspheres of the drug, 4% w/v aqueous sodium alginate solution, 10% aqueous CaCl2 solution, blend of 2% Span 80 and 1% Tween 20. Microspheres were spherical in shape, discrete, with a smooth surface and with a mean diameter favorable for intranasal absorption. Drug loaded microspheres had a higher degree of swelling compared to blank ones. Microspheres prepared by blending sodium alginate polymer with other mucoadhesive hydrogel; exhibited higher degree of swelling than microspheres formulated with pure sodium alginate polymer. Pronounced sustained effect of release over 8 hours was exhibited upon incorporation of Carbopol and HPMC with sodium alginate.

Conclusions:
The microspheres showed no severe damage of nasal epithelium after repeated administration to rabbits. The microspheres exhibited high swelling and good mucoadhesion properties making them suitable carrier systems for nasal delivery of salbutamol sulfate and similar drugs.

Key Words: Alginates; Salbutamol; Nasal delivery
Funding Agency: None

Pharmacy
Category: Clinical

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Pharmaceutical care in hospitals of Kuwait: Pharmacists' opinions and perceived barriers

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Introduction:
Pharmaceutical care practice has been accepted as the primary mission of the pharmacy profession. This study was designed to investigate hospital pharmacists' opinions about the importance of the various pharmaceutical care activities and the barriers to pharmaceutical care implementation in Kuwait.

Methods:
A descriptive, cross-sectional survey was distributed to all pharmacists working in the governmental hospitals in Kuwait (n=385). Data were collected via a pre-tested self-administered questionnaire and analyzed using SPSS, version 20. Statistical significance was accepted at a p value of <0.05.

Results:
The response rate was 64.9%. Pharmacists rated most of the pharmaceutical care activities as being important to very important, with overall mean (SD) responses of 3.5 (0.9) on a 4-point Likert scale. The perceived importance was highest for pharmacists' ability to verbally explain medical issues to the understanding of patients, 3.7 (0.6), the ability to obtain accurate information on all the medications taken by patients, 3.7 (0.7), to recommend dose adjustments, 3.7 (0.8) and to monitor medication side effects, 3.7 (1.2). Respondents rated performing limited physical examination as the least important activity, 2.9 (1.0). The perceived importance of these activities was significantly higher among females, Kuwait University graduates, young pharmacists (20-29 years) and those with practice experience between 1-5 years ($p<0.001$). The most significant barriers to the implementation of pharmaceutical care were lack of private counseling areas (87.6%), organizational obstacles (81.6%) and inadequate staff (79.6%).

Conclusions:
Hospital pharmacists appreciate the importance of the various pharmaceutical care activities. Collaborative efforts between health authorities and educational institutions, and the integration of innovative approaches in pharmacy management and education may overcome the barriers to pharmaceutical care implementation.

Key Words: Pharmaceutical care; Pharmacists; Kuwait
Funding Agency: None

Pharmacy
Category: Basic Sciences

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Ex vivo and in vitro evaluation of transdermal permeation of topcopherol formulations

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Introduction:
Alpha-tocopherol (T) plays important roles in the maintenance of skin physiological conditions. Formulation factors affects drug release and permeation.

Methods:
Different formulations (37) of oils, surfactants and cosurfactants were used for the development of self-emulsified drug delivery systems (SEDDS). These combinations were tested for physical compatibility and characterized for their particle size and turbidity when mixed with water. Solution formulations (21) were prepared in different combinations of propylene glycol (PG), ethanol, PEG 400, dimethyl formamide (DMF), dimethyl sulphoxide (DMSO), surfactants, and tocopheryl polyethyleneglycol succinate (TPGS). Permeation was studied in-situ using neonate rats stratum corneum in a diffusion cell. A two-levels three-factor experimental design was employed to evaluate the effects of considered variables, DMSO (X1), TPGS (X2) and T (X3) level on %-permeability (Y1). Mathematical elaboration of experimental data was carried out by the computer program DESIGN EXPERT®. Analysis of variance (ANOVA) was also performed on the resulting data.

Results:
SEDDS containing soybean oil showed good dispersability with no separation, but showed separation on mixing with ethanol, PG or PEG. Replacing soybean oil with oleic acid, the mixtures showed clear solution. The drug release and permeation of T from SEDDS was poor. Better permeation was observed with the solution formulations and the %-permeation ranged between 0.016 (F13) (SD=0.00769) and 0.07 (F19) (SD=0.010471). Permeatio showed best fit in interaction model with R2=0.9402. The theoretical and observed values were in good agreement. The equation that completely describes the system was: $Y1 = -0.086 + 0.039\ X1 - 0.045\ X2 - 0.044\ X3$.

Conclusions:
Drug-lipid formulations were inappropriate for transdermal delivery of T. Solution formulations exhibited better permeation and the percent of T, TPGS, and DMSO were the most important factors.

Key Words: Vitamin E; Transdermal Formulations; Permeation
Funding Agency: Research Sector, Kuwait University, PP01/09

Pharmacy
Category: Basic Sciences

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Synthesis and biological evaluation of novel oxazolidinone hydroxamic acid derivatives

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Introduction:
Oxazolidinones are antibacterial agents active against Gram-positive bacteria. Studies have shown that optionally varied C-5 substituted oxazolidinones resulted in comparable or enhanced antibacterial activity. Oxazolidinones are also plagued with unwanted monoamine oxidase (MAO) inhibition, due to structural similarity with MAO inhibitors, namely, toloxatone. In this study, we investigated the effects of optionally varied C-5 hydroxamate oxazolidinones on antibacterial and MAO inhibitory activities.

Methods:
Oxazolidinones were synthesized and evaluated for bacterial growth and monoamine oxidase inhibition. A susceptibility test was performed by the agar dilution method with discs containing 30 µg/mL test compounds and the diameter zone of inhibition (mm) measured. Computer model interactions of representative oxazolidinones at the bacterial ribosomal receptor site were performed using Molecular Operating Environment (MOE v 2012.10) software. MAO-A or -B inhibition was determined in 96 well microtiter plates using tyramine as a mixed substrate for MAO-A and -B. Blanks containing buffer instead of tyramine and controls containing distilled water instead of test compounds, were run parallel to the samples in a SunriseTM microplate absorbance reader at 498nm every minute for 10 minutes, then every 10 minutes for 20 minutes and every 20 minutes until 90 minutes.

Results:
Eight oxazolidinone hydroxamates and the N-carbamate precursors were tested. Compounds were devoid of antibacterial activity. Computer modeling showed that N-OH disrupted hydrogen bonding to the 5'-phosphate of G2540, due to steric overlap of the two oxygen atoms due to proximity (1.5 Å). The compounds showed weak to moderate MAO-A and -B inhibitions at 50 and 200 µM concentrations. MAO inhibitions ranged from 0 to 68.8% for both isoenzymes.

Conclusions:
The presence of a C-5 hydroxamic acid group in oxazolidinones is detrimental to antibacterial and MAO inhibitory activities.

Key Words: Oxazolidinones; Antibacterial activity; Monoamine oxidases inhibition
Funding Agency: KURA Grant #s PC01/09 (OAP) & Grant # GS 01/01, GS 01/03 and GS 01/05 (Science Analytical Facilities, SAF),

Pharmacy
Category: Basic Sciences

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Evaluation of triazolyl-oxazolidinones for anticonvulsant and antinociceptive activities

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Introduction:
Oxazolidinones are clinically useful as antimicrobial, psychotropic, and anticoagulant agents. They have also been reported to have anticonvulsant and analgesic properties. The objective of this study was to evaluate a series of triazolyl-oxazolidinones for anticonvulsant and antinociceptive activities.

Methods:
Twenty-seven oxazolidinones were evaluated using the NIH protocol on minimal clonic seizure (6Hz) test. Test compounds (100 mg/kg) were pre-administered to mice (n=4) by i.p. injection and each mouse was challenged with current delivered through corneal electrodes to elicit psychomotor seizures, at varying times. The animals were monitored for neurological behavior using the rotarod test. The ED50 (n=8) of 6 compounds was determined with appropriate descriptive statistics. Two compounds, PH66 and PH196 were tested for antinociceptive activity using the formalin test and compared to vehicle-treated mice (n =8 per group). The amount of time the mouse spent licking the affected hind paw in a two minute period at five minute intervals was recorded. The early (neurogenic pain) phase was from 0-10 minutes and the late (inflammatory pain) phase was from 15-40 minutes.

Results:
Neuroprotective data are presented as N/F (N=number of animals protected, F=number of animals tested) and any deaths are noted. Nine out of 27 compounds tested showed anticonvulsant activity, protecting between 1-3 mice out of 4. Of the 6 compounds selected for ED50 evaluation, PH66 and PH192 were the most active with ED50 (± STD Err) values of 52.47 (0.52) and 34.03 (0.62) mg/kg, respectively. These 6 compounds showed good safety profiles with 300 < TD50 < 750 mg/kg. Both PH66 and PH192 showed antinociceptive activity in both the early and late phases of the formalin test.

Conclusions:
Both PH66 and PH192 showed anticonvulsant and antinociceptive activities. Further investigations on the neuroactivity of the triazolyl-oxazolidinones are warranted.

Key Words: Oxazolidinones; Anticonvulsant activity; Antinociceptive activity
Funding Agency: Science Analytical Facilities (SAF), KU, RA Grant # GS 01/01, GS 01/03 and GS 01/05

Pharmacy
Category: Basic Sciences

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Isolation and characterization of new bioactive guaianolides from *Centaurea aegyptiaca*

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Introduction:
As a continuation for our research on *Centaurea aegyptiaca* that had shown cytotoxic activity against liver and larynx carcinoma cell lines, the isolation of two new guaianolides that may be responsible for the potent biological activity of *Centaurea aegyptiaca* extract are reported herein.

Methods:
The fresh aerial parts of *Centaurea aegyptiaca* were air-dried, coarsely powdered and extracted with ethanol (96%). The ethanol extract was partitioned against ethyl acetate. Then, the ethyl acetate fraction was chromatographed on a flash silica gel column eluted with an increasing strength of methanol in methylene chloride. Two compounds were isolated and identified using different spectral methods. Moreover, the cytotoxic activity of these compounds were evaluated against liver and larynx carcinoma cell lines using Skehan et al. protocol. IC_{50} (µmolar) of the two compounds were determined using doxorubicin as a positive control.

Results:
Two new guaianolide sesquiterpene lactones, $C_{20}H_{27}ClO_8$ (1) and $C_{20}H_{28}Cl_2O_8$ (2) were isolated from the ethyl acetate fraction and identified. Compound 1, the most potent of both, showed cytotoxic activity against liver and larynx carcinoma cell lines with IC_{50} values of 7.16 and 7.51 µmolar, respectively. However, compound 2 exhibited weaker cytotoxic activity against liver and larynx carcinoma cell lines with IC_{50} values of 24.24 and 32.40 µmolar, respectively.

Conclusions:
Phytochemical analysis of *Centaurea aegyptiaca* ethyl acetate fraction led to the isolation and identification of two new sesquiterpene lactones. Moreover, these compounds may be responsible for the cytotoxic activity shown by *Centaurea aegyptiaca* ethanol extract against liver and larynx carcinoma cell lines.
Acknowledgements: Spectral analyses were done at Faculty of Science General Facility, Grant numbers GS01/01 and GS01/03.

Key Words: Centaurea aegyptiaca; Cytotoxicity; New Guaianolides
Funding Agency: GS01/01 and GS01/03

Pharmacy
Category: Clinical

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Abnormal pattern of bradykinin forming components and nitric oxide in Kuwaiti patients with type 2 diabetes

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Introduction:
Bradykinin (BK), a pharmacologically active polypeptide, is released in the tissue and body fluids as a result of enzymatic action of kallikreins on kininogens. Diabetes is the most common risk factor leading to hypertension, nephropathy and retinopathy. The BK forming system has been proposed to protect cardiovascular and renal function. We, therefore evaluted various BK- forming components and nitric oxide (NO) in newly diagnosed untreated type 2 diabetic patients and healthy subjects.

Methods:
Fasting blood and urine samples were collected from healthy volunteers (N=20) and diabetics (N=8). Diabetics were newly diagnosed without treatment. The study was approved by the ethical committee of HSC and Ministry of health.Enzyme linked immunoassay was carried out to determine the various components, such as BK, tissue and plasma kallikrein, prekallikrein (PK), kininogens, kininase (KI) and NO.

Results:
The diabetic patients had elevated levels of glucose, body mass index and glycated hemoglobin. It was found that the concentration of plasma kininase, urinary and plasma kallikrein and plasma PK were significantly higher in diabetic patients without treatment when compared to healthy volunteers, while plasma and urinary NO and urinary kininogen (UK) levels were found significanlty lower in diabetics.

Conclusions:
The present investigation for the first time reports the abnormal activities in the BK forming system in Kuwiati patients with type 2 diabetes. High levels of plasma PK may be an indicator for having a risk factor for developing high blood pressure and nephropathy. The urinary kininogen levels were reduced and these alterations might reflect the utilization of UK to form BK. Reduction in NO level could be an indication of vasocontriction leading to hypertension. Higher KI levels may be an indicator of developing nephropathy.

Key Words: Diabetic; kallikrein; Nitric Oxide
Funding Agency: Kuwait University, RP(01/09)

Pharmacy
Category: Undergraduate

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The interaction between gabapentin and tetrodotoxin in the treatment of paclitaxel-induced neuropathic pain

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Introduction:
The use of paclitaxel in cancer treatment is often hampered by the development of a dose-limiting painful peripheral neuropathy. In animal models paclitaxel-induced neuropathic pain (PINP) manifests as thermal hyperalgesia and mechanical allodynia, which can be alleviated either by the calcium channel blocker gabapentin or sodium channel blocker tetrodotoxin (TTX). The objective of the present study was to analyze the interaction between gabapentin and TTX when coadministered to treat PINP.

Methods:
Paclitaxel (10 mg as a single dose) was administered intraperitoneally to female BALB/c mice (n = 74) to induce thermal hyperalgesia. Mice with paclitaxel-induced thermal hyperalgesia were treated with gabapentin (10 mg/kg) and TTX (3 and 6 µg/kg) alone or in combination or their vehicles (n=12-13 per treatment group) on the 7th day post paclitaxel administration. Thermal nociception was measured using the hot plate test.

Results:
Treatment with paclitaxel resulted in a significant reduction in reaction latency time to the hot plate test (thermal hyperalgesia) on the 7th day post administration compared to baseline latency and vehicle-treated animals ($p < 0.01$). Treatment with gabapentin (10 mg/kg) or TTX (6 µg/kg), but not 3 µg/kg of TTX, significantly reduced paclitaxel-induced thermal hyperalgesia i.e. produced a significant increase in reaction latency at 1 hour ($p<0.05$), compared to vehicle-treated mice. Coadministration of TTX 3 µg/kg and gabapentin 10 mg/kg had less effect than gabapentin alone ($p < 0.05$) and had no significant effect against paclitaxel-induced thermal hyperalgesia ($p > 0.05$).

Conclusions:
These results confirm that gabapentin and TTX attenuate paclitaxel-induced thermal hyperalgesia. The data also show that combined use of gabapentin with TTX has antagonistic effects on their antihyperalgesic activity, thus, combination therapy with gabapentin and TTX against PINP should be avoided.

Key Words: Paclitaxel-induced neuropathic pain; Gabapentin; Tetrodotoxin
Funding Agency: None

Pharmacy
Category: Basic Sciences

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Preparation and characterization of Cyclosporin A nanospheres to improve its solubility and dissolution

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Introduction:
Cyclosporin A (CyA) is a highly lipophilic compound. It is believed that its limited bioavailability and dissolution rate inconsistency are due to its poor solubility in water. Solubility and dissolution of CyA can be improved by inclusion in different hydrophilic polymer (HR).

Methods:
Nanospheres of CyA with different HR were prepared by co-precipitation from different solvents. The polymers used were Polyethylene glycol 4000 (PEG4000), Polyvinylpyrrolidone (PVP), Polyvinylpyrrolidone-polyvinylacetate copolymer (PVPAC), Chitosan (CH), α-Cyclodextrin (α-CD), β- Cyclodextrin (β-CD), and γ-Cyclodextrin (γ-CD) in drug polymer ratios 1:1, 1:2, and 1:3. The prepared formulations were analyzed for their encapsulation efficiency, solubility and dissolution in water and in PBS using HPLC. The formulations showed high encapsulation efficiency and significant increase in solubility and dissolution rates were characterized using particle size analyzer (PS), Zetameter, Fourier transform infrared spectroscopy (FTIR), X-Ray diffractometry (XRD) and Scanning electron microscope (SEM).

Results:
The encapsulation efficiency correlated inversely with the concentration of different polymers. The highest encapsulation efficiency was observed in case of α-CD 1:1(55.26%) and the lowest was in PVP 1:3 (21.31%). The solubility of all formulations was increased tremendously in range from 186.34 to 1015.25%. The PS was in nanorange (100-1000nm) and correlated inversely with solubility. The dissolution rate was improved and showed some correlation with solubility. The shape of the particles of most formulations was spherical and no interactions between CyA and polymers were observed as shown from the results of XRD and FTIR.

Conclusions:
The data indicate that by using HR and controlling the particle size, the solubility and dissolution of CyA could be improved. The prepared nanospheres may have high potential to improve CyA bioavailability.

Key Words: Cyclosporin A; Hydrophilic polymers; Solubility and dissolution
Funding Agency: None

Physiology
Category: Basic Sciences

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Partial progesterone deprivation up-regulates transcription of cell cycle control and pro-apoptotic genes in rat placentas

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Introduction:
Progesterone provides trophic support for fetoplacental growth and its low levels seem to manifest in intrauterine growth restriction. However, molecular mechanisms that mediate impaired placental growth due to low levels of progesterone are not clear. We investigated the gene expressions for proteins involved in cell cycle control and apoptosis in placentas of partial progesterone-deprived rats.

Methods:
Three groups of adult female SD rats were used as 1) control, 2) ovariectomized on day 15 of gestation (15GD) with supplementation of the physiological level of estrogen and subnormal progesterone levels (PRD), and 3) similar to group 2, but with supplementation of the physiological level of progesterone (PR). The placentas were retrieved on 19GD and gene expressions of estrogen receptors (ESR1 and ESR2), CDKN1A (p21), CDKN1B (p27), CTNNB1 (beta-catenin), CCND1 (cyclin D1), TP53 (p53), BCL2 and BAX were evaluated by RT-PCR according to standard procedures. Data were analyzed by one way ANOVA and LSD post hoc test with significance level set at $P<0.05$.

Results:
PRD reduced maternal body weight and placental weights ($P<0.05$), but not of fetuses, and PR recovered these effects. Both ESR1&2 were up-regulated in placental basal zones (BZ) in PRD and recovered in PR. The pro-apoptotic genes TP53 and BAX were up regulated in PRD and recovered in PR ($P<0.05$). Both CDKN1A and CTNNB1 were up-regulated in PRD and restored in PR. However, CDKN1B and CCND1 were up-regulated in BZ in PRD, but not in labyrinth zones (LZ), and restored in PR ($P<0.05$).

Conclusions:
Partial progesterone deprivation results in up-regulation of mechanisms responsible for cell cycle control and apoptosis in placentas. Interestingly, transcription of both pro-cell cycle arrest- and pro-proliferation-related genes occur in the placentas, which may finally lead to cell death and low weight placentas, but do not seem to affect fetal growth in rats.

Key Words: Cell cycle control; Placenta; Estrogen receptors
Funding Agency: MY02/08

Physiology
Category: Graduate MSc (Basic Science)

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Effects of lead exposure on the heart tolerance to ischemia reperfusion injury and its response to postconditioning protection

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Introduction:
Lead pollution is an issue of concern in the recent days. The toxicity and effects of lead on the heart are not completely understood. In this study we investigated the oxidative stress levels of lead toxicity and their effects on the tolerance and protection of the heart against ischemic diseases.

Methods:
Negative controls were not subjected to any treatment. Positive controls were subjected to 0.5% lead acetate in drinking water for 5 or 45 days. Hearts isolated from these rats were Langendorff perfused (n=6) and subjected to 30 minutes coronary occlusion and 30 minutes reperfusion. Control hearts were subjected only to ischemia reperfusion. Treatment was 3 cycles of 30 seconds left ventricle (LV) pacing alternated with 30 seconds right atrial (RA) pacing (pacing postconditioning, PPC). Left ventricular hemodynamics were computed by a data acquisition program. Infarct size was quantified by triphenyltetrazolium chloride (TTC) staining. Total antioxidants (TAS) and anti-oxidants (TOS) levels were evaluated using specific assay kits.

Results:
There were no significant difference between 5% lead acetated treatment for 5 days or 45 days on the tolerance of the heart to ischemic insult. Pacing postconditioning significantly ($p<0.05$) protected the 5 days lead-treated hearts. This protection was not seen in the 45 days lead-treated hearts. Interestingly the oxidant levels were significantly ($p<0.05$) higher in 5 days lead exposure compared to 45 days and untreated control. The levels of antioxidant were significantly lower ($p<0.05$) in 45 days lead exposure compared to the untreated control.

Conclusions:
Lead toxicity did not change the sensitivity of the heart to the ischemic insult. However, lead treatment for long periods abrogated postconditioning protection to the heart. The total oxidant level was significantly increased in 5 days lead exposed hearts and antioxidant level was significantly decreased in 45 days lead exposed hearts.

Key Words: Lead toxicity; Ischmia; Postconditioning
Funding Agency: College of Graduate Studies and grant number YM 02/13 from Research Administration, Kuwait University.

Physiology
Category: Basic Sciences

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The role of natriuretic peptides, nitric oxide and protein kinase G in the heart protection against ischemia reperfusion injury

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Introduction:
Brief periods of ventricular pacing during reperfusion phase (pacing-induced postconditioning, (PPC)) have been shown to protect the heart against ischemia reperfusion (I/R) injury. The aim of this study was to explore the role of natriuretic peptides (atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP)), protein kinase G (PKG) and nitric oxide (NO) in the protection of the heart against I/R injury and their effect on PPC.

Methods:
Langendorff perfused rat hearts (n=6) were subjected to 30 minutes coronary artery occlusion followed by 30 minutes reperfusion. PPC consisted of 3 episodes of 30 seconds left ventricular pacing alternated by 30 seconds right atrial pacing at reperfusion. Studied were control with only ischemia and reperfusion, PPC, PPC in combination with selective blockers of the ANP (H-[1,2,4]oxadiazole[4,3-a]quinoxalin-1-one (ODQ)), BNP (isatin) and NO (L-nitro-arginine-methylester (L-name)). Another sets of animals were treated with the agonists of ANP (ANP), BNP (Rat BNP-32), NO donor (S-nitroso-N-acetylpenicillamine (SNAP)) and PKG activator 8-(4-chlorophenylthio)-guanosine 3', 5'-cyclic monophosphate (CPT) at reperfusion. Hemodynamics were computed by a data acquisition program. Infarct size was determined using 2,3,5-Triphenyl-2H-tetrazolium chloride (TTC).

Results:
PPC significantly ($p<0.03$) improved cardiac hemodynamics and decreased the infarct size ($p<0.001$). The blockade of BNP and NO completely abrogated the protective effect of PPC. However, antagonism of ANP did affect the protection afforded by PPC. When applied exogenously ANP, BNP (Rat BNP-32), PKG activator and NO donor showed a significant ($P<0.03$) recovery in cardiac hemodynamics and a significant ($P<0.001$) decrease in the infarct size.

Conclusions:
Exogenous and endogenous BNP, NO and PKG protected the heart against I/R injury. However, ANP is protective when only infused at reperfusion.

Key Words: Ischemia Reperfusion; Naturalistic peptides; Postconditioning
Funding Agency: Kuwait University, Grant #MY 02/10

Physiology
Category: Basic Sciences

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11-beta-hydroxysteroid dehydrogenase-1 inhibition mediated intrauterine growth restriction parallels with altered expressions of cell cycle control genes in rat placentas

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Introduction:
Intrauterine growth restriction (IUGR) is one of the leading causes of neonatal deaths that occur worldwide. While maternal mechanistic changes responsible for IUGR are being unraveled, the placental factors contributing for poor fetal growth are not clear. The objective of the present study was to investigate placental cell cycle control genes in an experimentally induced model of IUGR.

Methods:
11-beta-hydroxysteroid dehydrogenase-1 (11HSD) was inhibited in pregnant Sprague-Dawley rats (N=5) by carbenoxolone administration (10 mg; ip) starting from gestational day 1 to 21. The fetuses and their respective placentas were collected on day 21 and weighed. The total RNA was extracted, reverse transcribed and the expressions of CDKN1A (p21), CDKN1B (p27), CTNNB1 (beta-catenin), CCND1 (cyclin D1), TP53 (p53), BCL2, and BAX were evaluated by RT-PCR according to established procedures in our laboratory. Data were analyzed by one way ANOVA and LSD post hoc test with significance level set at $P<0.05$.

Results:
Decreased maternal and fetal weights and increased placental weights ($P<0.05$) confirmed the induction of IUGR due to inhibition of 11HSD and up-regulated glucocorticoid levels. In placental basal zone (BZ), the expressions of CDKN1A and CCND1, not that of CDKN1B and CTNNB1, were decreased ($P<0.05$) and in labyrinth zone (LZ), the expressions of CDKN1B and CTNNB1, not that of CDKN1A and CCND1, were inhibited ($P<0.05$) indicating inhibited cell cycle control. Interestingly, in BZ, TP53 and BCL2, not BAX, were significantly expressed, but in LZ, the expression of TP53, not that of BCL2 or BAX, was inhibited indicating discordant effects on pro-apoptotic genes.

Conclusions:
Our results indicate that 11HSD deprivation-induced IUGR inhibits transcription of genes coding for the proteins necessary for cell cycle control and apoptosis. These altered pathways may be responsible for enhanced placental weight and may contribute for the induction of IUGR.

Key Words: Placenta; Cell cycle control, Apoptosis; Intrauterine growth restriction
Funding Agency: Kuwait University, Research Administration grant no. MY02/08

Physiology
Category: Graduate MSc (Basic Science)

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The anti-inflammatory effect of progesterone is dissociated from remyelination: a look at the maturation of oligodendrocyte progenitor cells

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Introduction:
Demyelinating diseases, such as multiple sclerosis, are characterized by a loss of myelin wrapping around axons of the nervous system and consequently a reduced axonal neurotransmission. The demyelinating lesions are associated with enhanced inflammatory response driven largely by resident microglia. Clinical strategies have been developed to dampen brain inflammatory response to promote remyelination. Remyelination requires induction of oligodendrocytes progenitor cells (OPC) and their differentiation into mature oligodendrocytes. In the present study, we investigated the role of progesterone on remyelination process as this steroid hormone has anti-inflammatory properties.

Methods:
Using a rat stereotaxic apparatus, 2 µl of either sterile saline or ethidium bromide (EB, 0.04%) solutions were injected into the corpus callosum of adult male rats. Each of these rat groups received daily injections of either oil or progesterone (5mg/kg). Rats were transcardially perfused with phosphate-buffered saline at 2, 7, 14 or 28 days post-EB injection. Myelin integrity and the lesion size were assessed using luxol fast blue staining. Immunofluorescent staining was used to detect OPC (NG2), mature oligodendrocytes (CC-1) and the microglia (Iba-1) at the site of the lesion.

Results:
Progesterone promoted a significant increase in the number of OPC at the site of the lesion and reduced inflammatory response (activated microglia). However, these cellular effects were not associated with maturation of OPC as neither mature oligodendrocytes, nor the size of the demyelinated lesions were significantly affected by progesterone treatment 14 and 28 days post-EB injection.

Conclusions:
These data suggest that progesterone promoted the recruitment of OPC to the demyelination site likely via its anti-inflammatory effect. However, the blunting of brain inflammatory response was dissociated from the process of maturation of oligodendrocytes.

Key Words: Oligodendrocytes; Myelin; Inflammation
Funding Agency: KU Research Sector grant # YM11/11 and Research Unit for Genomics, Proteomics and Cellomics Studies/Research Project No. SRUL02/13

Physiology
Category: Undergraduate

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Small blood vessels of the brain are surrounded by perivascular spaces: potential pathways for flow of brain interstitial fluid

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Introduction:
Accumulating evidence focus attention on perivascular spaces (PVS) as possible routes for a slow bulk flow of the interstitial fluid (ISF) of the brain towards the cerebrospinal fluid. However, how extensive PVS in the brain are remains unclear. The objective of this study was to explore if the PVS that are known to exist around larger blood vessels (Virchow-Robin spaces -VRS) extend further towards small blood vessels of the brain.

Methods:
Sprague-Dawley rats (n=6) were anesthetized with urethane (2g/kg, ip). Brains were fixed in 4% paraformaldehyde. Frozen sections (30um) were double immunostained using rabbit polyclonal anti-laminin (to stain pia mater) and mouse monoclonal anti - a-smooth muscle actin (SMA, to stain smooth muscle cells/pericytes) primary antibodies and appropriate secondary antibodies conjugated with cyanine dye Cy3 or fluorescein isothiocyanate. Sections were analyzed in LSM 510 Meta Confocal Laser Scanning Microscope.

Results:
Laminin stained pia mater was observed in all blood vessels (arterioles, venules and capillaries). There were clear circular gaps between blood vessels (SMA positive) and pia mater (laminin positive), which denotes perivascular space. Surprisingly, small clear gaps were notable between small arterioles and laminin-stained pia mater, indicating the presence of perivascular spaces. There were several circular structures, < 10 um in diameter, positive for laminin, but negative for SMA, which may be pial sheaths around SMA-negative capillaries.

Conclusions:
The data indicate that the pial invaginations that surround arteries and veins often extend further towards capillaries and form continuous perivascular space around small arterioles. These perivascular spaces could represent one of the routes for the bulk flow of the ISF towards the CSF.
Acknowledgements: We acknowledge the Research Core Facility, (KU Project SRUL 02/13) for providing confocal microscopy, and Jucy Gabriel for technical help.

Key Words: Brain interstitial fluid; Perivascular space; Laminin and alpha-smooth muscle actin
Funding Agency: Sunday, September 11, 2011

Physiology
Category: Undergraduate

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Impact of prenatal immune stress on remyelination during adulthood

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Introduction:
Early life immune stress can cause long lasting alterations in brain function and plasticity. A large body of data showed that the activation of maternal immune system has a long lasting impact on the offspring's brain development. However the impact of prenatal immune stress on myelin integrity has not yet been explored. In the present study, we explored whether prenatal immune stress alters the response of the central nervous system to a demyelination injury during adulthood.

Methods:
Pregnant Sprague Dawely rats were injected with either sterile saline solution or lipopolysaccharide (outer coat of Gram- bacteria; LPS) solution (100 µg/kg, i.p.) at gestation day 12 (GD12). Two months old male offspring received a stereotaxic injection of 2µl of the gliotoxin ethidium bromide (EB, 0.04%) into their corpora callosa. They were sacrificed 7 days post-EB injection, a time corresponding to the peak of demyelination. Assessment of the demyelination lesion size was performed using luxol fast blue staining, while myelinating cells (mature oligodendrocytes) were explored using immunofluorescent staining (CC1).

Results:
Rats offspring of mothers given LPS at GD12 (n=10) had a significantly reduced demyelination lesion size (from 0.857 mm^2 in saline-injected offspring to 0.491 mm2 in LPS-injected offspring, p=0.0445) compared to those born to mothers given saline (n=4). Interestingly this decrease in lesion size was also associated with an increase in the number of mature myelinating oligodendrocytes (p=0.031) at the site of the demyelinating lesion.

Conclusions:
These findings strongly suggest that the activation of maternal immune system has long lasting impact on the offspring's response to demyelination, likely by promoting enhanced levels of mature oligodendrocytes at the site of the lesion.

Key Words: Oligodendrocytes; Lipopolysaccharide; Microglia
Funding Agency: None

Physiology
Category: Basic Sciences

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Heart rate, MET levels, and glood pressure responses to stair climbing in females and males

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Introduction:
The Gulf Cooperation Council Countries have very high percentages of non-communicable diseases in the world. Namely, obesity and diabetes. As the United Nations identified four risk factors for these chronic diseases, in which inactivity is one of them. Therefore, the aim of our study was to explore whether climbing the stairs is safe to be used as a mode of physical activity especially for exercise prescription.

Methods:
A total of 11 females (F) with mean age of 25.6 ±5.2, and 8 males (M) with mean age of 33.3 ±2.3 years old participated in the study. Heart rate (HR) and energy expenditure in metabolic equivalent (MET) were measured or calculated for all subjects in each floor until the fifth floor. Blood pressure (BP) were measured in ground floor and in the fifth floor only.

Results:
No difference in resting HR were found between F and M. A significant difference in HR was shown in all four stair levels between the two sex groups. The HR as percentage of estimated maximal at the different stair levels were 62.9%, 67.5%, 69.9%, & 73.3% for M, and were 67%, 73.6, 78.0%, & 81.3% for F. Systolic BP increased significantly between the ground and the fifth floors in both F and M. The MET levels increased as subjects ascended the stairs. Only at the fifth floor, there was a significant difference between F and M. Comparing MET between floors, there were significant and gradual increases at all five stair levels in F. In M, the increases were only significant between the first two levels.

Conclusions:
Stairs may be safely used for exercise prescription as it was demonstrated. Climbing stairs may safely be used as a mode of exercise and physical activity especially for those who have no access or cannot afford joining exercise and sports clubs or facilities.

Key Words: Heart Rate; Blood Pressure; Stairs
Funding Agency: None

Physiology
Category: Basic Sciences

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Characterization of gallbladder stone, bile and tissue using time resolved fluorescence spectroscopy

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Introduction:
Laser-induced lithotripsy of gallbladder stone has the potential in expanding significantly with laser system, endoscopes, retrieval devices and modern imaging devices. The laser efficiency is the key parameter, such as pulse power, pulse width, and number of pulses, are specific for different types of stones. In addition, a guiding tool will be used to assist in discriminating the stone, the bile and the surrounding tissue. Time Resolved Fluorescence Spectroscopy (TRFS) can accommodate all these parameters and could be a new milestone in laser based lithotripsy.

Methods:
A femtosecond laser (wavelength = 400 nm) was used in this study. A bifurcated fiber was used for excitation as well as for fluorescence signal collection. The collected laser induced fluorescence light was then dispersed by a spectrometer, which is coupled to the streak camera detection system. Time resolved spectral data of the fluorescence signal was recorded to the computer for further analysis. For wavelength-domain comparison of the stone fluorescence signal, we used Ocean optics spectrometer. We also used inductively coupled plasma system to identity the stone chemical composition quantitatively.

Results:
Spectral- and time-resolved features were used to develop a new classification algorithm. The algorithm can be used to characterize gallbladder stones, and discriminate stone, bile and tissue. Moreover, the algorithm can be extended to set the most appropriate parameters for the laser lithotripsy, which is needed by the physicians in real-time stone fragmentation.

Conclusions:
This study demonstrates TRFS capable of characterizing and optimizing parameters in laser based lithotripsy. It can be one of the essential guiding tools in modern laser lithotripsy. Further research should be carried out to develop a single probe system to identify the type of stone and automatically set the optimum laser parameters in real-time laser lithotripsy of gallbladder stones

Key Words: Fluorescence Spectroscopy; Gallbladder stone; Femtosecond laser
Funding Agency: None

Psychology
Category: Basic Sciences

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Gender differences in neuroticism: A factorial Study

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Introduction:
Neuroticism (N) refers to six facets: Depression (sadness, guilt, hopelessness), Anxiety (fear, worry, tension), Angry Hostility (anger, frustration, bitterness), Self-Consciousness (shame, embarrassment, social discomfort), Impulsiveness (difficulty controlling cravings and urges, immoderation), and Vulnerability (stress reactivity). The research on personality factors shows a gender difference specifically in neuroticism. Therefore, the goal of the study is to determine the association between gender and neuroticism using the exploratory factor procedures with the faceted inventory of the NEO PI-R.

Methods:
The participants were 2109 (900 males & 1209 females) first year Kuwait University students. The genders were matched in age (20.19±1.56 & 20.67±1.25, t=0.94, p>.05). The Arabic versions inventory of the Big Five is Costa and McCrae's NEO PI-R (N) and demographic surveys were administered to participants in the class. Independent Sample t Test, the exploratory factor analysis, correlation matrices, are used in this study.

Results:
Internal consistency of NEO PI-R (N) was satisfactory for males and females (Cronbach's alpha = .71, .77). Females scored significantly higher on Anxiety (f=5.79, p<.001), Anger Hostility (f=3.01, p<.001), Depression (f=4.01, p<.001), Self-Consciousness (f=2.76, p<.001), Impulsiveness (f=2.64, p<.001), & Vulnerability (f=4.08, p<.001). A principal-axis factor analysis with oblique rotation of (N) faceted suggested one factor, accounting for 57.70% of males and 59.20% for females. Moreover, factor analysis re-classified the Neuroticism six facets for males (Vulnerability, Angry Hostility, Depression, Self-Consciousness, and Anxiety & Impulsiveness) while for females (Vulnerability, Depression, Angry Hostility, Impulsiveness, Self-Consciousness, & Anxiety).

Conclusions:
This study provides evidence for the association between gender and neuroticism and requires replication with clinical samples.

Key Words: Gender Differences; Neuroticism; Factorial Study
Funding Agency: None

Psychology
Category: Basic Sciences

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Psychometric properties of the arabic version of the Beck Anxiety Inventory (BAI) in Kuwait.

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Introduction:
The Beck Anxiety Index (BAI) is commonly used to measure the level of anxiety among adolescents and adults. A large number of studies in the West have shown interest in the psychometric characteristics of the BAI with various populations, specifically clinical and non-clinical population. This study aims at examining psychometric properties of BAI among Kuwaiti undergraduates.

Methods:
Data was collected from (612) Kuwaitis including (202) males and (416) females who studied at Kuwait University. The mean age of the sample was (20.93±2.52) years. The BAI has been administered in paper and-pencil form that consisted of 21 items (4-point Likert scale).

Results:
The exploratory factor analysis for the BAI showed the four subtest factors (neurophysiology, subjective anxiety, panic & autonomic) to load together 0.69. Reliability was confirmed (alpha coefficients: 0.90), and (test-retest correlation coefficients = 0.79). The BAI was positively correlated with the Kuwait University Anxiety Scale KUAS (r=0.54), Beck Depression Inventory-II BDI-II (r=0.43), Pessimism (r=0.30), and the Beck Hopelessness Scale BHS (r=0.39). The BAI score ranging from 1 to 50 had a mean (22.50 ±11.41). Furthermore, a significant gender difference in the BAI was found (f=8.57, p>.001) in which females scored higher means than males.

Conclusions:
This study provided evidence for the reliability and validity of the Arabic BAI for Kuwaiti undergraduates. The strengths of the 21 core items of the BAI include their brevity and ease of scoring, which make them practical to use in both counselling and research.

Key Words: BAI; Anxiety; Kuwait
Funding Agency: None

Research Methodology
Category: Graduate (Resident)

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Publication rate of abstracts presented at the health sciences center poster conference of Kuwait University between years 2006 and 2010

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Introduction:
Publication of abstracts presented at scientific conferences into full papers is considered as an indicator of the quality of the conference. Authors aim to measure the publication rate of abstracts presented at the annual Health Sciences Center's Poster Conference (HSCPC) of Kuwait University.

Methods:
During July 2013, PubMed search was done for abstracts presented at the HSCPC from years 2006 to 2010. We did an initial search of PubMed for the titles of all the abstracts presented during that period to document their publication in PubMed-indexed journals. If the title of the published paper, authors and abstract contained substantial similarities as those published in the HSCPC, the match was considered successful. Moreover, to ensure not missing any published paper, a search using the abstract's keywords with the name of each author was done when no match was found. Descriptive data were analyzed, and chi-square test was used to examine the association between abstracts' features and their publication using p-value of <0.05 as the cut-off level of significance.

Results:
A total of 1448 abstracts were included. Only 260 (18.0%) abstracts were published as full papers. Statistically significant higher publication rate was for abstracts from authors not enrolled in educational programs during the time of the research (p = 0.003), cohort studies (p = <0.001), and Psychiatry-related topics (p = <0.001), in which 19.7%, 50.0% and 50.0% abstracts of these categories were published, respectively.

Conclusions:
The publication rate in PubMed-indexed journals of abstracts presented at HSCPC was very low. Reasons behind this low rate should be addressed in order to improve the quality of this scientific meeting.

Key Words: Publication; Conference; Kuwait
Funding Agency: None

Surgery
Category: Basic Sciences

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The effect of EGCG on uncoupling protein 2 in acute liver injury

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Introduction:
The uncoupling protein 2, (UCP2) is an important protein that is involved in the mitochondrial production of oxygen free radicals. The aim of this study is to investigate the effect of Epigallocatechin gallate (EGCG) which is a major catechin contained in tea on acute liver injury.

Methods:
Twenty seven male Wistar rats were divided into three groups: control group (group A= 9 rats), acute liver injury (group B= 9 rats), acute liver failure group given EGCG two weeks prior to the induction by acute liver injury (group C= 9 rats). Acute liver injury was induced by the intraperitoneal injection of Thioacetamide TAA. The expression of liver UCP2 mRNA was detected by reverse transcription polymerase chain reaction. The levels of interleukins (IL) 6,10,12 and 18 were detected in the liver using enzyme linked immunosorbent assay. ANOVA test was used to compare data between groups. Liver histology was examined with Hematoxylin and eosin staining (H&E).

Results:
The expression of UCP2 in the liver of group C was the lowest when compared to other groups ($p \leq 0.005$).
There were no statistical differences between the levels of IL10 and IL18 between the groups. IL6 and IL12 levels were lowest in group C ($p \leq 0.005$). H&E staining showed a reduction in liver injury in group C when compared to group B.

Conclusions:
UCP2 is down regulated by EGCG. This could explain the beneficial effects of EGCG on acute liver injury.

Key Words: EGCG; UCP2; Hepatitis
Funding Agency: RIG

Surgery
Category: Clinical

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Hormonal and growth factor bioassay assessment in patients with long bone fractures and concurrent head or spinal cord injury

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Introduction:
The mechanism responsible for the clinical observation of accelerated healing of long bone fractures (LBF) in patients with concurrent head or spinal cord injury is not known. The aim of this study is to compare the serum levels of some hormones and growth factors in patients with LBF and concurrent head or spinal cord injuries with those with LBF only.

Methods:
Serum levels of parathyroid hormone (iPT), growth hormone, leptin, PDGF, adrenaline, activin A, human interleukin-1, cortisol, noradrenaline and VEGF were compared in 3 groups of patients: Group A were patients with severe head injuries (GCS of 8 or less) with concurrent LBF, Group B were patients with spinal cord injuries with paraplegia or quadriplegia and LBF and Group C were patients with LBFonly. Patients were matched for age, gender, extent of injuries and all LBF treated by internal fixation. Patients with significant pre-trauma comorbidities were excluded from the study. Serum samples were obtained at the following time points in the patients: within 24 hours of injury, then 7, 14, 21, 28 and 42 days after the injuries.

Results:
50,13 and 60 patients were recruited into groups A, B and C respectively. Patients in groups A and B had statistically significant higher levels of iPT and growth hormone compared to patients in group C ($p<0.001$). In all groups of patients the iPT and growth hormone levels declined and normalized over the next 6 weeks. Levels of all the other analytes listed above yielded inconsistent results.

Conclusions:
These results suggest that parathyroid and growth hormones may be part of the trophic substances released in massive quantities into the circulation resulting in stimulation of callus formation seen in patients with head and spinal cord injuries combined with LBF. Our findings suggest a possibility of hormonal mechanism to explain the accelerated healing of LBF seen in patients with associated severe head or spinal cord injuries.

Key Words: long bone fractures; brain spinal cord injury; hormones
Funding Agency: Kuwait Foundation for Advancement of Sciences Grant 2010/1302/04

Surgery
Category: Clinical

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The effect of head or spinal cord injuries on the healing rate of concomitant long bone fractures

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Introduction:
There is some clinical evidence to suggest that long bone fractures heal more rapidly in patients with associated head and spinal cord injuries. The aim of this study is to compare the healing rate and the amount of uniting callus formed in the long bones of patients with long bone fractures and concomitant head or spinal cord injuries with those with long bone fractures only.

Methods:
The mean time to union, healing rate of fractures, the amount of uniting callus formed were compared in three groups of patients: Group A were patients with severe head injuries with long bones fractures, Group B were patients with spinal cord injuries with paraplegia or quadriplegia and long bone fractures and Group C were patients with long bone fractures only. All fractures were internally fixed.

Results:
50, 13 and 60 patients were recruited into groups A, B and C respectively. The mean(range) time to union of long bone fractures in groups A, B and C patients was 6.9 (3-20), 6.2 (3-7.7) and 22.4 (13-41) weeks respectively; (A or B versus C: $p<0.001$). The mean(range) healing rate of long bone fractures in groups A, B and C patients was 4.5(0.2-10.6), 4.7 (2.6-7.5) and 0.38(0.11- 1) mm/ week respectively; (A or B versus C: $p<0.001$). The mean(range) thickness of callus formed at fracture sites of long bone fractures in groups A, B and C patients was 26(4-48), 29(10-48) and 8.1(2-20) mm respectively; (A or B versus C: $p<0.001$). There were no cases of delayed or nonunion in groups A and B patients. 5 of 69 fractures (7.3%) had delayed union in group C while 9/69 (13%) fractures in group C had nonunion.

Conclusions:
These results suggests that long bone fractures in patients with head or spinal cord injury heal faster and with more florid callus formation compared to those in patients with long bone fractures only and suggest a possibility of a neural or combined neuro- hormonal mechanism to explain it.

Key Words: long bone fractures; brain spinal cord injury; fracture healing rate
Funding Agency: Kuwait Foundation for Advancement of Sciences Grant 2010/1302/04

Surgery and Transplantation
Category: Clinical

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An audit of surgical operation notes in two general governmental hospitals in Kuwait

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Introduction:
The operative findings and post operative plans provide vital means of communication between health professionals. The objective of this study is to evaluate the quality and the completeness of operative notes document.

Methods:
A descriptive cross-sectional design with a quantitative approach was applied for the purpose of this study. The operative notes of patients underwent surgical operation at two general hospitals between June and September 2012 were reviewed. In the first part of the study, all selected operative notes were analyzed and audited taking the guidelines published by the Royal College of Surgeons of England as the reference. The second part of the study aimed to determine the completeness of operative sheet published by ministry of health of Kuwait which is coded (MR10), a check-list form was designed for this purpose.

Results:
A total number of 340 operative notes were analyzed. 100(29.4%) notes were written by assistant registrars, 158(46.5%) by registrars, 46(13.5%) by senior registrars, 22(6.5%) by specialists, and only 14(4.1%) by consultants. Date and time, type of surgery, name of the operating surgeon were not mentioned in 194(57.1%), 306(90%) and 24(7.1%) notes respectively.
Details of closure technique was missed in 202(59.4%) notes. Operative findings was not documented in 115(33.8%) notes, of which 63(54.76%) were written by assistant registrars, 42(36.5%) were missed by registrars and 8 (7.0%) were missed by senior registrars. Details of closure technique was not documented in operative notes by 82(40.6%) assistant registrars, 73(36.1%) registrars, 27(13.4%) senior registrars, 9(4.5%) specialists and 11(5.4%) consultants

Conclusions:
Most of the important operation details were missed by junior surgeons who did not had sufficient knowledge of the surgical procedures and the technique of writing, which necessitate training courses and implementation of clear guidelines.

Key Words: Audit; Operation notes; Good Surgical Practice
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Sirolimus rescue therapy after acute rejection in renal transplant recipients longterm follow up

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Hamed Al-Essa organ transplant center

Introduction:
Background: Conversion from calcineurine inhibitors (CNIs) to sirolimus (SRL) is proved to be effective in improving long-term graft outcome. SRL treatment of high risk renal transplant recipient (RTR) is still under investigation.
Aim: We studied the long-term effects of conversion from CNI to SRL as rescue therapy on RTR after treatment of biopsy proven acute rejections (BPAR).

Methods:
RTR converted from CNI, mycophenolate mofetil (MMF) as 2gm daily and steroid to SRL, MMF and steroid after treatment of BPAR were studied.

Results:
30 candidates were maintained on CNIs (24 were on cyclosporine-A and 6 on tacrolimus) after receiving anti-thymocyte globulin (80%) or basiliximab (13.3%) induction therapy. Mean follow-up period post-SRL was 43.46±17.9 months. The overall mean age was 35.1±13.5 y. Patients with multiple co-morbid conditions, black race (63.3%) and obesity (33.3% with BMI >30) were not excluded from the study. Mean time to convert to SRL was 10±18.8 months post-transplantation. Pre-conversion, all patients were reported to have BPAR with 16.7% steroid-resistant and 10% antibody mediated rejection episodes. Post-SRL rejection episodes were reported in 20% with 10% resistance to steroid treatment and 6.6% antibody mediated. Leucopenia, hypercholesterolemia and hypertriglyceridemia increased significantly post-SRL (p 0.031, 0.0001 and 0.007 respectively). Graft and patient survival were 100 % each. There were significant improvements in estimated creatinine clearance from 58±22.1to 69.6±22.2 ml/min/1.7^2 (MDRD formula) at one year (p 0.001) and to 72.9 ±21.9 ml/min/1.7^2 by the end of the study (p <0.0001). SRL had to be discontinued in 33.1% of candidates mainly due to its adverse effects or planning pregnancy (10%).

Conclusions:
Conversion to SRL as rescue therapy after treatment of BPAR is proved to be effective as a CNI free regimen for high risk RTR during long-term follow up.

Key Words: Sirolimus; Immunosuppression; Renal transplant
Funding Agency: None

Original Research Case Report By Subject Area

Dentistry
Category: Clinical

167

Plasma Cell Gingivitis: A Rare Case Report

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CASE REPORT

Background:
Plasma cell gingivitis (PCG) is a rare benign condition of the gingiva. It is marked by a dense infiltrate of normal plasma cells. Though the exact etiology is not known, allergic reaction seems to be a plausible explanation.

Case summary:
We present a case of 12-year-old Kuwaiti girl presented to Amiri Dental Center on August 2013 with swollen gingivae. It was asymptomatic initially, later she started to experienced discomfort and bleeding on eating and toothbrushing. Medical history was non-contributory. Oral examination showed sharply demarcated erythematous and edematous gingival overgrowth localized to maxillary arch. The lesion was extending to the mucogingival junction on the left side. Panoramic image was unremarkable. Oral hygiene was good. Differential diagnosis was diverse and series of laboratory tests were carried out and all were negative to known granulomatous diseases, leukemia and allergy. Oral rinse dexamethasone (0.5mg/5ml) was prescribed for 2 weeks. Subsequent reduction in the size of gingival growth was striking. Gingivectomy was carried out after 5-day-discontinuation of the steroid. Histologically, it revealed diffuse and massive infiltration of plasma cells into sub-epithelial connective tissue. Immunohistochemistry stain of plasma cell marked its reactive process. After 3 months of follow up, the gingival condition were stable and no evidence of recurrence.

Conclusions:
PCG may mimic more serious conditions. Plaque control and periodontal surgery alone will not cure this disease as long as the causative agent has not identified. Hence, prognostic state is vague and long-term follow up is recommended. Topical steroid use in unavoidable in some cases.

Key Words: Gingival overgrowth; Plasma cell; Steroid

Dentistry
Category: Clinical

168

Micro-marsupialization: minimally invasive method for treatment of sublingual ranula

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CASE REPORT

Background:
Ranula is a pseudocyst that is caused by the extravasation of mucus from the sublingual gland. Trauma or obstruction of the sublingual gland results in the accumulation of saliva in the surrounding tissues followed by an inflammatory reaction leading to the formation of a pseudocyst wall. Management of ranulas include marsupialization, laser ablation, cryotherapy, OK-432 sclerotherapy and excision of the lesion with or without sublingual gland removal.
The classic marsupialization or simple excision of the pseudocyst leads to unacceptable high recurrence rate of up to 67%. Sublingual gland excision together with dissection of the pseudocyst had much more favorable recurrence rates of 1-2%. However, the rate of tongue paresthesia resulting from dissection in the vicinity of lingual nerve increased from 2.1% to 11.6%.
The micro-marsupialization as an alternative to traditional surgical methods was described by Morton and Bartley in 1995 and modified subsequently by several authors.

Case summary:
We treated 2 patients with large sublingual ranulas by aspiration of mucous content followed by placing multiple thick sutures through the dome of the pseudocyst. These sutures were left in place for 1 month, which led to in-growth of epithelium and formation of several new draining path tracks. Both patients tolerated the procedure well and no recurrence or deleterious side effects were observed during 6 months follow-up.

Conclusions:
Micro-marsupialization is simple and safe technique applicable under topical or local anesthesia in a cooperative patient. It obviates the danger of lingual nerve injury associated with radical surgical treatment while providing minimal recurrence rates.

Key Words: ranula; marsupialization; lingual nerve

Forensic Medicine
Category: Clinical

169

Superior Blowout Fracture of the Orbit: The Blowup Fracture.

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CASE REPORT

Background:
Blowout fractures of the Orbit occur when direct blunt force is applied to the globe and orbit by an object of larger diameter than the globe. This may involve the bones of the eye socket leading to fracture of the orbital floor, walls, or much less common orbital roof "The blowup fracture".

Case summary:
Two principal mechanisms have been proposed to explain blowout fractures, the buckling and the hydraulic mechanisms caused, respectively, by trauma to the orbital rim and the globe of the eye. We describe a Twenty-one-year-old dark skinny male who sustained a blowup fracture of the right orbital roof without an orbital rim fracture. External examination revealed right periorbital ecchymosis and edema, and no visible displacement of the bone was apparent on plain X-ray film. Autopsy showed a fracture of the midportion of the right orbital roof with displacement of the fracture fragment into the anterior cranial fossa and herniation of the intraorbital fat and the globe through the fracture. Histologic sections of the brain and meninges revealed antemortem fresh meningeal hemorrhage with bruising of the base of the right frontal lobe adjacent to the site of fracture.

Conclusion:
We present the autopsy findings associated with a rare fracture of the superior orbital roof: the blowup fracture to evaluate the role of such injuries in causing death even with minimal external signs.

Key Words: Forensic; Blowout fracture Orbit; Blowup Fracture

Medicine
Category: Graduate (Resident)

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Bartter Syndrome: A Case report

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CASE REPORT

Background:
Bartter syndrome is an uncommon inherited condition resulting from abnormalities of chloride channels at the thick ascending lobe of Henle.The classical Bartter syndrome occurs in early childhood with polyuria, polydipsia, vomiting, constipation, salt craving, and a tendency to dehydration.We are reporting a case of Bartter syndrome diagnosed early in the neonatal period by characteristic deranged biochemical profile in spite of absence of antenatal or postnatal medical problems

Case summary:
A male child who was completely healthy and admitted to hospital at the age four months with upper respiratory tract infection and mild respiratory distress. Since the family has two children affected with Bartters syndrome, this patient underwent complete biochemistry work up to look up for the condition. Clinically he was thriving well and had no signs of dehydration or electrolyte disturbance. He had initial laboratory finding of hypokalemia, hypochloremia and metabolic alkalosis. Then the diagnosis was confirmed by raised plasma renin level and plasma aldosterone level. Regarding his family history, two out of five siblings were affected, and both of them were symptomatic when they were diagnosed and had biochemical profile changes.
Our patient is now on replacement treatment and following up with Pediatrics outpatient department. In the last visit when he was nine months, of age, he was growing well and symptom free.

Conclusion:
Although Bartter syndrome is an uncommon condition, it should be suspected in case of deranged biochemical profile with hypochloremia, hypokalemia and metabolic alkalosis. Even with the absence of symptoms and signs in such patients, physician must further investigate the renin and aldosterone level. Having the disease in the family is justified to screen other members with basic biochemical profile. Early recognition and appropriate intervention with replacement or medical therapy aid better outcome of the disease and reduce the morbidity

Key Words: Bartter syndrome; Hypochloremia, hypokalemia and metabolic alkalosis; Asymptomatic, absence of signs

Medicine
Category: Clinical

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Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Diagnosis and Treatment: Two Case Reports from Kuwait

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CASE REPORT

Background:
MERS-CoV routine screening is based on the detection of viral RNA upstream of the E protein gene (upE) by real-time reverse-transcription polymerase chain reaction (rRT-PCR) with confirmation by detection of open reading frame 1a (orf 1a). MERC-CoV has no proven therapies except for general supportive care. Based on literature review, monotherapy is the first line therapy.

Case summary:
Patient 1: A 47 year old Kuwaiti male, with known co-morbidities, presented with lower respiratory tract (LRT) symptoms with travel history to Saudi Arabia. Patient rapidly progressed to acute respiratory distress syndrome (ARDS) and acute renal failure. Endotracheal secretion (ET) and bronchoalveolarlavage (BAL) were screened positive and confirmed for MERS-CoV. The MERS-CoV viral load using upE assay was lower compared to orf 1a assay. Patient was started on peg-INF α 1a subcutaneously and a low dose of oral ribavirin. Patient improved gradually and combination treatment discontinued following two consecutive MERS-CoV negative ET samples.
Patient 2:A 52 year old Kuwaiti male with known co-morbidities presented with LRT symptoms and acute renal failure was admitted with recent history of travel to Saudi Arabia. A BAL sample was screened and confirmed for MERS-CoV. Patient was started on peg-INF α2b. He deteriorated; IVIG was added to the second dose of peg-INF α2b, followed by oral ribavirin. As he improved, all MERS-CoV treatment combination was discontinued. However, the patient's ET samples showed fluctuations of MERS-CoV viral load, with upE assay showing lower viral loads and disappearing earlier compared to orf 1a assay. Eventually, patient ET samples were MERS-CoV negative by both assays.

Conclusions:
- ORF 1a assays were found to be more sensitive in gauging the viral loads during the management of these two particular patients compared to upE.
- Treatment with peg-INF α plus a low dose of ribavirin is recommended instead of the current recommendation.

Key Words: MERS-CoV; upE and orf 1a; peg-INF and ribavirin

Medicine
Category: Clinical

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Thrombocytosis and cerebral haemorrhage

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CASE REPORT

Background:
intracerebral hemorrhage occurs when a diseased blood vessel within the brain bursts, allowing blood to leak inside the brain. The sudden increase in pressure within the brain can cause damage to the brain cells surrounding the blood. If the amount of blood increases rapidly, the sudden buildup in pressure can lead to unconsciousness or death.

Case summary:
69-year old gentleman, with past history of hypertension, chronic kidney disease, essential thrombocytosis of unknown clear cause, admitted with left sided weakness. On examination he was conscious, oriented, blood pressure 170/50, motor power 2/5 and left extensor plantar response. Both pupils were equal and reactive to light. Computerized tomography scan of the brain done and showed right parieto-temporal haematoma surrounded by oedema, with positive mass effect in the form of compression of the right basal ganglia, right thalamus, 3rd and right lateral ventricle. There was slight midline shift to the left side by about 6mm. The patient was given dexamethasone and mannitol and showed good recovery.Follow up computerized tomography scan of the brain showed minimal increase in size, midline shift as well as the surrounding oedema.Previous investigations done for the essential thrombocytosis in the form of bone marrow biopsy which showed active bone marrow. JACK-2 was negative.

Conclusion:
Thrombocytosis is a condition in which there is an excessive number of platelets that can form a clot. With the presence of platelet dysfunction and high blood pressure, cerebral haemorrhage can occur. So prompt treatment of thrombocytosis and good control of blood pressure can prevent serious stroke in the future.

Key Words: Stroke; Thrombocytosis; Haemorrhage

Medicine
Category: Graduate (Resident)

173

Mediastinal seminoma

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CASE REPORT

Background:
Gonadal cell tumours (GCT) commonly occur in the gonads. However, 2-5% of them arise in extragonadal regions, preferentially in midline structures such as the mediastinum, retroperitoneum, pineal gland and sacral area. Histologically, extragonadal GCT are categorized into seminomas and nonseminomatous GCTs. In this case report, we describe a rare case of mediatinal seminoma in a young male diagnosed and treated in Kuwait.

Case summary:
Mr.A.A. is a previously healthy 19 year old Kuwaiti gentleman who was admitted to Mubarak Al-Kabeer hospital, department of internal medicine, complaining of a 2 day history of pleuritic chest pain, abdominal pain, fever and shortness of breath. In addition, he also had a 1 week history of night sweats and 1 month history of unintentional weight loss (not quantified). A chest x-ray performed in the casualty prior to admission revealed a large right lung/mediastinal mass. On examination, the patient's vital signs and all system examination, including lymph node and genital examinations, were unremarkable. Investigations revealed an elevated LDH. His CT chest confirmed the presence of a huge anterior mediastinal mass. The patient then underwent CT guided core needle biopsy of of this mediastinal mass, which revealed a malignant thymic germ cell tumour (seminoma). Tumour marker beta-human chorionic gonadotropin was found to be elevated. The patient also underwent an ultrasound of the testes which failed to reveal any primary tumor or suspicious mass. Prior to the histopathology report, the patient had been initially managed with IV Rocephin 2mg, Klacid 500mg PO and prednisone 40g OD. However, these medications were stopped after diagnosis of mediastinal seminoma was made and the patient was transferred to Kuwait Cancer Control Center for treatment options.

Conclusion:
Although this case is rare, seminoma should be considered in the differential diagnosis of a mediastinal mass, even in the absence of testicular lesions.

Key Words: mediastinal seminoma; mediastinal mass; germ cell tumour

Medicine
Category: Graduate (Resident)

174

Atrial myxoma presenting with symptoms of palpitation in a 55 year-old caucasian male

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CASE REPORT

Background:
Atrial myxomas are the most common primary cardiac tumors. They are usually small or moderate in size by the time of the diagnosis, exhibiting nonspecific cardiac or systemic symptoms, and are most frequently soft and friable without microscopic signs of ossification. We describe herein rare case of a large left atrial myxoma with hemorrhage inside the tumor.

Case summary:
A 58-year-old male with history of hypertension , was referred to the cardiology clinic because of palpation of 2 months duration. An ECG was done which showed normal sinus rhythm, left ventricular hypertrophy and infrequent PVC's. An echo-cardiography was done to rule out hypertensive heart disease. A 4x4 cm mobile mass was seen in the left atrium attached to the inter atrial septum and protruding into the left ventricle. The patient was referred to the cardiac surgeon, and a coronary angiography was done prior to the surgery revealing normal coronaries. The mass was excised and pathological examination revealed a benign atrial tumor (myxoma) measuring 5 x 4 cm with heamorrhage within the mass and a gelatinous capsule at the top of the mass

Conclusion:
We consider our case as extremely rare because of the asymptomatic course despite the large size of the tumor, with obstruction of the mitral orifice

Key Words: Palpitaion; Left atrial myxoma; Surgical removal

Medicine
Category: Clinical

175

Right atrial thrombus in a 50 years old female removed surgically

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CASE REPORT

Background:
Right atrial thrombi may develop within the right atrium or may have peripheral venous origins that, on their way to the final destination site lodge in, right atrium. Right atrial thrombosis is classified as two type: A (mobile, thin) and B (non mobile and attached to atrial wall) that they are probably of cardiac origin due to local pathology, indwelling catheter, atrial fibrillation, stasis, rheumatological or hematological disease like protein C or S deficiency.

Case summary:
A female patient, 50 years old, with history of hypertension and bronchial asthma and recent hospitalization for calcular cholecystitis presented to the emergency room with history of sudden onset of shortness of breathing with chest pain. ECG showed sinus tachycardia with non specific ST-T changes and cardiac markers were mildly elevated. She was admitted to the CCU as a case of acute coronary syndrome. D -Dimer was done which was high (2000 ng) Routine echo cardiography revealed a large mobile mass in the right atrium measuring 5 x 2 cm differential diagnosis was right atrial thrombus versus right atria myxoma. Lower limb venous Dupplex revealed recanalized DVT of the right popliteal vein. The patient was referred for Surgical excision due to size and mobility of the mass. Surgical excision was done revealing a large thrombus 12 x 2 cm extending from the inferior venae cava and filling the right atrium.

Conclusion:
We consider our case as extremely rare because of the size and shape of the thombus resembling an atrial myxoma

Key Words: Right atrial mass; Thrombus; Surgical removal

Medicine
Category: Clinical

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Severe unconjugated hyperbilrubinemia: Gilbert syndrome is possible

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CASE REPORT

Background:
Gilbert syndrome is benign, often familial condition characterized by recurrent but asymptomatic mild unconjugated hyperbilirubinemia in the absence of haemolysis or underlying liver disease. We present an unusual case of Gilbert presented with sever symptomatic unconjugated hyperbilirubinemia.

Case summary:
A 15-year-old previously healthy girl presented with complaints of anorexia, abdominal discomfort, yellowish discolouration of the eyes and dark urine over the past 2 weeks. There was no history of fever prior to onset of jaundice. She gave history of receiving fluconazole 150mg once weekly for 6 weeks for scalp fungal infection .Over the last two weeks she was on special dietary regimen for weight loss. General physical examination revealed sever jaundice and no pallor. Abdominal examination did not show any organomegaly. Routine laboratory work-up showed sever unconjugated hyperbilirubinemia (Total bilirubin 181.8umol/L (normal range 3-34 umol/L), indirect bilirubin 174.2 umol/L. Liver enzymes, serum albumin, prothrombin concentration and serum ammonia were within normal limits. Apart from mild microcytic hypochromic anaemia (Haemoglobin: 11.4 g/dL), other CBC parameters were within normal. Serum LDH and coomb's test were normal. The patient was maintained on proper IV fluid and normal caloric diet allowed .Next day after admission she was dramatically improved and her postprandial levels of bilirubin were within the normal range (Total bilirubin 22.5umol/L and indirect bilirubin 18.9 umol/L).

Conclusion:
Gilbert's syndrome should be considered to the differential of severe unconjugated hyperbilirubinemia.

Key Words: Gilbert's syndrome; Unconjugated hyperbilirubinemia; Fluconazole side effect

Medicine
Category: Clinical

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Undifferentiated nasopharyngeal carcinoma presenting as Cervical Lymphadenopathy in a young lady.

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CASE REPORT

Background:
Malignant lesions of the nasopharynx are perhaps the most commonly misdiagnosed, most poorly understood, and most pessimistically regarded of all tumours of the upper respiratory tract. Early diagnosis of Nasopharyngeal Carcinoma (NPC) is usually difficult attributed to its insidious onset and non-specific features in initial stages. The incidence variability of NPC, among different geographical and ethnic groups, indicates a combination of genetic susceptibility, infection by Epstein-Barr virus and environmental factors.

Case summary:
33 years lady presented with gradual progressive bilateral neck swellings over the last six months. She had no history of fever, weight loss, tinnitus, reduced hearing or epistaxis. The patient had unremarkable family and past medical history. Clinical examination revealed bilateral nodular masses in the posterior cervical region suggestive for enlarged lymph nodes. Flexible nasopharyngeal endoscopy showed left sided nasopharyngeal mass arise mainly from the nasopharyngeal roof , extending down along the posterior pharyngeal wall and laterally to fossa of Rosenmuller. Her laboratory workup was normal apart from mild normocytic normochromic anaemia and high ESR up to 64. CT sinus, neck, chest and abdomen post IV contrast revealed cervical and mediastinal lymphadenopathy with heterogeneous post contrast enhancement and with a nasopharyngeal area of similar enhancement pattern. Our differential diagnoses included metastatic nasopharyngeal carcinoma, lymphoma or Castleman disease. FNAC from the posterior cervical lymph nodes was suggestive of metastatic poorly differentiated carcinoma. Biopsy of the nasopharyngeal mass revealed nasopharyngeal carcinoma undifferentiated type.

Conclusion:
Early diagnosis of NPC is difficult due to its concealed location of this disease & the wide spectrum of nonspecific and sparse symptoms associated it. Clinicians should keep NPC in mind when making the differential diagnosis of neck masses

Key Words: Cervical lymphadenopathy; Nasopharyngeal carcinoma.; Head and neck malignancy

Medicine
Category: Clinical

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Superior vena cava and jugular venous thrombosis

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CASE REPORT

Background:
The diagnosis of superior vena cava and jugular venous thrombosis can be confirmed by computed tomography, by venography, and clinically. Bright intraluminal signal intensity seen throughout the course of the affected jugular vein on magnetic resonance images.

Case summary:
92-year old male patient with past history of hypertension, hypothyroidism, diabetes mellitus, ischaemic heart disease, coronary artery bypass graft, end stage renal disease on regular haemodialysis, chronic atrial fibrillation not on warfarin. Admitted because of disturbed level of consciousness with glascow coma scale 6/15. Blood pressure was initially elevated 190/110 and was controlled with labetalol infusion and when dropped, it was maintained with nor-epinephrine infusion. Computerized tomography scan of the brain repeated and showed extensive right cerebral infarction with mass effect, but no midline shift sparing the right basal ganglia. The patient was intubated and ventilated. Lasix 20 mg intravenous was given. Electrocardiography showed atrial fibrillation. Echocardiography showed ejection fraction 10 - 15%, global hypokinesia, sclerotic aortic valve, pulmonary artery systolic pressure was 40 mmHg. There was bilateral upper limbs oedema for which chest and neck computerized tomography scan done and showed superior vena cava and jugular venous thrombosis, treated with plavix tab 75 mg once daily and clexane 0.4 ml subcutaneous once daily.Because of the high risk of haemorrhagic transformation, computerized tomography scan of the brain repeated and showed extensive right middle cerebral artery territory, left occipital and left cerebellar infarcts, no haemorrhage and no midline shift.

Conclusion:
patients with hypercoagulable state especially those with chronic atrial fibrillation are prone to venous thrombosis and risk of pulmonary embolism. So good anticoagulation should be prescribed early to avoid venous thrombosis, keeping in mind the side effects of anticoagulant.

Key Words: Thrombosis; Jugular; Vena cava

Medicine
Category: Clinical

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Unilateral Opercular Infarct Presenting With Anarthria and Drooling of Saliva

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CASE REPORT

Background:
The opercular syndrome is a rare disorder due to bilateral lesions of opercular cortex surrounding the insula.First described by Magnus in 1837, Foix-Chavany-Marie syndrome (FCMS) is a facio-labio-glosso-pharyngolaryngo-brachial paralysis or cortical type of pseudobulbar paralysis. Most of the reported cases are due to cerebrovascular disease, CNS infections, developmental disorders like neuronal migration defects, reversible form with epilepsy and rarely neurodegenerative diseases.We report a case of a healthy right handed young man who had a typical presentation, but imaging showed an unilateral lesion on the dominant hemisphere.

Case summary:
31 years old male, previously healthy with no risk factors presented with sudden onset of difficulty in swallowing and inability to speak . He went to bed and woke up with these symptoms and neck pain on the left side. On admission, he was conscious, able to understand but couldn't speak. He had a weak smile and drooling of saliva. Extraocular muscles and pupils were normal. Cranial nerve examination revealed mild right facial paresis with significant bilateral bulbar and tongue weakness, facial sensations were normal. Deep tendon reflexes were elicitable and sensory system examination was normal. Right plantar response was equivocal. Other neurological examination were unremarkable. Vital parameters were normal except tachycardia of 115 beats /minute.The possibilities of botulism, vertebral dissection, and myasthenia were ruled out by appropriate investigations.MRI brain revealed diffusion restricted lesion on the left opercular region. Brain stem was normal.Magnetic resonance angiogram and venogram were unremarkable.

Conclusion:
This case is of considerable interest because of its presentation mimiking other neurological conditions with rapid recovery. Unilateral lesion can be explained by transhemispheric diaschisis. A condition with dysfunction of cerebral metabolism on the contralateral hemisphere.

Key Words: Unilateral; Opercular; Diaschisis

Medicine
Category: Clinical

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Unexpected complication of pulmonary embolism

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CASE REPORT

Background:
Pulmonary embolism can be life-threatening, but prompt treatment can greatly reduce the risk of death. Pulmonary embolism can be associated with unusual complications such as syncope and paraplegia.

Case summary:
63-year old patient, with past history of diabetes, hypertension and ischaemic heart disease, admitted with shortness of breath of gradual onset and progressive in course accompanied with chest discomfort of two days duration. He had also pain in the left leg and lower abdomen. Electrocardiography showed right bundle branch block. Doppler ultrasound showed left deep venous thrombosis. So Computerized tomography pulmonary angiography done and showed bilateral massive pulmonary embolism. The patient received thrombolytic therapy. Then he developed hypotension and flaccid paralysis of both lower limbs. Magnetic resonance imaging of the lumbo-sacral spine done and showed ischaemic myelopathy mostly due to anterior spinal artery occlusion. The patient is bed bound and can move the lower limbs with power 2/5Laboratory investigations showed normal liver and renal functions. Normal complete blood count. Computerized tomography angiography of the abdomen done and showed patent superior mesenteric vessels. Echocardiography done and showed ejection fraction 59% and diastolic dysfunction. Because of lower abdominal pain and dysuria, colonoscopy done and was normal. Urinary bladder biopsy done and showed chronic cystitis with eosinophil in the lamina propria. No evidence of malignancy. Tumor markers done and were within normal range. The patient is mildly improving with intensive physiotherapy and he is kept on oral anticoagulant.

Conclusion:
Taking measures to prevent deep venous thrombosis can help protect against pulmonary embolism. Although pulmonary embolism can be treated with thrombolytic therapy with remarkable recovery, yet in rare situations it can lead to paraplegia especially in those who have hypercoagulable state.

Key Words: Embolism; Thrombolysis; Paraplegia

Microbiology, Virology and Immunology
Category: Clinical

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Nocardial infections in the immunocompromised

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CASE REPORT

Background:
Localized and multi-system nocardiosis is an opportunistic disease that occurs commonly in immunocompromised patients. Here we report 2 cases of nocardial infections in such patients

Case summary:
Case 1: A 43 year old Bangladeshi female diagnosed with multiple myeloma in April 2013 and received 5 cycles of chemotherapy, presented on November 12, 2013 with convulsions and right sided weakness. CT brain revealed multiple brain lesions in frontal and parietal regions. On 15 November a left frontal craniotomy was done and.thick yellow pus was evacuated from one lesion and was sent to the Ibn Sina Microbiology lab. Gram stain of pus showed weakly Gram positive branching filamentous bacteria. Modified Ziehl Neelson stain showed branching, beaded acid-fast bacilli. Culture after 48 hrs. grew chalky-white dry colonies on blood agar which was identified as Nocardia farcinica . Patient was started on aggressive triple antibiotic therapy which included amikacin, meropenem and co-trimoxazole. Repeat CT brain on December 4, 2013 revealed massive regression of the lesions.
Case 2: A 44 year old, female Kuwaiti presented on November 18, 2013 with a history of fever, swelling on the right thigh since 5 days. She underwent a renal transplant in August 2000 and was on immunosuppressive therapy. Ultrasound of the right thigh revealed a deep intramuscular abscess. An ultrasound guided aspiration was done and 40 ml of thick yellow pus was sent to the microbiology lab of Ibn Sina hospital. Gram stain of the pus showed Gram positive branching filaments. Modified Ziehl Neelson stain showed branching, beaded acid-fast bacilli. Culture grew chalky cream coloured colonies which was identified as Nocardia asteroides complex. She was started on IV meropenem 500 mg 8 hrly and oral septrin double strength 12 hrly for 2 weeks followed by oral septrin for one year.

Conclusion:
Nocardiosis should be suspected in immunosuppressed patients who present with abscesses in multiple organs.

Key Words: Nocardia; Immunocompromised; Abcesses

Microbiology, Virology and Immunology
Category: Clinical

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Cryptococcus gattii meningoencephalitis in an immunocompetent patient in Kuwait

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CASE REPORT

Background:
Cryptococcosis is the most common fatal mycosis worldwide. It is caused by two species of Cryptococcus: C. neoformans and C. gattii. C. gattii appears to infects individuals with no identifiable immune deficiency.

Case summary:
A 34 year-old Filipino male was admitted to Farwaniyah Hospital; Kuwait, with history of generalized headache and drowsiness for the 3 days. He was previously healthy. He came to Kuwait 3 years before and worked as a baker. On examination, his vital signs were all within normal. He had mild neck stiffness with positive Kernig's sign. His blood test were all normal. He was initially given ceftriaxone, vancomycin and acyclovir intravenously, and lumber puncture was performed. India ink examination, culture and latex agglutination were positive for Cryptococcus. CSF examination showed elevated protein and WBC, mainly lymphocytes. His general immunological tests and for human immunodeficiency virus infection were negative. The isolate appeared susceptible to amphotericin B, voriconazole (VOR), but showed reduced susceptibility to fluconazole by E-test. The patient was started liposomal amphotericin B and VOR. Clinically patient was improving. He left the hospital against medical advice and readmitted three months later with similar symptoms. Liposomal amphotericin B was started with 5-flucytosine. After 3 weeks of therapy, the cultures were negative. The patient improved and left the hospital on oral voriconazole therapy. The isolates obtained grew on canavanine-glycene-bromothymol blue medium suggesting their identity as C. gattii, which was subsequently confirmed by amplified fragment length polymorphism fingerprinting as C. gattii genotype VGII.

Conclusion:
A Filipino male with meningoencephalitis caused by C. gattii, genotype VGII is described. This is the first report of C. gattii infection diagnosed in Kuwait and suggests that the disease may have a prolonged incubation period in immunocompetent individuals.

Key Words: Cryptococcus gattii; Genotype VGII; Immunocompetent

Neurology
Category: Clinical

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Case Report: Acute Inflammatory Demyelinating Polyneuropathy with Bilateral Extensor Plantar Reflexes

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CASE REPORT

Background:
Guillain-Barr´e syndrome (GBS) usually presents with lower motor neuron (LMN) symmetrical weakness, areflexia, and hypotonia. GBS has rarely been reported with up going planters' response. We report a case of GBS with up going planters during the course of the disease.

Case summary:
A 52-year-old woman developed acute paralysis with areflexia following a diarrheal illness. There was no fever at the time of the onset. She developed numbness and asymmetrical weakness of both lower limbs which progressed to involve the upper limbs bilaterally. There were no cranial nerves, respiratory or sphinecteric involvements. Few days later, the planters became upgoing bilaterally, with absent of other upper motor neuron signs. Cerebrospinal fluid (CSF) analysis showed albuminocytological dissociation. Early Nerve conduction study (NCS) showed absent H-reflex, dispersed F-waves with prolonged maximum F-latencies and M-amplitude showed no clear block. MRI brain and spine were unremarkable. She was treated with intravenous immunoglobulin (IVIG). Repeated NCS two weeks after the onset, definitely confirmed conduction block. She was able to walk with support three weeks after the onset.

Conclusion:
GBS should be considered as a differential diagnosis in a patient with acute quadriparesis, even if there is asymmetrical muscle weakness and extensor planters' response.

Key Words: Guillain-Barr´e syndrome; Upgoing planters' response; Asymmetrical weakness

Neurology
Category: Clinical

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Aneurysmal Subarachnoid Hemorrhage Management Associated with Unsuspected Aortic Coarctation

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CASE REPORT

Background:
Aortic Coarctation (AC) rarely goes undiagnosed until adulthood. A 5-fold increase in the incidence of intracerebral aneurysms (IA) is observed in patients with AC, whereas the incidence of AC in patients with IA is as low as 0.45%. The risk of aneurysmal rupture is increased in this patient population.

Case summary:
We present a case of a 47-year-old male, with aneurysmal subarachnoid hemorrhage (aSAH) and initially unnoticed AC. Impossibility of crossing the aortic arch with a catheter was experienced during digital subtraction angiography via the femoral route along with an observed difference in the arterial blood pressures between the upper and lower limb which raised the suspicion of AC. CT angiography confirmed juxtaductal complete occlusion of the aorta and extensive collateral network via both subclavian arteries. Although the left MCA aneurysm was successfully clipped during an uneventful intraoperative course, the neurocritical care stay was challenging and complicated by severe symptomatic cerebral vasospasm necessitating treatment including endovascular targeted intra-arterial milrinone.

Conclusion:
This paper aims at increasing the awareness of the association between undiagnosed AC and aSAH in middle age patients. Furthermore, it describes the challenging neurointensive care management of severe cerebral vasospasm in an uncorrected AC patient.

Key Words: Aneurysmal subarachnoid hemorrhage; Aortic coarctation; Intra-arterial milrinone

Neurology
Category: Clinical

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Milrinone for Cerebral Vasospasm in a Ruptured Unsecured Cerebral Aneurysm

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CASE REPORT

Background:
Cerebral vasospasm in the setting of a ruptured unsecured aneurysmal subarachnoid hemorrhage is rare in the current treatment paradigm of early aneurysmal obliteration. Preventing cerebral infarction due to vasospasm and avoiding re-rupture of the unsecured vascular lesion in this difficult setting is challenging as treatment aims are in conflict. Limited studies have shown the safe use of hypertension-hemodilution treatment in these unsecured aneurysm cases yet the risks associated with endovascular management and other modalities still remain unaddressed.

Case summary:
We present the case of a 28-year-old female with a surgically difficult-to-manage left internal carotid artery aneurysm during a period where our interventional neuroradiologist was unavailable. Cerebral vasospasm was diagnosed both clinically and radiologically on the 4th post-incident day which was initially treated with blood pressure augmentation to maintaining a target systolic blood pressure of 130-160mmHg. When clinical improvement was limited, an escalating-deescalating intravenous infusion of milrinone was maintained. CT angiography and perfusion scans were performed at a 3 day interval to guide and assess the response of the treatment.

Conclusion:
We report the safe use of intravenous milrinone in a patient with vasospasm secondary to a ruptured unsecured cerebral aneurysm.

Key Words: Ruptured Unsecured Cerebral Aneurysm; Cerebral vasospasm; Milrinone

Nuclear Medicine and Radiology
Category: Clinical

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Case Report: Chagas Heart disease

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CASE REPORT

Background:
Chagas disease, caused by the parasite TrypanosomaCruzi, is a serious health problem in Latin America and is an emerging disease in non-endemic countries. The disease was described in 1909 by Brazilian physician "Carlos Chagas". Dilated cardiomyopathy is the most important and severe manifestation of human chronic Chagas disease and is characterized by heart failure, ventricular arrhythmia, heart blocks,apical left ventricular aneurysm with or without thromboembolic phenomenon, & sudden death.

Case summary:
A 20 year-old female patient visited the cardiac outpatient clinic complaining of chest pain. Echocardiography revealed dilated left ventricle. She was refereed to our clinical radiology department for cardiac CT assessment.
ECG-Gated CT scan of the heart was done and revealed cardiomegaly with left ventricle and left atrium configuration showing a large aneurysm involving the left ventricle arising from the infero-posterior wall and the apical portion near to the mitral valve (sub-valvular area). The aneurysm shows two components; the larger component contains soft tissue thrombus and the smaller component shows a calcified thrombus. Another smaller aneurysm was seen arising from the anterior wall close to the interventricular septa & the aortic valve. Of note, ulceration of the left coronary sinus was present most likely secondary to inflammation.

Conclusion:
Chagas disease is a zoonosis transmitted primarily through parasite laden secretions from hematophagoustriatomine insects. These insects, which serve as vectors, are present in South & Central America, Mexicoand Southern United State. The disease can also be transmitted through blood transfusion, organ donation, and from mother to child at birth, which is the matter in non-endemic regions. Oral transmission has recently been recognized as a cause of sporadic small human outbreak, mostly in Amazon region. Chagas disease clinically present in acute followed by chronic form. Acute disease occurs in less than 1% and clinical manifestation

Key Words: Chagas disease; Cadiomyopathy; Aneurysm

Nuclear Medicine and Radiology
Category: Clinical

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Coronary Sinus Aneurys

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CASE REPORT

Background:
Aneurysm of the valsalva sinus (aortic sinus) can be congenital or acquired. It's a rare condition seen more in men than women and among Asians than other ethnic populations. First described in 1839 by Hope et al, it has been found in (0.09%) of 8138 autopsy subjects and in (0.15%-3.5%) of patients who underwent open heart surgery. Most cases are diagnosed on the basis of echocardiography with or without angiography. Both ECG-gated computed tomography (CT) and magnetic resonance imaging (MRI) can provide an excellent anatomic depiction.

Case summary:
A 39 year-old female patient has long history of rheumatoid arthritis with severe aortic regurgitation. She underwent gastric band surgery in 2009. The operation was complicated by a non-healing wound for about 8 months. Meanwhile she developed sudden onset of chest tightness, shortness of breath and severe sweating. Echocardiography revealed bipartite left ventricle (LV) with a partition extending from Aortic root (left coronary sinus) into the (LV).

Conclusion:
Aneurysm of the valsalva sinus is either congenital or acquired. Congenital aneurysm may result from localized weakness of the elastic lamina or an underlying deficiency of normal elastic tissue. Acquired aneurysmis commonly caused by infections such as bacterial endocarditis, syphilis, and tuberculosis. Other causes include cystic medial necrosis and injury from deceleration trauma. Ruptured and non-ruptured valsalva sinus aneurysms are associated with potentially fatal complications; however, the prognosis is excellent.
The clinical manifestation of valsalva sinus aneurysm can present at any age. Symptoms vary widely and when present they are often related to the aneurysm rupture or mass effect on the adjacent cardiac structures. The commonest site of rupture is the right ventricle. Other signs include cardiac murmur, chest pain, dyspnea and palpitation. Aortic regurgitation is a common complication of both ruptured and non-ruptured aneurysm.

Key Words: Valsava sinus; Coronary sinus; Aneurysm

Nuclear Medicine and Radiology
Category: Graduate (Resident)

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Safeguarding the performance of Tc-99m MAG3 diuretic (Lasix) renogram by using a condom catheter in a male patient

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CASE REPORT

Background:
The diuretic renal dynamic study also known as Lasix Renogram is used for non-invasive evaluation of obstruction in a dilated pelvicalyceal system. Technically, it involves administration of frusemide (Lasix) at some time-point related to injection of the radiotracer (Tc-99m MAG3) and acquiring dynamic imaging for 30 minutes. In children, pre-insertion of a urinary catheter (Foley) is recommended to ensure completion of the study without interrupting image acquisition due to the urge to void after administration of the diuretic. In adults inserting a Foley catheter, which carries some invasiveness, is usually not done. Instead, we report for the first time in Kuwait the use of an alternative way in a male patient in the form of a condom catheter that was proved to be non-invasive, simple and relatively cheap.

Case summary:
A 32-year-old male had a history of left flank pain, dysuria, and hematuria. Previously, he had a DJ-stent placed which was removed subsequently. A Tc-99m MAG3 dynamic renal study with a diuretic was ordered to evaluate for urinary outflow obstruction.
The study was performed with the patient well hydrated prior to start. Lasix was injected, however, the patient had urgency to void and the study was aborted early in the diuretic phase, which was not adequate to evaluate the presence of obstruction.
The whole study was rescheduled for another day. In the second attempt, a condom catheter was put in place by the patient who had the procedure explained to him. The repeat study was completed successfully and the patient was diagnosed with urinary obstruction that required further intervention.

Conclusion:
A condom catheter is an alternative non-invasive means for draining the urinary bladder to insertion of a Foley catheter in male patients undergoing diuretic renal studies that could eliminate repeating the study due to interrupted imaging after Lasix administration.

Key Words: Lasix Renogram; Obstruction; Condom catheter

Nuclear Medicine and Radiology
Category: Clinical

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Persistent thyroid on a Tc-99m sestamibi parathyroid scan. In vivo clues and the importance of radiopharmaceutical quality control

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CASE REPORT

Background:
Tc-99m sestamibi parathyroid scan is commonly used to identify the location of hyperfunctioning parathyroid tissue (HFPTT) in patients with hyperparathyroidism. It involves early and delayed imaging of the neck after injection of the radiotracer. Relying on differential washout between the thyroid, which is visualized only on the early images, and HFPTT, which is seen on both early and delayed images, persistent focal uptake would point to HFPTT such as adenoma or hyperplasia. The kinetics of Tc-99m sestamibi as described are observed in the majority of cases, however, occasionally delayed visualization of the thyroid is observed, which interferes with the identification of HFPTT. We present a case of faulty Tc-99m sestamibi, where the injected preparation behaved similarly to pertechnetate. The detection of such occurrence could be done by testing the product after preparation as follows: Upon chelation to sestamibi, Tc-99m pertechnetate changes from +7 oxidation state to +1. This can be confirmed using thin liquid chromatography (TLC). A C18 TLC plate is spotted with the radiopharmaceutical and developed in an organic solvent. Pertechnetate will stay at the origin, while sestamibi moves with to the solvent front.

Case summary:
A 39 yr old female who had a history of hypercalcemia and hyperparathyroidism was referred for a Tc-99m sestamibi parathyroid scan with SPECT/CT for exact localization of the lesion. The Tc-99m sestamibi scan showed persistent uptake in the thyroid. Imaging of the abdomen revealed gastric uptake, confirming a faulty radiopharmaceutical preparation with high pertechnetate content. A repeat study identified an adenoma and its location was defined by SPECT/CT.

Conclusion:
The performance of the Tc-99m sestamibi radiopharmaceutical quality control would prevent cases of a faulty preparation that could exhibit pertechnetate behavior and persistent thyroid uptake, thus causing an uninterpretable parathyroid scan.

Key Words: Parathyroid scan; Technetium sestamibi; Thin liquid chromatography

Nuclear Medicine and Radiology
Category: Clinical

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Functional-structural correlation using a Tc-99m HDP bone scan with SPECT/CT for a suspected bone tumor on the plain film of the frontal and maxillary sinuses

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CASE REPORT

Background:
The use of medical imaging for evaluation of various complaints can lead to discovery of hidden abnormalities in the body, also known as incidental findings, which necessitate further diagnostic work up usually involving more sophisticated and invasive tests. Such a case is presented in which a patient complaining from headache had a plain x-ray of the sinuses. A large shadow was seen in the right frontal sinus raising the possibility of a bone tumor in that region. The choice of what test could resolve the issue was considered and the decision was taken to obtain a bone scan with SPECT/CT of the head. The added advantage of the bone scan was in its ability to evaluate the whole skeleton for additional lesions. SPECT/CT would provide exact function-structure correlation for the putative abnormality.

Case summary:
A 65 yr old female had a history of on and off diffuse headache. She also complained of pain in the lower back and ankle. A plain x-ray of the facial sinuses for evaluation of sinusitis was obtained by her primary care physician. The plain film of the sinuses showed an irregular hazy shadow in the right frontal sinus. The patient did not have a clinical complaint on that side. A Tc-99m HDP whole body bone scan including a SPECT/CT of the head did not show a corresponding mass lesion. However, extensive hyperostosis was seen in the skull and some degenerative changes in the lower lumbar spine and joints of the lower extremities.

Conclusion:
The choice of a functional-structural imaging modality, such as a bone scan with SPECT/CT, would enable a more efficient evaluation of incidental radiographic findings in the skeleton. Changes attributable to normal variants such as hyperostosis seen in the skull can be readily identified. This was aptly shown in the case presented.

Key Words: Bone scan SPECT/CT; Hyperostosis; Tumor

Nuclear Medicine and Radiology
Category: Clinical

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Special adaptation of the lung scan protocol for evaluation of lung ventilation-perfusion in a child with Scimitar syndrome

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CASE REPORT

Background:
Scimitar syndrome, known also as hypogenetic lung syndrome, is a congenital anomaly with right pulmonary venous return to the inferior vena cava through the scimitar vein appearing as a Turkish sword on chest x-ray. It is associated with a hypoplastic right lung and blood supply from the celiac artery to the right lung base. Various imaging modalities are used to assess the abnormalities present including: plain chest film, echocardiography, CT-, MR- and contrast angiography. The role of the lung scan is in ascertaining the function of the lungs in terms of perfusion and ventilation and in providing quantitation of function and whether ventilation-perfusion match is present.

Case summary:
A 12 yr old boy with a history of Scimitar syndrome was referred for a lung Ventilation-Perfusion scan after corrective surgery to assess the relative function of each lung. The Perfusion part of the study was performed twice on 2 separate days in order to check whether the superior and inferior venous circulation provided the same pattern of lung perfusion. The first time, the perfusion radiotracer (Tc-99m MAA) was injected through a peripheral vein in an arm followed by imaging the chest in multiple views. In the second time, the radiotracer was injected in a vein in a foot and imaging of the chest repeated as in the first time. On a third day, a ventilation study was performed using Tc-99m Technegas and static imaging of the chest. The perfusion scans done in the first and second time showed no uptake in the right lung. The ventilation scan showed, however, that the right lung ventilation is 20% of the total.

Conclusion:
The lung scan provided important information on differential lung perfusion and ventilation in a case of Scimitar syndrome. The simple adaptation of the perfusion scan for assessing upper and lower body venous return into the lungs provided a more complete evaluation of this condition.

Key Words: Scimitar syndrome; Lung scan perfusion ventilation; Venous return

Nuclear Medicine and Radiology
Category: Clinical

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Clinical implication of incidental hypertrophic osteoarthropathy (HOA) found on Tc-99m hydroxydiphosphonate (HDP) bone scan in a patient with rheumatoid arthritis (RA)

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CASE REPORT

Background:
The radionuclide bone scan is used to evaluate a variety of skeletal conditions including arthritis, such as RA, to identify distribution and severity of joint involvement. Increased uptake is seen on the blood pool images in the joints denoting inflammation and on delayed images in the bone surfaces of the joints related to reactive changes. Usually, the small joints of the hands are affected and images of the whole body are acquired. A case of RA is presented in which the bone scan showed a pattern of hypertrophic osteoarthropathy: "railroad tracks" especially in femurs and tibias. There was no clinical complaint related to it or other known pathologies.

Case summary:
A 58 yr old female had a history of RA, treated on and off with anti-inflammatory drugs and methotrexate for 10 years. The patient complained of pain in the shoulders, hands and feet. There was no history of cancer. A Tc-99m HDP bone scan showed increased uptake in the left wrist and left ankle on blood pool images. The delayed images showed uptake in multiple joints and the lumbar spine. The long bones of the lower extremities showed increased cortical pattern suggestive of HOA. A more thorough search for other pathologies did not identify a concomitant illness especially a tumor. A search of the literature revealed reports of rheumatoid manifestations that can predate the diagnosis of cancer. This is in addition to the well known association of HOA with lung cancer. However, whether isolated presentation of HOA on the bone scan without clinical manifestation can be predictable of malignancy has not been reported previously.

Conclusion:
Due to known association between some musculoskeletal syndromes especially HOA and malignancy, the presence of occult cancer should be kept in mind in management of such patients. However, the significance of isolated HOA by bone scanning would still require more confirmatory studies before it be considered as a reliable predictor of cancer.

Key Words: Bone scan; Rheumatoid arthritis HOA; Cancer

Nuclear Medicine and Radiology
Category: Clinical

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Bilateral Itralobar Sequestration

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CASE REPORT

Background:
Intralobar pulmonary sequestration is characterized by the presence of nonfunctional parenchymal lung tissue, receiving systemic arterial blood supply. It lacks normal communication with the tracheo-bronchial tree. Failure to diagnose and treat this condition can lead to recurrent pneumonia and fatal hemoptysis. The aim of this case report is to increase awareness about the condition and to review criteria of its definitive diagnosis and subsequent treatment.

Case summary:
Bronchopulmonary sequestration is a benign, rare lung abnormality. Anatomically it is classified into intralobar and extralobar sequestration; intralobar sequestration is more common accounting for up to 75%, usually seen during adolescence, presenting with recurrent chest infection secondary to inflammation and bronchial obstruction & it is seldom associated with other anomalies. Conversely, extralobar sequestration is always congenital, has a separate pleural investment, and is often associated with other anomalies including congenital diaphragmatic hernia, congenital cystic adenomatoid malformation, and fistulous connection to the esophagus or stomach. It presents during the neonatal period. This case, a bilateral intralobar sequestration in neonate is reported because of its rare occurrence.

Conclusion:
11 months old a baby boy diagnosed with a complex congenital cyanotic heart disease, tetralogy of fallot, pulmonary atresia and Majot Aorto-pulmonary Collateral, supraventricular tachycardia with multiple surgical repair. After two months he suffered from recurrent severe wheezy chest, frequent plain chest X-rays showed bilateral broncho-pneumonia and isotope lung scan revealed bilateral reduced lung perfusion. Follow-up by computed tomography angiogram (CT) of the chest revealed bilateral lower lobes sub-segmental consolidations with feeding arteries coming from the descending thoracic aorta and draining veins in to the pulmonary venous circulation

Key Words: Pulmonary Sequestration; Intralobar; Extralobar

Nuclear Medicine and Radiology
Category: Clinical

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An unusual case of coronary artery fistula (CAF); one with the main Pulmonary artery and the other with the left atrium, diagnosed with 64-MDCT Coronary Angiography

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CASE REPORT

Background:
Coronary-pulmonary artery fistula is an uncommon cardiac anomaly that can originate from any of the three major coronary arteries. This report describes a case of complex coronary-pulmonary artery fistula with one feeding vessel from the proximal part of the right coronary. Traditionally, conventional angiography has been used for the diagnosis of coronary anomalies. With use of 64 multi-detector computed tomography (MDCT) in cardiac imaging, the number of incidentally found coronary artery fistulas has been increasing.

Case summary:
A 49-year-old woman was referred to Chest Diseases Hospital for CT coronary Angiography. She had a history of subtle chest pain and arrhythmia. CT coronary angiography was performed using a 64-slice MDCT scanner.The anatomy of the coronary artery-pulmonary artery fistula was complex but was well demonstrated after detailed analysis. The right coronary artery originates from the right coronary sinus, the left coronary artery originated from the left coronary sinus which bifurcates to LAD and LCx.There was right coronary dominance. The fistula was seen arising from the proximal RCA and courses horizontally anterior to the main PA till its left lateral aspect just above the pulmonary valve Finally, it ended by joining to a 20-mm bulbous dilatation over the lateral aspect at the base of the main pulmonary artery before draining into the main pulmonary artery.

Conclusion:
CAFs have an estimated prevalence of 0.002% in the general population, but they are present in 0.05%–0.25% of patients who undergo coronary angiography. There is no race or sex predilection for CAF.Coronary fistulae may lead to serious complications, including myocardial ischaemia, congestive heart failure and rupture of aneurysmal fistulae. Coronary CTA is a relatively new imaging modality that has been used for non-invasive coronary artery imaging since 2000. With the introduction of (MDCT) many problems with image quality have been overcome.

Key Words: CAF= Coronary to pulmonary artery fistula; MDCT= Multi-detector computed tomography; LAD= Left anterior descending, LCX= left circumflex, RCA= right coronary artery

Nuclear Medicine and Radiology
Category: Clinical

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Bilateral carotid artery aneurysm in mirror image appearance. Case Report.

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CASE REPORT

Background:
Bilateral intracavernous aneurysms of the internal carotid artery are very rare. To our knowledge, no such case has been reported from Kuwait so far. We report a case of a bilateral intracavernous aneurysms of the internal carotid artery appearing as mirror image on MRI/MRA imaging.

Case summary:
A 57 year old female patient presenting with headache and ophthalmic symptoms was referred to the radiology department for MRI/MRA examination of the brain and the orbits. The study revealed bilateral aneurysm of the cavernous segment of the internal carotid arteries. The MRI examination of the brain was normal.

Conclusion:
Bilateral internal carotid artery aneurysms in the cavernous segments of the vessel are rare. The case is presented for its rare nature.

Key Words: Carotid artery; Aneurysm; Cavernous sinus

Obstetrics and Gynecology
Category: Clinical

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Skene gland cyst, case report

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CASE REPORT

Background:
Skene's glands (periurethral) are located adjacent to the distal urethra. Cysts form if the duct is obstructed, usually because the gland is infected. They occur mainly in adults. Cysts may form abscesses or cause urethral obstruction and recurrent UTIs. Most cysts are <1 cm and asymptomatic. Some are larger and cause dyspareunia. The first symptoms may be those of urinary outflow obstruction (eg: hesitancy, dribbling, retention) or of UTIs. Abscesses are painful, swollen, tender, and erythematous but usually do not cause fever.

Case summary:
32 year old Ethiopian lady otherwise healthy. She initially presented to our gyn clinics complaining of a painful swelling in the perineum. This swelling was increasing in size over the last 3 months. Patient didn't notice any bleeding or abnormal discharge with this swelling. No urinary symptoms were noted by the patient except for pain when sitting down. Careful perineal examination revealed a 1.5x1.5 cm swelling (cyst) noted to be at the left inner aspect of the labial fold near the urethra. Suspicion of urethral diverticulum was noted and a decision to treat the patient as a multidisciplinary team was conducted. Consultant urologist from Amiri hospital was contacted to further evaluate the patient and accordingly an MRI was requested. MRI confirmed the presence of this swelling (gartner cyst) and no urethral invasion was confirmed. Patient underwent surgery in the presence of consultant urologist. Careful dissection of this cyst was done but unfortunately it ruptured while manipulation. Patient was discharged home with a urinary Foley catheter in second post op day. She was evaluated in both gyn and urology clinics post operative. Final histopathology reveled the cyst to be of skene glands.

Conclusion:
Skene gland tumors can represent a challenge for it's treating gynecologist in view of its proximity to the urethra. The importance of treating the patient as a multidisciplinary team conjunction with a urologist is evident.

Key Words: Skene gland; Gartner cyst; Urethral diverticulum

Obstetrics and Gynecology
Category: Clinical

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Acute abdominal pain, OHVIRA syndrome (Obstructed hemivagina and ipsilateral renal anomaly)

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CASE REPORT

Background:
OHVIRA syndrome (obstructed hemivagina and ipsilateral renal anomaly) is a rare development anomaly of the mullerian system. It consists of uterus didelphis with obstructed hemivagina and ipsilateral renal a genesis.

Case summary:
A 13 years old Egyptian female, known to have a single kidney, presented to the emergency room with acute lower abdominal pain of one day duration. Abdominal examination revealed supra public fullness that was tender on touch. Ultrasound revealed uterus didelphys and heamatocolpus. Urgent MRI revealed the presence of ipsilateral kidney, uterus didelphys along with transverse and longitudinal vaginal septae. Her lab work up was within normal. First surgical intervention which included resection of the most prominent part of the vaginal septae, aided in relieving patients symptoms. A Foley catheter was inserted and kept for 1 week. Unfortunately 6 months later, patient returned with the same initial complaint of abdominal pain and a repeat ultrasound confirmed heamatocolpus. Second surgical intervention involved complete removal of both longitudinal and transverse vaginal septae. Three months later, a repeat ultrasound was requested as part of her follow up and have revealed the presence of another small collection which was managed conservatively and was spontaneously resolved with menses.

Conclusion:
In the middle eastern communities, diagnosis of OHVIRA and its management represents a challenge for its treating gynecologist. Importance of radiological investigations are key essential tools in the diagnosis and provides a road map to its management. Surgical treatment also plays a significant role in its management and follow up.

Key Words: OHVIRA; Adolescent gynecology; HWW syndrome

Obstetrics and Gynecology
Category: Graduate (Resident)

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Mayer-Rokitansky-Kuster-Hauser syndrome (MRKH)

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CASE REPORT

Background:
Mayer-Rokitansky-Kuster-Hauser syndrome or MRKH is a congenital malformation of Müllerian agenesis characterized by a failure of the Müllerian duct to develop, resulting in a missing uterus and variable malformations of the upper portion of the vagina. It is a rare condition that occurs in 1 in 16,000 pregnancies, but normal ovarian function

Case summary:
We report a case of a 23 year woman, a university graduate, who presented at the Gynaecology clinic with primary amenorrhea and inability to get pregnant. She has been married to a 25 year old Engineer for two years and they have been cohabiting without use of contraception, but she has been experiencing severe dyspareunia. Examination revealed a healthy looking, intelligent and well developed young lady, with height 156 cm and weight 58kg, giving a body mass index (BMI) of 23.8 and normally developed breasts at Tanner grade 5. Investigations revealed the following results. Karyotype showered normal female XX and hormone: FSH 3. 4 IU/L, LH 7.4 IU/L, prolactin 386 pg/ml, TSH, FT4 and SHBG. Pelvic ultrasound confirmed presence of normal sized ovaries harbouring multiple follicles. A uterus like structure is seen-39x27x32 mm posterior to urinary bladder. MRI is highly recommended for further anatomic delineation. MRI findings were Absent uterus and upper two thirds of the vagina picture suggestive of Mayer-Rokitansky-Kuster-Houster Syndrome. Both ovaries show multiple follicles picture suggestive of PCO but no urinary malformations. The clinical implications were discussed with the couple, emphasizing the options of assisted reproductive technology (ART) and surrogacy, the future of uterine transplant, and religious view.

Conclusion:
Mayer-Rokitansky-Kuster-Houster Syndrome is a serious clinical problem because of the association with sterility. Our patient has MRKH type 1 which has no associated urinary malformation

Key Words: Mullerian Agenesis; Primary Amenorrhea; Sterility, Surrogacy

Orthopaedic Surgery
Category: Clinical

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Extracorporeal shock wave therapy relieved pain in patients with coccydynia: A report of two cases

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CASE REPORT

Background:
Extracorporeal shock wave therapy (ECSWT) has been used widely for musculoskeletal conditions; however, no reports are available about its use for coccydynia. We aim to study the effect of ECSWT in relieving pain of coccydynia.

Case summary:
ECSWT was used for two male patients, patient (A) and patient (B), who failed to respond completely to other conservative management of coccydynia. Numerical pain scale (NPS) and visual analogue scale (VAS) were used to assess the pain. Consent to publish the data was obtained from both patients. Before starting ECSWT, patient (A) reported pain intensity of 6/10 and 5.1/10 on NPS and VAS respectively, while the intensity of pain of patient (B) was 7/10 and 6.9/10 on NPS and VAS respectively. Four weeks following the proposed treatment protocol of ECSWT, patient (A) reported complete relief of pain on NPS and VAS while patient (B) reported pain intensity of 1/10 on NPS and 0.8/10 on VAS. The same intensity of pain was reported by both patients after 12 months follow-up.

Conclusion:
ECSWT relieved pain of coccydynia in our patients.

Key Words: Coccydynia; Coccyx; Extracorporeal shock wave therapy

Pathology
Category: Clinical

200

Metastatic medullary thyroid carcinoma to the breast in a patient with combined medullary and papillary carcinoma of thyroid - a case report

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CASE REPORT

Background:
Metastatic tumours in the breast from extramammary sites are rare(0.2 – 1.3%). Thyroid carcinoma metastatic to the breast is extremely rare with only a few cases reported in the literature. Here we report a case of metastatic medullary thyroid carcinoma (MTC) to the breast, diagnosed by fine needle aspiration cytology (FNAC) and subsequent excisional biopsy .

Case summary:
A 66 year old Kuwaiti woman presented in October 2009 with a nodule in the right lobe of thyroid. Ultrasound, guided FNAC revealed a neoplastic lesion, most likely papillary thyroid carcinoma (PTC). She underwent total thyroidectomy and neck dissection. Histopathology revealed combined papillary (<25%) and medullary (>75%) thyroid carcinoma pT3N1bMX. In 16 of the 35 lymph nodes examined metastatic carcinoma was identified, MTC in 11 and PTC in five. No germline mutation in the RET gene was detected on genetic testing, hence her clinical presentation was of a sporadic MTC. She received external radiotherapy to neck and upper mediastinum followed by an ablative dose of I131in January 2010. There was progressive rise in serum calcitonin and CT/PET scan reported hypermetabolic paratracheal / suprasternal lesions in addition to multiple pulmonary non avid lesions and a lesion in the right breast. The right breast mass (1.5 x 1cm), was aspirated in January, 2011.FNAC revealed a carcinoma favouring metastasis from the MTC. She underwent wide local excision of the breast mass in February, 2011 which confirmed metastatic MTC. In view of progressive metastatic disease and rising calcitonin levels she was started on Vandetanib since February, 2012.

Conclusion:
MTC commonly metastasizes by both hematogenous and lymphatic spread. Involvement of the breast is extremely rare and only 13 cases have been reported in the literature. This case is peculiar as it was a combined papillary and medullary carcinoma of the thyroid of which the medullary component metastasized.

Key Words: Metastatic medullary carcinoma thyroid; Breast; Fine needle aspiration cytology

Pathology
Category: Graduate (Resident)

201

Incidental minute GIST in a ceacal diverticulum

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CASE REPORT

Background:
Gastrointestinal stromal tumors (GISTs) represent 80% of mesenchymal tumors of the digestive tract. They commonly arise in the stomach and small intestine, and less frequently in the colon and rectum. Incidental microscopic GISTs, also known as GIST tumorlets, are preclinical lesions that need additional stimuli to evolve into clinically relevant GIST. Minute GISTs can be multiple or solitary, mostly discovered in stomach specimens resected for malignancy or at autopsy examination. Herein we are reporting a case of an incidental GIST tumorlet in a cecal diverticulum, which was resected due to complications of perforation.

Case summary:
A 58 year old woman presented with acute abdominal pain and fever. Intra-operatively, a cecal diverticulum was seen, associated with omental adherence and abscess formation. A right hemicolectomy and omentectomy were performed. Histopathological evaluation confirmed the presence of a cecal diverticulum showing serosal inflammation and abscess formation, compatible with perforation. Microscopically, an incidental spindle cell lesion was noted, measuring 3 mm in maximum dimension, arising from the muscularis propria. The lesion showed proliferation of uniform spindle cells in short fascicles and the differential diagnosis was that of a minute GIST vs a benign nerve sheath lesion. Immunohistochemical stains showed diffuse positivity for CD117 and CD34, an immunoprofile that is diagnostic of GIST. S100 stain was negative ruling out a nerve sheath tumor.

Conclusion:
There is an increasing awareness, of small incidental spindle cell lesions in the GIT that may or may not be associated with clinically apparent GISTs. These silent GISTs are more frequently seen at the gastro-esophageal junction. In addition, they can be associated with inherited forms of GIST; however, less commonly can be seen sporadically.

Key Words: GIST; Minute GIST; Ceacal diverticulum

Pathology
Category: Graduate (Resident)

202

Squamoid eccrine duct carcinoma and angiolymphoid hyperplasia with eosinophilia. Rare case

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CASE REPORT

Background:
Squamoid eccrine duct carcinoma (SEDC) is an extremely rare primary cutaneous tumor, with only few cases have been reported in the literature. This type of tumor exhibits both squamous and adnexal duct differentiation. Here we report an unusual case of squamoid eccrine duct carcinoma associated with angiolymphoid hyperplasia with eosinophilia (ALHE), which is also known as epithelioid hemangioma. It is an uncommon idiopathic condition that can occur at any body site. The morphology of both entities is described in this case.

Case summary:
A 15-year-old young girl presented in April 2013 with a left eyebrow nodular swelling with a maximum diameter of 1.0 cm. The lesion was surgically removed. Histopathological evaluation revealed coexistence of two different histopathological morphologies SEDC and ALHE with eosinophilia. The first entity consists of duct-like structures and squamous proliferation with atypia, infiltrating through the dermis. The nuclei have low-grade morphology. The tumor is admixed with circumscribed collections of thin and thick walled blood vessels, which are lined by plump endothelial cells, and surrounded by chronic inflammatory cells, lymphoid follicles with germinal centers and numerous eosinophils. A diagnosis of low-grade squamoid eccrine duct carcinoma and angiolymphoid hyperplasia with eosinophilia is made.

Conclusion:
Possible explanation of angiolymphoid hyperplasia in a squamous cell tumor is attributed to release of angiogenic factors by tumor. To our knowledge this peculiar case with collision morphology has not been published in the literature.

Key Words: Squamoid variant; Eccrine duct carcinoma; Angiolyphmoid hyperplasia

Pathology
Category: Clinical

203

Uncommon metastases of papillary thyroid carcinoma: Report of two 2 cases.

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CASE REPORT

Background:
Papillary carcinoma of the thyroid (PTC) usually remains localized and distant metastases is reported ranging from 4 – 15%. We report two cases of PTC with local lymph node involvement which metastasised to the chest wall and pleura.

Case summary:
Case 1: A 73 years old male had total thyroidectomy (TT) for PTC and received ablative dose of I131. Within four months on follow up he was detected to have pleural thickening and chest wall mass on CT scan which was aspirated and reported as metastatic PTC.

Case 2: A 36 year old male presented with soft tissue lesion related to pleura and enlarged mediastinal lymph nodes. He gave history of having had a TT for PTC with lymph node excision 7 years ago and had also received ablation dose of iodine. The pleural mass was aspirated and found to be a metastatic PTC.

Conclusion:
PTC ordinarily behaves in an indolent manner but can have unusual metastatic presentations and patterns. Rare case report of metastases to the pleura has been documented.

Key Words: Papillary thyroid carcinoma; Metastases; Pleura

Pathology
Category: Clinical

204

Undifferentiated Carcinoma of the Breast Masquerading as Interdigitating Dendritic Reticulum Cell Sarcoma in Fine Needle Aspiration Smears: Report of Three Cases.

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CASE REPORT

Background:
Dendritic cells (DC), positive for S100 protein, are the most potent antigen-presenting cells. Infiltration of the tumors by DC reflects the host immune defense mechanism; the more DC infiltrate the tumor, the better the prognosis. Quantitative assessment of tumor-infiltrating dendritic cells (TIDC) have been correlated to prognosis in a variety of human neoplasms. The number of S100+ TIDC has been found to vary according to grade of the breast cancers as follows: GRIII>GRII>GRI. Recently we observed three cases of breast carcinomas with dense TIDC infiltration in fine needle aspiration (FNA) smears, leading to the erroneous cytodiagnostic label or differential diagnosis of dendritic cell sarcoma.

Case summary:
The three women with breast masses were aged 34 years, 32 years, and 65 years, respectively. The FNA smears showed presence of highly pleomorphic cells, mostly in the form of bare nuclei with prominent nucleoli. The cells were usually in singly dispersed form but occasional discohesive clusters were observed in two of the cases. Variable number of cells with dendritic cytoplasmic processes and nuclear characteristics with features similar to those of bare nuclei were present along with lymphocytes and/or plasma cells. Immunocytochemical staining for leukocyte common antigen (LCA), CD68, S100 protein (in two cases) and vimentin yielded positive reaction in the cells with intact cytoplasm and dendritic processes. Occasional group of cells were positive for EMA in one case. The cytodiagnsis was dendritic reticulum cell sarcoma in two cases and dendritic cell sarcoma versus medullary carcinoma in one. The histopathological diagnoses were medullary carcinoma in two cases and invasive ductal carcinoma (NOS), grade III in one case.

Conclusion:
Undifferentiated carcinoma with dense, tumor-like dendritic cell infiltration can lead to an erroneous FNA cytodiagnosis of dendritic cell sarcoma, even if immunocytochemical parameters are adopted.

Key Words: Carcinoma of the Breast; Interdigitating Dendritic Reticulum Cell Sarcoma; Fine Needle Aspiration Cytology

Pathology
Category: Clinical

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Metastatic Nasopharyngeal Carcinoma with Extensive Langerhans Cell Reaction: Initially Diagnosed by Fine Needle Aspiration Cytology.

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CASE REPORT

Background:
Langerhans' cells (LCs) are specialized myeloid-derived dendritic cells or antigen-presenting histiocytes in the body characterized by dendritic cytoplasmic processes and residing in the skin and the mucosa of certain organs. Rare studies involving proliferation of LCs in nasopharyngeal carcinoma (NPC) link this phenomenon to Epstein-Barr virus (EBV) infection as well as better prognostic outcome. We report a case revealing dense infiltration of LCs in a metastatic NPC, which was initially diagnosed by fine needle aspiration (FNA) cytology.

Case summary:
A 30-year-old man presented with a 3 x 3 cm. left cervical mass of four weeks duration in February 2009. FNA smears showed small groups as well as singly scattered atypical cells with mild to moderate nuclear pleomorphism and indistinct to prominent nucleoli along with a polymorphous population of lymphoid cells and numerous LCs which were positive for S100 protein. In the cell block preparation, the neoplastic cells were positive for cytokeratin, and epithelial membrane antigen (EMA). The routine cytodiagnosis was metastatic epithelial malignancy of nasopharynx or salivary gland origin. The histopathological diagnosis was metastatic undifferentiated nasopharyngeal carcinoma in the left cervical lymph node. Immunohistochemical staining on archival lymph node biopsy material showed positive reaction for pan CK, EMA, and EBV latent membrane protein (LMP) in the neoplastic cells; the infiltrating Langerhans cells were positive for S100 protein, CD1a, myeloperoxidase, LCA, and vimentin, but negative for CD68. CT-scan revealed a tumor arising out of the left fossa of Rosen Muller and left cervical lymphadenopathy. The patient received chemo-radiotherapy in UK and followed-up at Kuwait.

Conclusion:
To the best of our knowledge, this is the first reported case to highlight the diagnosis of a metastatic NPC with extensive Langerhans cell reaction by FNA cytology.

Key Words: Nasopharyngeal Carcinoma; Langerhans Cell Reaction; Fine Needle Aspiration Cytology

Pediatrics
Category: Graduate (Resident)

206

A Case of Glycogen Storage Disease Ib in a 14- Month-Old Girl

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CASE REPORT

Background:
Glycogen storage disease (GSD), type Ib, an extremely rare autosomal disorder affecting the glucose-6-phosphatase complex, presents with the key features of hepatomegaly, fasting hypoglycemia, lactic acidosis, failure to thrive/growth retardation, and muscular hypotonia as a result of impaired glycogenolysis and gluconeogenesis.

Case summary:
A case of glycogen storage disease type Ib in a 14-month-old girl, diagnosed based on clinical and biochemical abnormalities, is reported. She presented with a doll-face resemblance and symptoms of fasting hypoglycemia with hepatomegaly. The key laboratory findings in this case were hyperuricemia, lactoacidemia, elevated liver enzymes and neutropenia. Ultrasonography revealed hepatomegaly. Subsequently, she was maintained on essential dietary therapy, which consisted of uncooked cornstarch, frequent feedings, and nocturnal gastric drip infusion.

Conclusion:
Complications of GSD are common with age and early diagnosis, by genetic analysis, is important to initiate effective treatment in order to prevent long-term complications. Metabolic control is of utmost importance with treatment of complications as they arise. Treatment consists of dietary therapy to achieve metabolic control with long-term implications such as liver and hepatocyte transplantation.

Key Words: GSD; Metabolism; Chemistry

Pediatrics
Category: Clinical

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A Case Report of Pediatric Ebstein Barr Virus (EBV) related Cholestasis from Al-Adan Hospital, Kuwait

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CASE REPORT

Background:
Infectious mononucleosis is an acute illness due to Epstein Barr virus infection, which occurs commonly in young adults . Our objectives of writing this case is to alert pediatrician about different presentation of a common viral illness and to increase awareness of serious complication of EBV infection in these age group.

Case summary:
A 7 years old girl previously well, was admitted to our hospital with a history of fever for 10 days, decreased appetite, malaise and abdominal pain.. On admission she was looking well but irritable ,hydrated , febrile with stable vital sign, abdominal examination showed enlarged liver 3 cm. .Initial blood investigation showed, CBC normal white count Hb:109 g/L, platelet 126.,liver function test (LFT) showed mild elevation of liver enzyme ,.The child underwent extensive investigations including viral serology screening (CMV and EBV). Few days. Later on her abdominal pain was increasing along with persistent fever . U/S abdomen revealed hepatosplenomegaly, contracted gallbladder with thick edematous wall. Blood investigation revealed elevated white count with lymphocyte predominance and borderline platelet count at, peripheral blood film showed reactive lymphocytosis. A repeat of her liver profile showed total: Bilirubin-: 103 µmol/L with predominant direct fraction, Her LFT showed mainly a cholestatic pattern. coagulation profile: showed significant coagulopathy consistent with acute liver failure of INR 2.2 Blood virology previously done confirmed acute EBV infection. (PCR+IgM). She had gradual clinical improvement and was discharged in stable condition. The girl underwent a repeat of liver function tests and U/S abdomen 2 weeks after discharge both of which were normal.

Conclusion:
This case report illustrates some of the challenges in diagnosing a common disorder that presents in an uncommon presentation. All pediatricians should be aware of various presentations of common viral childhood infection in order to provide a comprehensive cascade of investigation and supportive management

Key Words: Children; Ebstein Barr Virus; Infection

Surgery
Category: Graduate (Resident)

208

Post-Traumatic Ulcer on the dorsum of the hand, biopsy?!

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CASE REPORT

Background:
The variable presentation of cutaneous leishmaniasis (CL), a parasitic infection caused by the Leishmania species, poses a diagnostic challenge when it resembles other post-traumatic skin lesions. The aim of this report is to raise the awareness of CL presenting as an isolated post traumatic skin ulcer, especially among those at risk of the infection.

Case summary:
A 40 year old Pakistani male with no known medical issues, presented to the hand surgery clinic, after being referred from a primary healthcare service with a cutaneous lesion on the left wrist. He gave a history of a left wrist swelling following a blunt trauma while being in Pakistan three months ago. He described that within the last 20 days it was increasing in size until the overlying skin has sloughed. The lesion was initially managed as a skin infection with topical anti-biotics and dressing prior to the referral. On examination, the patient was found to have a 4.5*6 cm cutaneous erythematous lesion overlying the dorsal aspect of the left wrist extending to the left hand. Around the center of this lesion there was a 1.5*1 cm superficial ulcer with a sloughed base with an underlying nodular, firm subcutaneous mas measuring 2.5*1.5 cm. There were no enlarged lymph nodes in the ipsi-lateral upper limb. There were no similar lesions on the rest of the skin and the rest of the examination and other investigations and blood work were normal. The initial diagnosis was that of a post-traumatic granuloma, and thus after a trial of systemic antibiotics and conservative management, the lesion was excised and biopsied revealing CL by pathology. The patient was thereafter referred to dermatology for further management.

Conclusion:
Proper history and examination, along with diagnostic suspicion should identify those presenting with ulcers due to CL for dermatological consultation prior to excision. Post-traumatic skin changes have been identified to facilitate atypical presentations of CL.

Key Words: HAND; ULCER; LEISHMANIA

Surgery
Category: Clinical

209

Functional surgery for traumatic brachial plexus injury in adults. Case report and literature review.

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CASE REPORT

Background:
Traumatic brachial plexus injuries are frequents, especially after high-velocity accidents. Different surgical treatments are used: nerve transfer or nerve graft, tendon transfer or muscle transfer, and arthrodesis. In the literatures, there are different approaches for the reconstructive surgical techniques of the traumatic brachial plexus injuries depending on the experienced surgical team.

Case summary:
A 44 years old male, had a motorbike accident in May 2008 with bilateral involvement of the brachial plexus: left complete sensorimotor paralysis and right partial injury (middle and lower trunk). First surgery at 9 months: neurotization of the first left 4 intercostal nerves on the left musculo-cutaneous nerve to re-innervate the left biceps muscle. No motor recovery at 22 months. Then 2nd surgery after 20 months on the right side: arthrodesis of M1 to M2 and trapezo-metacarpal right (to keep the opening of the first commissure), tendon transfer of flexor carpi radialis on flexor digitorum profundus (for a P3/P2 flexion) and brachioradialis on flexor pollicis longus (for flexion of the thumb P2/P1). Result: grip of I-II fingers with good resistance, grip of I-III possible without resistance. At 3 months after surgery, the functional scale of Kapandji for the right hand = 18/60.

Conclusion:
Functional surgery for traumatic brachial plexus is becoming more complex. Monitoring over several years, requires a "specialized “team.
We must try to get "at least":

- A stable shoulder.
- Flexion-extension of the elbow.
- Aesthetic hand without pain.

We made literature reviews and summarized the indications, the advantages and the inconveniences for each surgical method.

Key Words: brachial plexus; nerve graft and transfer; muscle graft and transfer

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KEYWORD INDEX

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