

**FOURTEENTH HEALTH SCIENCES CENTRE
POSTER CONFERENCE 2009**

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Organising Committee

- Dr. Mariam HM Yousif (Vice Dean Research)
- Prof. M. John Albert (Chairman)
- Dr. Edet E Udo (Coordinator, Scientific & Publications)
- Dr. Nowall Hassan (Coordinator, Finance)
- Dr. Sana Al-Mutairi (Coordinator, CME)
- Dr. Halit Canatan (Coordinator, Logistics)
- Dr. Khalaf Al-Shammari
- Dr. Alyaa M A Moussa
- Dr. Entesar Hussain
- Dr. Kamal Matar
- Dr. Ahmed M Al-Kandari
- Mr. Jassim Al-Khorafi
- Mr. Dheya HA Al-Hasan
- Ms. Amna Safar

Special Acknowledgements

- Prof. Abdulla Behbehani, Vice-President, Health Sciences Centre
- Mr. Adel Al-Moosad, Director, Service Department
- Mrs. Teena Sadan, Technical Staff, CRC, Faculty of Medicine

Photograph of Organising Committee



Front row, from right to left

Dr. Nowall Hassan, Prof. M John Albert, Dr. Mariam HM Yousif, Dr. Alyaa M A Moussa, Dr. Entesar Hussain

Second row, from right to left

Dr. Halit Canatan, Dr. Kamal Matar, Dr. Sana Al-Mutairi

Members not shown in the picture

Prof. Fuad M Hasan, Dr. Khalaf Al-Shammari, Dr. Edet Udo, Dr. Ahmed M Al-Kandari, Mr. Dheya HA Al Hasan, Mr. Jassim Al-Khorafi, Ms. Amna Safar

Message from the Dean, Faculty of Medicine

I am delighted to see the **14th HSC Poster Conference** ready to unfold. This landmark annual event came into existence in 1996. The purpose of the conference was to display and disseminate the fruits of research activities of the staff and the students of this Faculty. Over the years, the Poster Conference proved to be an effective medium for researchers from different departments to put their heads together and come up with innovative ideas where basic science translates into clinical applications.



To add icing to the cake, every year we invite a keynote speaker who talks about a global issue relevant to research and health. This year we are truly honored and privileged to have **Professor R. Brian Haynes**, Professor of Clinical Epidemiology and Medicine, Chief of Epidemiology, McMaster University, who will be talking to us about “**Evidence-based Medicine and knowledge translation research for better healthcare**”. Translational research is exactly what the Faculty of Medicine encourages its staff to carry out, and evidence based medicine is what we expect our graduates to practice. I am certain that **Prof. Haynes’** presentation will inspire young bench-side researchers and clinical investigators to develop a strategic vision for research priorities in this faculty taking into consideration the pressing health problems facing our community.

I am confident that as you attend this meeting, you will find answers to many questions related to healthcare. But I am equally hopeful that the Poster

presentations will also stir more questions in the minds of the participants in order to invigorate research activity in this institution.

I also thank the President of Kuwait University **Prof. Abdulla Al Fuhaid** and the Director General of the Kuwait Foundation for the Advancement of Science **Dr. Ali Al Shamlan** for their generous support.

Finally, I would like to express my appreciation of the hard work and dedication of the organising committee chaired by **Prof. M John Albert**.

Professor Fuad Hasan
Dean
Faculty of Medicine
March 2009

**Message from the Vice Dean for
Research,
Faculty of Medicine**



This year we are holding the 14th Health Sciences Poster Conference and we are honoured to have Prof. R. Brian Haynes, Professor of Clinical Epidemiology and Medicine, Chief of Health Information Research Unit, Faculty of Health Science, McMaster University, Canada, to be our Keynote Speaker.

The title of the keynote lecture is *"Evidence-Based Medicine and Knowledge Translation Research for Better Health Care"*. The 20th century focused on basic research resulting in many great discoveries, but now the 21st century focus has to become translating basic science discoveries into improved human health. In the past, it often took many years for laboratory discoveries to make their way into the practice of medicine. The goal of the medical institutions must include support to programmes to rapidly and efficiently translate laboratory discoveries into improved patient care.

I am sure that this conference will provide an excellent opportunity for the researchers in Health Sciences Centre and other health institutions in Kuwait to obtain knowledge about the current research activities and to discuss chances for future collaborations.

Finally, I would like to thank the organising committee chaired by Prof. M. John Albert, for its hard work and commitment to make this conference another successful event.

Wish you all very fruitful days of stimulating discussions and sharing of knowledge.

Dr. Mariam H. M. Yousif
Vice Dean for Research
Faculty of Medicine
March 2009

Message from Chairman of 14th HSC Organising Committee



It is with great pleasure that I pen this brief message. The Health Sciences Centre's annual poster conference has become a seminal event in our research and academic activities. This year's is no exception. We are honoured to have Professor R. Brian Haynes from the Faculty of Health Science, McMaster University, Hamilton, Ontario, Canada, deliver the keynote address on "Evidence-based medicine and knowledge translation research for better health care". He is a pioneer in the field of evidence-based medicine which has come to occupy a pivotal role in the practice of modern medicine.

As usual, there was an enthusiastic response to the call for abstracts. We hope to see most of the work eventually published in good international journals. This is a testimony to the calibre of work we do and the recognition by our peers.

We could not have succeeded without the help and support from various quarters-especially, the Dean, Vice-Dean for Research, and the administrative support service, Faculty of Medicine. We acknowledge the financial support from Kuwait University, Kuwait Foundation for Advancement of Science (KFAS) and Kuwait National Petroleum Company (KNPC). The judges perform a very difficult job of selecting posters for various awards. I thank them. The members of the poster organising committee participated enthusiastically in sharing the responsibilities. I am indebted to them.

The metric of success of the conference will be measured by how we answer the question, “Was the conference rewarding?” I am confident that it will be answered in the affirmative. Have a great conference!

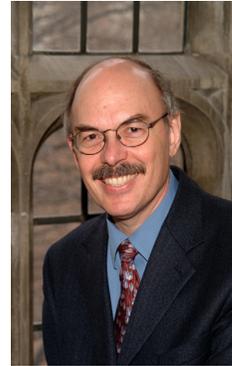
Professor M. John Albert
Chairman
14th HSC Poster Conference

Keynote Speaker

14th Annual HSC Poster Conference 2009

Professor R. Brian Haynes

R. Brian Haynes is Professor of Clinical Epidemiology and Medicine, Chief of the Health Information Research Unit at McMaster University, Hamilton, Ontario, Canada. He is on the active medical staff of Hamilton Health Sciences, Hamilton, Ontario, where he specializes in diabetes care. His main research interests are in improving health and health care through enhancing the validation, distillation, dissemination and application of health care knowledge. He is one of the originators of evidence-based medicine and is founding editor of ACP Journal Club, Evidence-Based Medicine, and EBM Updates.



Keynote Abstract

Evidence-Based Medicine and Knowledge Translation

Research for Better Health Care

High fidelity evidence-based information systems provide the starting point, and an essential ingredient, for improving healthcare. However, knowledge translation (KT) processes are also needed if evidence-based medicine is to become a reality. KT processes include developing clinical and health care policy, developing applications to deliver the policy, and incorporating the applications into the care of individual patients and populations.

For example, strong evidence shows that optimal stroke care prevents strokes, and reduces mortality and disability from strokes, but achieving these benefits in usual practice settings requires knowledge translation by and for policy makers (forming and implementing evidence-based policy), managers (working across traditional financial and jurisdictional boundaries), the public (being aware and seeking care when needed), practitioners (developing new skills and assuring quality), and patients (adhering to recommended treatments).

This presentation will describe the evolution and current status of information systems that provide the building blocks for evidence-based health care. It will then describe the knowledge translation steps needed to improve the implementation of evidence in practice.

Best Poster Award Winners -2008

Dr. Nael Al-Naqeeb Award for Best Undergraduate Research

- Al-Baaly H, Al-Khateeb A, Al-Mutairi L, Al-Zayer E: Knowledge, Beliefs and Attitude Towards Consanguinity and Premarital Screening for Hereditary Diseases Among Kuwaiti University Students

Graduate Research in Basic Sciences (Masters)

- Taqi Z, Al-Ali W, Jacob S, Al-Mulla F: Microarray Profiling of siRNA-knockout of RKIP in primary HEK293s cell line

Graduate Research in Basic Sciences (PhD)

- AL-Rifaiy AI, Al-Merjan J, Szucs G, Al-Nakib WS, Pacsa A: Heterogeneous adenovirus serotypes cause conjunctivitis in Kuwait

Graduate Research for Resident Doctors

- Marafi FA, Syed SA, Esmail AA, Elgazzar AH: Scintigraphic Patterns of Poliomyelitis on Bone Scan

Basic Sciences

- Benter IF, Canatan H, Yousif MHM, Anim JT, Akhtar S: Microarray based transcriptome analysis reveals global gene upregulation associated with kidney damage in DOCA-salt-induced hypertensive rats occurs via signaling cascades involving epidermal growth factor receptor and RasGTPase
- Hanif SNM, Al-Attiyah R, Mustafa AS: Characterization and Immunogenicity of RD1 Encoded Antigens of *Mycobacterium tuberculosis*

Clinical Sciences

- Uthaman B, Abushaban L, Al-Qbandi M, Al-Hay A, Rathinasamy J, Selvan J :Scimitar syndrome: The impact of interruption of anomalous systemic arterial supply on further management of symptomatic infants
- Omu AE, Al-Azemi MK, Kehinde EO, Anim JT, Oriowo MA, Mathew TC: Effect of obesity on outcome of antioxidant therapy in men with Asthenozoospermia
- Marafie MJ, Al-Awadi SA, Al-Mosawi F, Al-Ali W, Behbehani A, Al-Mulla F: Establishment of high throughput screening for MLH1 and MSH2 gene mutations for detection of HNPCC

Case Report

- Al-Kanderi SR, Pandey T: Intracranial calcification in central diabetes insipidus: Case Report

Past Poster day Keynote Speakers and Lectures

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.

Past Poster day Keynote Speakers and Lectures, Cont.

2003

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

2002

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

2001

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

2000

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

1999

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

1998

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

Past Poster day Keynote Speakers and Lectures, Cont.

1997

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

**Original Research Abstracts List
By Subject Area**

Allied Health

1

*Al-Obaidi SM, Hassan NA, Sinan T, Ben-Nakhi H, Al-Mandeel M: Effectiveness of McKenzie Treatment Intervention for Chronic Low Back Pain: A Comparison of Selective Physical and Psychological Measures (Clinical)

2

*Al-Rashidi R; Khudada S; Dashti F; Hassan N: The Prevalence of Work Related Musculoskeletal Disorders Affecting the Upper Body Among the Dental Professionals (Undergraduate)

3

*Khalifa NM, Mittal R, Omar S, Al Basmy A: Outcome of children with Wilms' Tumor: A 10 years analysis of from a single institution in Kuwait. (Clinical)

4

*Manee F, Rintala D, Hersch G, Chan J, and Reed K: Cross Cultural Perspectives of Quality of Life between Kuwaitis and Americans with Spinal Cord Injuries (Basic Sciences)

5

*Nadar MSH, Asbeutah A, Al-Obaidi S: The Effect of fingers flexion on Median Nerve compression within the Carpal Tunnel (Clinical)

Anatomy

6

*Renno WM, Al-Banaw AG, George P, Abu-Ghefreh AA, Benter IF, Yousif MHM and Akhtar S: Angiotensin-(1-7) Prevents the Diabetes-induced Decrease in Astrocyte GFAP Immunoreactivity in Hippocampal Formation (Basic Sciences)

Biochemistry

7

*Alansari ES: Development of an Assay for Detecting Alpha -2- Macroglobulin (Basic Sciences)

8

*Ali D, Sequeira F, Thomas M, Craik J, Benov L: The role of glyceraldehyde-3-phosphate dehydrogenase in hyperglycemia-induced kidney damage (Graduate: MSc Basic Sciences)

9

*Al-Maghrebi M, Kehinde EO, Anim JT, Eapen RM, John SJ, Prasad A: Vasectomy is associated with induction of germ cell apoptosis via modulation of survival genes in a rabbit model (Basic Sciences)

10

*Sequeira F, Thomas M, Craik J, Benov L: Rhodanese has a function as an antioxidant (Basic Sciences)

11

*Thomas M, Sequeira F, Batinic-Haberle I, Benov L: Modulation of biological actions of Mn-porphyrin superoxide dismutase mimics (Basic Sciences)

12

Thomas M, Sequeira F, Batinic-Haberle I, *Benov L: Superoxide dismutase mimics can substitute for the natural enzyme (Basic Sciences)

Community Medicine

13

Al-Failakawi B, Al-Mutairi M, *Al-Shraifi M, Al-Mohanna Z, Al-Sabah R, Al-Mahmoud S: Prevalence and associated risk factors of postpartum depression among mothers in Kuwait (Undergraduate)

14

Al-Awadi A, Al-Amiri R, *Al-Otaibi O: Low Back Pain among Male Taxi Drivers in Kuwait (Undergraduate)

15

Al-Awadi E, *Al-Haqqaan A, Al-Merdasi N, Al-Ottaibi H: First aid and cardiopulmonary resuscitation (CPR) knowledge and practice among elementary and intermediate school teachers in Kuwait (Undergraduate)

16

AlJassim A, *AlKandari M, AlSayed Omar A, Hussain A, Doi S, Bouhaimed M: Metabolic risk factors among adults participating in a national walking marathon in Kuwait (Undergraduate)

17

Al-Kandiri AK, Zubaid EM, Al-Ajeel FK, *Al-Najjar SJ, Shukkur M, Thalib L: Body image, body satisfaction and self-esteem in female university students in Kuwait (Graduate: MSc Basic Sciences)

18

*Al-Kharji S, Al-Ajeel F, Bu Rizq S, Al-Enizi M, Al-Ghunaim M, Al-Jaser W, Al-Mazeedi S, Al-Tammar F: Health risk behaviors among Kuwait University students (Graduate: MSc Basic Sciences)

19

*Al-Mazeedi H, Bouhaimed M: Putting medical negligence on the map: The spectrum of available information in Kuwait (Graduate (Resident))

20

*Al-Rashidi S, Abdulhakeem A, Al-Otaibi N, Hussain F, Doi SA, Thalib L: Patterns and symptoms of menopause among Kuwaiti women aged 45 to 65 years (Undergraduate)

21

*Baqeri FA, Al-Kazemi FU, Mughadam RA, Al-Mohri ZMJ, Ziyab AH, Akhtar S: Self-rated health and associated factors among faculty members and support staff of Kuwait University (Undergraduate)

22

*Mehraj S, Al-Awadhi E, Sadeqi M, Al-Fahad F: Knowledge and awareness of colorectal cancer in ministries complex employees in Kuwait (Undergraduate)

23

*Mohammad M KH E A Eid: Optimal Waist Circumference Cut-off Points to Predict the Risk of Diabetes Type 2 in Kuwaiti Adult Population (Graduate (Resident))

24

*Shah NM, Badr H, Behbehani JB, Shah MA: Chronic illness and functional disability among older Kuwaitis: how strong is the association? (Basic Sciences)

25

*Thalib L: Survival of Male Breast Cancer Patients: Population Based Cohort Study (Clinical)

Dentistry

26

*Akbar A, Bishara F, Al-Shammari KF: Dentist Awareness and Application of Current Guidelines for Antibiotic Prophylaxis Prescription (Undergraduate)

27

*Al-Khabbaz A, Al-Shammari KF: Dental and Medical Students Knowledge about Periodontal Disease and Diabetes (Basic Sciences)

28

*Al-Ansari JM, Al-Shammari KF, and Kamber F: Dentist and physician awareness of periodontal disease and pregnancy complications (Basic Sciences)

29

*Al-Awadhi SA, Loza Y: The effect of cell wall components of Candida albicans on the adhesion to Poly(methyl methacrylate) resin (Clinical)

30

*Al-Kharafi L, Al-Hajery D, Al-Azemi R: Patient Information vs. Patient Satisfaction among Orthognathic Patients Treated in Ministry of Health Clinics in Kuwait (Undergraduate)

31

*Al-Khatrash A, Badran B, Alomari Q: Variability in Diagnosis and Treatment of Occlusal Caries among Dentists in Kuwait (Undergraduate)

32

*Al-Marshed M, Al-Marshed S, Hasan AA: Child Oral Health Impact Profile (COHIP) for Preschool Children with Anterior Tooth Caries .(Caregiver's version) (Undergraduate)

33

*Al-Mutawa SA, Shyama M, Al-Duwairi Y, Soparkar P: Oral hygiene status of Kuwaiti schoolchildren in different governorates (Clinical)

34

*Alomari QD, ElDaraa EK: Randomized clinical trial of in-office dental bleaching with or without light activation (Clinical)

35

*AlQabandi A Kh: Profile of Antibiotic Prescriptions at a Dental Center (Clinical)

36

*Alsane' MA, Abd-Alsalam M: Infant Oral Health Knowledge of Expectant Mothers in Kuwait (Basic Sciences)

37

Alsane' MA, *Andersson L: Knowledge of Traumatic Dental Injuries Management among Dentists in Kuwait (Clinical)

38

*Al-Shammari KF, Al-Khabbaz A, Al-Jtaily M: Prevalence and risk indicators for alveolar bone loss in Kuwait (Basic Sciences)

39

Al-Shammari KF, *Kamber F, And Al-Ansari JM: Female patient awareness of periodontal disease and adverse pregnancy outcomes (Basic Sciences)

40

*Al-Shammari MS: Cusp deformation by composite resin restorations in MOD cavity model. (Basic Sciences)

41

*Årtun J, Al-Azemi R: Behavioral Risk Factors for Incisor Trauma Prior to Adolescence (Basic Sciences)

42

*Dileep Thomas, Rino Roy, Nancy V Thomas: Esthetic smile (Clinical)

43

*Ellepola AN, Khan Z, Joseph B, Chandy R, Philip L: Oral Carriage of Candida in patients attending the Kuwait University Dental Clinic: Preliminary Data. (Basic Sciences)

44

*Ellepola AN, Joseph BK, Devipriya B, Sharma P: Knowledge and attitudes of HIV/AIDS among Kuwait University dental students (Basic Sciences)

45

Gad M, *Mohamed Sh: Determining the superior temporomandibular joint space in centric relation using lateral tomogram in edentulous patients (Graduate: PhD Basic Sciences)

46

*Ghadanfar A: Assessment of dental surgeons' referrals to the orthodontic clinic in a dental center (Clinical)

47

Haron I, *Sabti M, Omar R: Knowledge and attitudes of dentists practising in Kuwait towards evidence based dentistry (Undergraduate)

48

Joseph BK, *Devipriya B, Sharma P: Oral cancer awareness among dentists in Kuwait. (Basic Sciences)

49

*Kullman L, Al-Sane M: Association between chronological age and third molar development in a Kuwaiti population using panoramic radiographs- a pilot study (Basic Sciences)

50

*Mohamed Sh: Comparing two designs of Mandibular Advancement sleep apnea appliances (Graduate: PhD Basic Sciences)

51

*Shyama M, Al-Mutawa SA, Al-Duwairi Y, Soparkar P: Age specific caries experience of Kuwaiti Kindergarten schoolchildren in different governorates (Clinical)

52

*Suresh R, Jones K, Newton T: An intervention to improve adherence to daily flossing regimen among patients in Kuwait University Dental Center (Graduate: MSc Basic Sciences)

Genetics and Molecular Biology

53

*Suad AlFadhli, Iman Hussein: Genetic diversity in two different ethnic groups (Arab and Persian) using 15 STR markers (Graduate: MSc Basic Sciences)

Health Education and Ethics

54

*Yaiesh S, Abdulrazak R, Bouhaimed M: Do You Know Your Blood Type: It Can Save Your Life! (Undergraduate)

Imaging (Nuclear Medicine and Radiological Science)

55

*Ali L, Khalil M, Hadi N, Al-Anteri I, Al-Kanderi A: Improvement of lesion detection in Ga67 imaging using two energy photopeaks in patients with lymphoma disease (Clinical)

56

*Ali L, Loutfi I, Hadi N, Al-Mutairi A: Scintigraphic localization of parathyroid lesions in patients with chronic renal failure using a magnified pinhole technique (Clinical)

57

*Al-Kandari F, Javaid A, Al-Shemmeri I, Al-Banna A, Ahmad AH, Al-Bargash K, Al-Reshidy M: Radiosynovectomy: Another approach to treat inflamed Knee joint (Clinical)

58

*Al-Mardoof A, Rizvi SAM, Loutfi I: Importance of ischemia detection by gated myocardial perfusion imaging in chronic renal disease with cardiac dysfunction (Graduate: MSc Basic Sciences)

59

*Al-Saeedi F, Loutfi I: Liver function evaluation using Tc-99m colloid and HIDA imaging in diabetic rats. Experimental model and findings. (Basic Sciences)

60

*Gupta R, Marouf R, Adekile AD: Influence of Frequent Vaso-Occlusive Crisis and Avascular Necrosis of the Femoral Head on Bone Mineral Density in Sickle Cell Disease Patients (Clinical)

61

*Galal AM, Doweidar AA, Abu-Shadi HM, Al-Kandery SR: Imaging of peripheral nerve entrapment (Clinical)

62

*Ismaiel AM, Abu-El-Nasr AK, Al-Kandery SR: MRI evaluation of ACL graft complications: correlation with clinical assessment and arthroscopic findings (Clinical)

63

*Khalil MM, Attia A, ALi M, Ziada G, Omar A, Elgazzar A: Echocardiographic correlation of Four Quantitative Gated SPECT Methods in the estimation of the left ventricular Ejection Fraction. (Basic Sciences)

64

Khurshed MA, *Javaid A, Naeem M, Mehmood N, Irum F, Umar S, Roohullah, Burdy GM, Khan ZT, Chohan ZA: Use of 99Tcm MIBI Spect for diagnosis of silent myocardial ischemia in diabetic patients (Clinical)

65

*Loutfi I, Al-Feeli M: Partially-reversible myocardial perfusion defects: clinical and electrocardiographic correlates (Clinical)

66

*Mustafa Sayed, H. R.Fargaly, MD: Success Rate Of 131i Ablation In Patients With And Without Preliminary Diagnostic Whole Body Scan (Clinical)

67

*Sheikh M, Ben-Nakhi, Shukkur AM, Sinan T, Al-Rashdan I: Accuracy of 64-multidetector row CT in the diagnosis of coronary artery disease. (Clinical)

68

*Usmani S, Khan HA, Al Mohannadi S, Javed A, Marafi F, Al Nafisi N, Abu Huda F, Amanguno HG: Intraoperative gamma probe localization of parathyroid using Tc-99m MIBI in patients with primary hyperparathyroidism (Clinical)

Medical Education

69

*Mohammed AM, Ware J: Kuwait University medical students do benefit from printed topics for their learning (Basic Sciences)

70

*Mohammed AM, Ayed A, Ware J: Some of what we do may not be necessary: writing five option multiple-choice questions (Basic Sciences)

71

*Waheedi MA, Al-Tmimy AM, Enlund H: Perceived preparedness for the smoking cessation role among students of health professions in Kuwait (Basic Sciences)

Medicine

72

Abalkhail SI*, Hilali N, Al-Kandari N, Doi SA, Al-Duaij S, Hafez MF, Nair VS, Ali AH, Al-Shoumer K (1, 3): Oscillations On Osteocalcin Levels In Uremic Patients Maintained On Regular Hemodialysis (Clinical)

73

*Abdel Ghani AH, Nessim J, Gupta RK, Ziedan J, Al Waheeb S, Ranjan B, Hussain N, A Helal B1, A Azmi M, Johny K V : Renal biopsies in Mubarak A Kabeer Hospital indications and clinical significance (Clinical)

74

*Abdel Ghani AH, Al Hilali N, Fouda M, Hussain N: Bacterial spectrum of permcath catheter related infection among hemodialysis patients (Clinical)

75

*Abdella NA, Mojiminiyi OA, Al-Mulla F, Al-Mohammedi H, Al-Arouj M, Nakhi AB, Pinto C, Al-Rammah T: Gender has significant impact on obesity-related metabolic abnormalities and phenotypic traits in healthy first-degree relatives of Type 2 Diabetes patients (Clinical)

76

*Abdella NA, Mojiminiyi OA, Al-Mulla F, Al-Mohammedi H, Al-Dahi W, Pinto C, Al-Rammah T: Evaluation of Adiponectin as a potential component of the criteria for the Metabolic Syndrome (Clinical)

77

*Abutiban F, Mokaddam K, Ameen E, Moussa M, Alsaied K: Comparison between familial and sporadic systemic lupus erythematosus in Kuwaiti patients (Clinical)

78

*Al Mutairi SS, Mojiminiyi OA, Shihab-Eldeen A, Al Rammah T, Abdella NA: Putative Roles of Circulating Resistin In Patients With Asthma, COPD and Cigarette Smokers. (Clinical)

79

*Al-Ghunaim MM, Al-Fraij AK, Bouhamra SW, Mohammad RT: A Case-control Study of the Risk Factors for Developing Diabetic Foot in Type 2 Diabetes Patients in Kuwait (Undergraduate)

80

*Al-Hilali N, Hussain N, Abdul-Kawy Y, Al-Azmi M: Safety and efficacy of novel dose regimen of cinacalcet in the treatment of hyperparathyroidism in hemodialysis patients (Clinical)

81

*Al-Mutairi N: Clinical spectrum and management of cutaneous leishmaniasis in Kuwait (Clinical)

82

*Al-Mutairi N, Al-Doukhi A: Comparative study on the efficacy, safety and acceptability of Imiquimod 5% cream versus cryotherapy for Molluscum Contagiosum in children. (Clinical)

83

*Alshemmari S, Mehrez J, Alqallaf D, Bhuksh F, Ameen R: JAK2 V617F mutation in Polycythemia vera in Kuwait: Molecular versus conventional diagnosis. (Clinical)

84

*Hussain N, Al-Hilali N, Ali I, Attia, Fathi V, Abdul Ghany A, Al-Azmi M, Johny KV: Trends in the left ventricular structure before and after spironolactone treatment in peritoneal dialysis patients (Clinical)

85

*Masocha W, Parvathy SS: Assessment of LPS induced monoarthritis in mice using the Catwalk video based gait analysis system. (Basic Sciences)

86

*Nahar I, Al-Saleh K, Al-Herz A, Al-Jarallah K, Al-Awadhi A Shehab D: Does Vitamin D have a role in patients with musculoskeletal pain? (Clinical)

87

*Nair MP, Al-Otaibi T, Said T, Halim M, Moneim MA, Elsayed A, Nawas KM, El-Kholy O, Nampoory MRN: Chronic antibody mediated rejection (CAMR) in renal transplants (Clinical)

88

*Al-Mutairi N and Al-Doukhi A: Combination of split skin grafting and excimer laser for the treatment of chronic stable localized vitiligo in children (Clinical)

89

*Rashed W, Zubaid M, Almahmeed W, Al-Lawati J, Sulaiman K, Al-Motarreb A, Amin H, Al Suwaidi J: Impact of Gender on Treatment and Clinical Outcomes in Acute Coronary Syndrome Patients in the Middle East (Clinical)

90

*Shehab D, Mini A: Nerve conduction studies in diabetic patients- A single centre experience (Clinical)

91

*Surrin SK, Jaufeerally FR, Kwok B, Koh TH, Sim LL: Singapore general hospital heart failure registry (Clinical)

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**Original Research Abstracts
By Subject Area**

1

Effectiveness of McKenzie Treatment Intervention for Chronic Low Back Pain: A Comparison of Selective Physical and Psychological Measures

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Introduction:

Although many studies were published on the effectiveness of the McKenzie intervention, the long term impact on cognitive components of the pain experience appear to be an assumption associated with the well behavior that follows. This assumption merits further examination. Objectives: To assess the influence of the McKenzie intervention on selected biobehavioral and physical performances in individuals with Chronic Low Back Pain (CLBP) demonstrating pain centralization.

Methods:

Prospective comparative design with two follow-up assessments at the end of the 5th and 10th weeks after the interventions. Sixty two subjects with CLBP (28 men and 34 women) age range of (37.29 – 41.92) years. Pain related fear and beliefs were assessed using the Disability Belief Questionnaire (DBQ) and Fear Avoidance Belief Questionnaires (FABQ). McKenzie standardized assessment, evaluation, diagnosis, intervention as well as advises and home programs were provided. Repeated sit-to-stand, forward, bending, customary and fast walking times were recorded. Pain (anticipated vs. true felt), were measured before and after the performance of a task. Measurement protocols were repeated at the end of the 5th and 10th weeks after completing the treatment. Performance time scores were compared to those of healthy matched individuals based on age, height and weight. Descriptive statistics as well as analysis of variance with post hoc analysis were used (alpha = 0.05).

Results:

Significant improvements were reported at the end of the 5th week for all variables (P<0.05). Anticipation of pain and FABQ (Physical Activity subscale) were the strongest predictors for task performances. There was a tendency for performance time and bio-behavioral factors to regress after the end of the 10th week.

Conclusions:

Our results support the short term influence of the McKenzie intervention in CLBP, However, the long-term effectiveness merits further studies.

Key Words: Pain centralization; McKenzie exercises; Fear-avoidance belief
Funding Agency: None

The Prevalence of Work Related Musculoskeletal Disorders Affecting the Upper Body Among the Dental Professionals

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Introduction:

There is a high risk of Work-related musculoskeletal disorders (WMSDs) due to the different types of mental stresses and physical stresses affecting the body. The aim of this study was to investigate the prevalence of physical, psychosocial, and individual characteristics of dental students and staff in Kuwait.

Methods:

A questionnaire was distributed at different locations in Kuwait such as hospitals, clinics and Kuwait University. A sample size of 370 was calculated a-priori. The questionnaire was formulated to investigate the physical and psychosocial workload on general health and duty characteristics. It also included specific and general questions concerning the lifestyle of dental professionals as well as work load characteristics. Data was analyzed using SPSS 14.0 to describe means, standard deviations, and percentages. While Chi-Square test was used to analyze the relationships between variables.

Results:

A total of 390 questionnaires were completed and returned. Of the respondents, 40.5% were male and 59.5% were female with 43.2% of respondents were 20-30 years. 43% of respondents were Kuwaiti, 31.5% were Asian and the remaining respondents were of other nationalities. Respondents were categorized as: 20% students, 6.9% academics, 19.9% general dentists, 21.7% specialists, and 31% hygienists or dental nurses. Most respondents reported experiencing at least one WMSD (73%) with Low Back Pain (LBP) as being the most prevalent (40.7%) followed by neck pain (26.7%), upper back pain (15.6%), hand/wrist pain (7.4%) and shoulder/elbow pain (9.6%). Almost one quarter of respondents (22.2%) sought medical care. Almost 2 in 10 respondents (14.6%) reported taking sick leave because of a WMSD. The majority of respondents (99.7%) reported experiencing physical loads during work (repetitive movements, awkward postures, strenuous arm movements and use of vibration tools). No association between psychological load and WMSD, sick leave, or medical care was found. There was a significant association between WMSD and gender ($p < 0.004$), and repeated movements ($P < 0.032$), awkward postures ($p < 0.009$), and strenuous arm movements ($p < 0.039$). The use of vibration tools was significantly associated with shoulder pain ($p < 0.040$).

Conclusions:

The results of this study suggest that WMSD represent a major occupational health issue for dental professionals in Kuwait. WMSD was shown to be effected in almost three quarters of the dental professionals in this study. Further research is now needed to clarify the impact of WMSD's in dental professionals as well as to help determine effective measures for reducing these disorders in this population group.

Key Words: Work-related musculoskeletal disorder; Dental Professionals; Physical Therapy
Funding Agency: None

Outcome of Children with Wilms' Tumor: A 10 Years Analysis of from a Single Institution in Kuwait.

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Introduction:

Wilms' tumor is the most common renal tumor during childhood. Over the past three decades, there have been significant improvements in the survival of children suffering from this tumor. This is largely attributed to the introduction of chemotherapy based protocols by the international cooperative groups, mainly National Wilms' Tumor Study group (NWTS), and the International Society of Pediatric Oncology (SIOP). The long term survival from this tumor is in the range of 80 – 90%. This study was conducted to evaluate outcome of our patients with Wilms' tumor.

Methods:

We analyzed the data of 32 patients over a 10 years period (January 1998-December 2007). Majority of children were treated adopting the SIOP protocols. Five children underwent primary nephrectomy and were treated on alternative protocols.

Results:

The median age was 38 months (range from 22-54 months); males and females were equal in number (16 each). There were 10 children with stage I (31%), 8 with stage II (25%), 7 with stage III (21.8%), 4 with stage IV (12.5%), and 3 with stage V (9.3%). One child had congenital aniridia. Favourable histology was seen in 25 patients (78%), unfavourable in 6 patients (19%), one patient had CMN (3%). Twenty seven children were treated at our centre using SIOP protocols, while 5 children travelled abroad and had primary nephrectomy followed by chemotherapy. Nine children (28%) also received radiotherapy. All surviving children are followed up at our centre. Ten years EFS was 81%, and with OS of 84%. There were 5 deaths, out of which three were metastatic at presentation. Two died due to refractory disease, 2 died of relapse and one due to therapy related septicemia.

Conclusions:

The survival of our children with wilms tumor are comparable with results from reported results in literature. The patients with metastatic disease due to delayed presentation had poor outcome.

Key Words: Wilms' tumor; Outcome; Children

Funding Agency: None

Cross Cultural Perspectives of Quality of Life between Kuwaitis and Americans with Spinal Cord Injuries

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Introduction:

Quality of life (QOL) is considered one of the outcomes in occupational therapy and has long been of central focus to occupational therapists. Spinal cord injury (SCI) survivors are one of the common groups that occupational therapists treat. A spinal cord injury is an unexpected injury that can occur among young adult males. It is a nationwide issue and the annual incidence of SCI worldwide has been reported to be between 11.5 and 57.8 cases per million population. Such injury can result in significant and permanent life changes for the injured individuals including his/her physical, psychological, and social aspects. Since client satisfaction is considered an important health outcome, more research is necessary to compare the QOL of persons with SCI across a variety of cultures. Currently, there is no study that assesses and compares QOL between an Arabic country and that of a more developed country. Due to growing numbers of SCI survivors in Arabic countries and the need to preserve their long-term QOL, it seems necessary to study and compare the QOL between survivors of SCI in the USA and Kuwait. The aim of this study was to compare QOL scores between adult Kuwaitis and Americans with spinal cord injuries.

Methods:

This study was quantitative in design. The health-related quality of life (HRQOL) of adult Kuwaitis with SCI living in the community as measured by the 36-item Short Form Health Survey (SF-36) were compared to American general population norms and the results from American survivors with SCI reported in the Forchheimer et al study using the means and standard deviation scores.

Results:

Kuwaiti survivors with SCI results' were compared to the results of American survivors with SCI that were published in a study by Forchheimer et al using the means and standard deviation scores of the SF-36 scores. T-test analysis showed a significant decrease in QOL scores of the Kuwaitis compared with Americans on three scales of the SF-36: social functioning, role emotional, and mental health as well as the mental component summary measure.

Conclusions:

QOL is an important outcome and improving it is often stated as the major goal of therapy. Cross cultural QOL studies can help our understanding of QOL for persons with chronic disabilities. This present study may encourage policy makers in Kuwait to develop new health policies to improve services and rehabilitation outcomes in Kuwait. Also this methodology introduces a new area of research for occupational therapists cross-culturally. Such cross-cultural studies can help in generating many new hypotheses regarding occupational therapy health care issues. Further investigation on the impact of the occupation, environment, and adaptation on the QOL of persons with SCI both nationally and internationally could lead to better, healthier and more productive lives.

Key Words: Spinal cord injury (SCI); Quality of life (QOL); Occupational therapy

Funding Agency: None

The Effect of Fingers Flexion on Median Nerve Compression within the Carpal Tunnel

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Introduction:

During finger flexion, the lumbrical muscles enter the carpal tunnel and cause an increase in carpal tunnel pressure, a mechanism that has been suggested to contribute to the etiology of Carpal Tunnel Syndrome (CTS). Purpose: To measure the immediate effects of pressure change in the carpal tunnel, as increased by finger flexion, on median nerve sheath area (MNSA).

Methods:

Twenty - three healthy volunteers (10 males, 13 females) participated in this experimental study. The MNSA was measured at the level of hook of hamate using ultrasonography during four different finger positions.

Results:

A significant change in MNSA during different finger positions ($F = 20.073$, $p < 0.001$) was found, indicating change in pressure exerted on the nerve. The biggest difference in MNSA was recorded between full finger extension and forceful full finger flexion (mean difference = 1.174 mm, $p < .001$).

Conclusions:

Finger flexion resulted in decrease in MNSD, possibly indicating a median nerve compression. Hand therapists need to consider modifying their conservative treatment of CTS by limiting hand function activities and immobilizing the wrist AND fingers to minimize lumbrical insertion into the Carpal Tunnel, thus, limiting pressure increase on median nerve.

Key Words: Carpal Tunnel Syndrome; Lumbricals; Median nerve

Funding Agency: None

Anatomy

Category: Basic Sciences

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Angiotensin-(1-7) Prevents the Diabetes-Induced Decrease in Astrocyte GFAP Immunoreactivity in Hippocampal Formation

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Introduction:

Diabetes increases the risk of central nervous system (CNS) disorders such as stroke, seizures, dementia, and cognitive impairment. Astrocytes are proving critical for normal CNS function, and alterations in their activity could contribute to diabetes-related disturbances in the brain. A key indicator of this response is the alteration in the level of glial fibrillary acidic protein (GFAP) and number of GFAP-immunoreactive (IR) astrocytes. We have previously shown that chronic treatment with angiotensin-(1-7) [Ang-(1-7)] reduced blood pressure and improve renal, cardiac and vascular function but its role in diabetes-induced alterations in the CNS is unknown. This study examined the effect of Ang-1-7 treatment on the number of GFAP-IR astrocytes in hippocampal formation of streptozotocin (STZ)-induced diabetes.

Methods:

Male Wistar rats weighing about 300g were used. Animals were divided into the following groups (N=10/group):

1. Wistar Control,
2. Wistar + STZ (55 mg/kg body weight)
3. Wistar STZ + Ang-(1-7); treated daily with (ip) injections of Ang-(1-7) (576 ig/kg/day ip)
4. Wistar STZ + DX-600 (ACE2 inhibitor; 40 mg/kg/every other day subcutaneously)
5. Wistar STZ + A779; treated daily with A779 (Ang-(1-7) receptor antagonist; 0.8 mg/kg/day ip).

Results:

Results demonstrated a significant ($P < 0.001$) decrease in the number of GFAP-IR astrocytes in the CA and dentate gyrus of the hippocampal formation of diabetic rats when compared with the hippocampal areas of control group. This decrease was significantly ($P < 0.02$) elevated after Ang(1-7) treatment in the hippocampal formation areas of the diabetic group.

Conclusions:

These results suggest that the induction of diabetes is associated with a reduction in GFAP-IR astrocytes in the hippocampal formation which may affect the functional support and role of astrocytes in the CNS. In addition, Ang(1-7) treatment could be an important therapeutic strategy to lessen pathological changes associated with diabetic state in the CNS.

Key Words: Hippocampal formation; Astrocytes; Diabetes

Funding Agency: Departmental support

Development of an Assay for Detecting Alpha -2- Macroglobulin

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Introduction:

Diagnosis of kidney problem is usually made depending on clinical history, medical examination, X-ray and laboratory tests. One of these laboratory tests is the presence of blood (haematuria) and proteins (proteinuria) in urine. Proteins especially the one with large size, are reabsorbed in the urinary tract and don't present in urine of healthy people except when there primary or secondary kidney problems. We tried to develop an ELISA assay for the measurement of alpha -2- macroglobulin in urine and evaluate its performance. Testing alpha-2- macroglobulin as marker for haematuria.

Methods:

Method was established using commercial reagents, equipment and appropriate standards. Standard prepared by adding 0.2ml plasma calibrator to 2ml of 1% BSA/PBS to give concentration of 181.8 mg/l alpha -2- macroglobulin . Serial dilution of the curve was done to give a range from 0.04 µg/l - 874 g/l. The assay was optimized using different regants and conditions. Urine samples from patients with kidney problems were tested for alpha -2- macroglobulin. The results were compared to blood content measured using urine strips. All results were tested statistically using analyze-it.

Results:

Standard curve constructed using serial measurement of the standard with optimum conjugated antibody concentration 0.049 µg/ml and 14.2 µg/ml for coating antibody. Ova-albumin was chosen as a blocker. Sensitivity of the assay was 0.05 µg/ml, analytical recovery 86-110%. Dilution experiments showed parallism in standard curves. Intra and inter- assay were 1.9-5.1% and 9.9-20% respectively. Alpha -2- macroglobulin measured using the assay correlated with haematuria ($p < 0.05$; Spearman correlation) and proteinuria ($p < 0.01$). alpha -2- macroglobulin correlated with proteinuria in those who were positive for haematuria $p < 0.01$.

Conclusions:

Positive correlation with proteinuria excludes alpha -2-macroglobulinn from being used as a sole marker for haematuria.

Key Words: ELISA; alpha -2-macroglobulinn; kidney

Funding Agency: None

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The Role of Glyceraldehyde-3-Phosphate Dehydrogenase in Hyperglycemia-Induced Kidney Damage

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Introduction:

Glyceraldehyde-3-phosphate dehydrogenase (GAPDH; EC 1.2.1.12) is a ubiquitous enzyme that plays an important role in glycolysis and gluconeogenesis by reversibly catalyzing the conversion of D-glyceraldehyde-3-phosphate to 1, 3-bisphosphoglycerate. A highly reactive thiol at its active site renders GAPDH sensitive to modification by a variety of compounds with subsequent loss of enzyme activity. It has been hypothesized that inactivation of GAPDH is the key factor triggering a series of reactions leading to diabetic complications. The aim of this work was to investigate the effect of diabetes on kidney GAPDH, the mechanisms of its inactivation and the possible consequences.

Methods:

Streptozotocin diabetic rats, and superoxide dismutase (SOD)-, catalase (CAT)-, and GSH-deficient *E. coli* strains were used as model systems. Mn(III) 5, 10, 15, 20-tetrakis(N-methylpyridinium-2-yl)porphyrin (MnTM-2-PyP) was used as a superoxide/peroxynitrite scavenger. In vivo MnTM-2-PyP was administered s. c. at a daily dose of 1.0 mg/kg for two months. Tissue and cell homogenates were used to estimate GAPDH activity. Proteinuria was used as a marker of kidney damage. Student's t-test was used for data analysis and $p < 0.05$ was accepted as statistically significant.

Results:

GPDH activity was suppressed to ~ 60% in diabetic animals, but remained unaffected in SOD-, CAT- and GSH-deficient cells. MnTM-2-PyP did not protect GAPDH against inactivation, and did not prevent proteinuria.

Conclusions:

Diabetes caused significant loss of GAPDH activity in the kidney. This inactivation was not a consequence of direct -SH oxidation by reactive oxygen or nitrogen species. Inactivation of GAPDH leads to increase of upstream glycolytic intermediates, which in turn can activate four major pathways of hyperglycemic damage.

Key Words: Glyceraldehyde-3-phosphate dehydrogenase; Diabetes; Kidney damage

Funding Agency: Grant MB 07/04 from Kuwait University

Vasectomy is Associated with Induction of Germ Cell Apoptosis via Modulation of Survival Genes in a Rabbit Model

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Introduction:

Vasectomy is a widely used method of male contraception that has been postulated to be associated, in the long term, with increased risk of prostate cancer. This disease is linked to disruption of the mechanism regulating the balance between cell proliferation and apoptosis in prostatic cells. Since vasectomy might alter this balance, this study evaluates the long term effect (6 months) of this contraceptive procedure on apoptosis, survival gene expression and spermatogenesis in a rabbit model.

Methods:

Groups of four adult NZW rabbits (6-12 months old) were sham-operated, unilaterally vasectomized or bilaterally vasectomized. The testes were harvested six months after vasectomy. Germ cell apoptosis was evaluated by TUNEL assay and electrophoresis assay of DNA fragmentation. Spermatogenesis was evaluated using the histological Johnsen scoring system. The relative gene expression of survival genes (survivin, Bax and Bcl-2) was quantified using RT-real time PCR.

Results:

In the two post vasectomy groups, spermatogenesis impairment was associated with increased apoptotic score. The total number of positive TUNEL cells in vasectomized groups was greater than that in sham-operated group ($P < 0.05$). Also, the number of spermatozoa and spermatids in testicular biopsies were significantly lower (Johnsen score < 5 ; $P < 0.05$) than in sham group. An elevated bax/bcl2 ratio and a low level of survivin gene expression were present in testicular tissue after vasectomy coinciding with increased apoptotic score.

Conclusions:

These findings demonstrate that six months post vasectomy could enhance damage to spermatogenesis and apoptotic death of testicular tissue in adult rabbits through modulation of the expression of survival genes.

Key Words: Vasectomy; Apoptosis; Survival genes

Funding Agency: Kuwait University Research Grant No. MB01/05

Rhodanese has a Function as an Antioxidant

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Introduction:

Rhodanese (Rho) (thiosulfate sulfurtransferase; EC 2.8.1.1) is a ubiquitous enzyme present in all living organisms, from bacteria to man. The exact biological role of Rho is not known, but it is suggested to play a role in cyanide detoxification. The active site of Rho contains a tryptophanyl residue in close proximity to an essential -SH group. This makes the enzyme sensitive to inactivation in vitro. Little is known however, about the status of rhodanese in vivo, at conditions of oxidative stress. The aim of this study was to investigate how endogenous production of reactive oxygen/nitrogen species affects Rho activity.

Methods:

Two types of systems were used throughout this study - superoxide dismutase (SOD)-, catalase-, soxRS-, and oxyR- deficient Escherichia coli strains, and diabetic rats. Rho activity was assayed by a standard colorimetric procedure in cell-free extracts and tissue homogenates. Student's t-test was applied for data analysis and $p < 0.05$ was accepted as statistically significant.

Results:

In vitro, in cell-free extracts and tissue homogenates, Rho was rapidly inactivated by superoxide and hydrogen peroxide, or by short-chain glucose metabolites. The activity of Rho was, however, elevated in SOD-deficient cells, and in cells subjected to oxidative stress, as well as in diabetic rat liver.

Conclusions:

Irrespective of its vulnerability to inactivation, in vivo Rho is maintained active even during severe oxidative stress. Since the enzyme repairs oxidatively damaged Fe-S proteins involved in energy production, it can be considered an antioxidant and its activity is essential for the survival of the cells during oxidative stress.

Key Words: Rhodanese; Oxidative stress; Antioxidant

Funding Agency: Grant MB03/07 from Kuwait University

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Modulation of biological actions of Mn-porphyrin superoxide dismutase mimics

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Introduction:

Mn porphyrins (MnP) are among the most effective functional catalytic antioxidants, and comprise a relevant class of synthetic modulators of redox-signaling pathways. Their mode of action has been attributed to their ability to regulate redox-active transcription factors and to scavenge reactive species. Together with the free radical-scavenging activity, MnP bioavailability is a major determinant of their in vivo efficacy. The aim of the present study was to investigate how substitutions on the porphyrin ring would affect biological actions of Mn(III) meso-tetrakis(N-alkylpyridinium-2-yl)porphyrin.

Methods:

Manganese(III) meso-tetrakis(N-alkylpyridinium-2-yl) porphyrins and Mn(III) meso-tetrakis(N-alkylpyridinium-3-yl) porphyrins with ethyl, methyl, propyl, butyl, and hexyl substituents were used in this investigation. The effects of the MnP were tested on SOD-deficient (JI132) and SOD-replete (AB1157) *E. coli* strains by monitoring cell growth and viability. Student's t-test was applied for data analysis and $p < 0.05$ was accepted as statistically significant.

Results:

The increase of hydrophobicity from methyl- to hexyl-substituted MnP practically did not affect the O₂·⁻ scavenging activity, and hence in vitro antioxidant potency of the SOD mimetics. It, however, dramatically changed MnP's biological effects. While the hydrophilic ethyl and methyl analogs fully substituted for SOD at the concentration range of 20 – 30 μ M, the hexyl-substituted MnP worked as an antioxidant at a very narrow range ($\leq 0.5 \mu$ M), but exerted strong bactericidal action at concentrations $\geq 1.0 \mu$ M.

Conclusions:

Aliphatic substituents at meso-position of the porphyrin ring profoundly affect the biological properties of the MnP. Replacement of the shorter chains (methyl, ethyl) with longer chains (hexyl) converts MnP SOD mimics to highly potent antibacterials. Among the reasons is the higher lipophilicity of hexyl analogues, which affects cellular uptake and distribution.

Key Words: SOD mimic; Antioxidant; Antibacterial

Funding Agency: Grant MB03/07 from Kuwait University

Superoxide Dismutase Mimics can Substitute for the Natural Enzyme

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Introduction:

Oxidative stress has been implicated in a variety of pathological conditions including diabetes, ischemia-reperfusion injury, chronic inflammation, neurodegenerative disease, and aging. The potential medical utility of a compound that would reduce oxidative stress has led to the development and testing of a variety of Mn-containing coordination compounds that have been termed superoxide dismutase (SOD) mimics. The aim of this study was to use a very simple model system – bacteria (*Escherichia coli*) in order to test the ability of Mn-containing SOD mimics to substitute for the natural enzyme.

Methods:

Wild-type *E. coli* have Fe- and Mn-containing cytosolic SODs. *E. coli* lacking both of these cytosolic SODs exhibit several phenotypes that can be directly attributed to the loss of SOD activity, e.g. poor aerobic growth and auxotrophies for certain amino acids. We used those features to determine the effect of the SOD mimics by assessing the aerobic growth in media lacking specific amino acids. SOD activity was assayed by the cyt. c reduction method, and growth was measured turbidimetrically. All experiments were repeated at least 3 times with 3-5 replicates.

Results:

For the compounds tested, log k cat for dismutation of superoxide was in the range 6.6 - 8.85. The enzyme SOD has a log k cat around 9.0. The SOD mimics with higher catalytic activity demonstrated higher efficiency in relieving the oxygen-dependent phenotypic deficits exhibited by the SOD-deficient cells.

Conclusions:

For most compounds tested, high catalytic activity paralleled with high efficiency in protecting the SOD-deficient cells against superoxide-induced damage.

Key Words: SOD mimic; Catalytic activity; Superoxide dismutase

Funding Agency: Grant MB03/07 from Kuwait University

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Prevalence and Associated Risk Factors of Postpartum Depression among Mothers in Kuwait

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Faculty of Medicine

Introduction:

This cross-sectional study aims to investigate the prevalence and associated factors of postpartum depression among mothers in Kuwait as well as to assess the level of their awareness.

Methods:

Participants included mothers who are 0-6 months postpartum and who had living infants 6 months or younger. These mothers were chosen from randomly selected vaccination clinics at the primary care centers distributed throughout the six governorates of Kuwait. Participants completed a five-part questionnaire assessing socio-demographic information, pregnancy- and delivery-related variables, postpartum depression status (Edinburgh Postpartum Depression Scale (EPDS)), availability of social support (Multidimensional Scale of Perceived Social Support), as well as awareness of PPD.

Results:

The prevalence of PPD in Kuwait was found to be 53.4% (EPDS cut-off score of 12). Five risk factors were strongly associated with high scores on EPDS; low total family income (less than 500KD) (OR=3.231), having more than 4 children (OR=2.556), stressful life event(s) (OR=3.04), lower social support scores (OR=0.955), and medical complications during last pregnancy and/or delivery (OR=3.787). Among the sampled mothers, 84% have heard about PPD, however, the majority of them know a little about PPD.

Conclusions:

This study suggests that PPD is common in Kuwait. However, other studies on PPD conducted in Kuwait have found varying prevalence rates. Therefore, further studies on PPD should look into using standardized diagnostic criteria for PPD to more accurately assess the prevalence rate among mothers in Kuwait. There is also a strong need to educate the public and physicians about PPD.

Key Words: prevalence; income

Funding Agency: None

Low Back Pain among Male Taxi Drivers in Kuwait

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Introduction:

Vehicles' drivers are susceptible to Low Back Pain (LBP) because of prolonged sitting in a restricted position, car vibration, shocks from roads, and mental stress associated with driving. Little is known about LBP among vehicles' drivers in Middle East.

Aim:

Estimate the prevalence of LBP among male company-employed taxi drivers in Kuwait and investigate the associated risk factors.

Methods:

Cross-sectional survey on conveniently selected group of taxi drivers using self-administered questionnaire. Questions about LBP were adopted from Nordic Questionnaire while Roland-Morris questionnaire was used to estimate the disability due to LBP.

Results:

Out of 301 participants the one-year prevalence and the one-week prevalence was 34.9% (95% CI: 29.5%- 40.6%) and 21.3% (95% CI:15.3-24.5%) respectively. Half of those with LBP in the last 12 months have sought medical care which represent 17.3% of all drivers. Factors that were significantly associated with LBP are age, nationality, smoking, BMI, and job satisfaction.

Conclusions:

LBP is common among taxi drivers in Kuwait with more than one in three drivers suffers from LBP. Health promotion including smoke cessation, encouraging healthy weight, and dealing with issues related to job satisfaction may reduce the risk of LBP among taxi drivers.

Key Words: Low Back Pain (LBP)

Funding Agency: None

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First Aid and Cardiopulmonary Resuscitation (CPR) Knowledge and Practice among Elementary and Intermediate School Teachers in Kuwait

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Introduction:

To measure the level of knowledge and the extent of practice of elementary and intermediate school teachers about First aid and cardiopulmonary resuscitation (CPR). Also, to study the association of knowledge and practice about First aid/CPR with sociodemographic characteristics of teachers.

Methods:

A cross-sectional sample survey was conducted during the month of January 2009. A specially designed self administered structured questionnaire was used to collect data from elementary and intermediate school teachers in Capital and Al-Jahra governorates. The questionnaire included 3 sections: sociodemographic characteristics, knowledge of school teachers about First aid/CPR and practice of First aid/CPR among school teachers. A total of 474 teachers were included in the study with response rate of 74.1%.

Results:

The mean First aid/CPR knowledge score among elementary and intermediate school teachers was 45.9% with a maximum score 77%. The mean knowledge score of elementary teachers was significantly higher than that of intermediate school teachers ($p = 0.008$). Also, the mean knowledge score of female teachers was significantly higher than that of male teachers ($p < 0.001$). Teachers were more knowledgeable in the management of falls (72.0%), bee sting (67.9%), electrical burns (57.4%), bleeding wounds (55.3%) and fainting (48.6%), while they were less knowledgeable in managing poisoning (29.2%), dental injury (14.5%), and seizure (8.7%). 13.1% of teachers attended a First aid/CPR training course and only 36.5% reported the existence of a protocol for emergency situations.

Conclusions:

The overall First aid/CPR knowledge among elementary and intermediate school teachers in Kuwait is insufficient. It is recommended that health authorities would provide repeated training courses through official institutions distributed all over Kuwait and provide schools with a protocol to be followed in emergency situations.

Key Words: Cardiopulmonary resuscitation (CPR); Sociodemographic characteristics

Funding Agency: None

Metabolic Risk Factors among Adults Participating in a National Walking Marathon in Kuwait

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Introduction:

Cardiovascular diseases (CVD) are the major causes of morbidity and mortality worldwide and are the leading cause of death in Kuwait. Modifiable risk factors for CVD include smoking, obesity, hypertension, diabetes, hypercholesterolemia, poor dietary habits and lack of exercise. The objective of this study was to assess some of these factors among adults participating in a walking marathon in Kuwait.

Methods:

A cross-sectional study was conducted in 2008. Participants visiting the Kuwait Heart Association screening unit during the registration period for the marathon were approached. Weight and height were measured and body mass index was computed. Blood pressure (BP) cut off point was more than 140 mmHg for systolic BP or more than 90 mmHg for diastolic BP. For random blood sugar the cut off level was more than 11.1 mmol/l and more than 200 mg/dl for total cholesterol level. The Statistical Package for Social Sciences (SPSS), Version 16 for windows [SPSS Inc, Chicago, IL, USA] was used for analysis. The statistical significance was considered to be $P < 0.05$.

Results:

Two-thirds of the population was at least overweight and males were more obese than females. Amongst the participants, a fifth had high blood pressure, a quarter had high cholesterol values and a few had elevated random blood sugar values. The ratio of having more than two risk factors to having nil risk factors was 6:1 in adults, while in the teenagers group it was the reverse and approximately 1:5. Although the association between gender, age and the number of metabolic risk factors were not statistically different, nevertheless, about half of the teenagers, three-quarters of the young adults and the vast majority of the adults had at least one metabolic risk factor.

Conclusions:

The prevalence of CVD metabolic risk factors is significant even in this relatively young and self selected healthy population.

Key Words: Metabolic risk factors; Young adults; Kuwait

Funding Agency: None

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Body Image, Body Satisfaction and Self-esteem in Female University Students in Kuwait

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Introduction:

With increasing global prevalence of overweight and obesity, the psychological consequences associated with poor body image and satisfaction with body image has become an important public health issue. Dieting behavior has become the focus of concern among health professionals because of its increasing prevalence. Very little data exists regarding the relationship between obesity and overweight status and the perception of self, particularly in the Arab region.

Methods:

A cross sectional survey was conducted on 772 female students in three universities in Kuwait. Data were collected using self-administered questionnaires. Predictors for low self-esteem, satisfaction with body image and the use of weight control measures were assessed using logistic regression models.

Results:

Half of the population perceived themselves as overweight or obese while only 26% of them had BMI levels higher than normal. About 55% were also not satisfied with their body image particularly among the overweight and obese; 72% desired a normal image, and 16% wanted to be underweight. Multivariate stepwise logistic regression models identified that the body image perception of being obese or overweight, the wish to become thinner and the desired image predicted the level of body image dissatisfaction. Body image satisfaction and perceived image in turn were the independent predictors of low self-esteem, as well as the use of extended weight control methods.

Conclusions:

Our findings suggest that perceived body image, in particular thinner body ideal and associated satisfaction with body image and low self-esteem, have more significant effects on dieting than being actually overweight does. Public health consequences associated with poorly perceived body image could be important. Thus, this association should be further investigated and emphasized to confirm causal relationships.

Key Words: Satisfaction with body image; Low self-esteem; Desired and perceived body image
Funding Agency: None

Health Risk Behaviors among Kuwait University Students

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Introduction:

The majority causes of death in Kuwait can be controlled by modifying different risk factors and health-related behaviors, which are implemented and reinforced in the adolescence period. The aim of this study, which is part of the first GCC Youth Risk Behavior assessment research, is to determine the prevalence of health risk behaviors among youth population in Kuwait.

Methods:

In this cross-sectional study, random sampling method was used to select Kuwait University students from all colleges. Data analyses were performed using SPSS version 16. Total sample=1196 students; 9.6% were female. Self-administered questionnaire was used to assess different health-risky behaviors.

Results:

The prevalence of major health risk behaviors like smoking, illegal substances use, alcohol drinking, violence, sexual health, mental health and unhealthy lifestyle were assessed.

Conclusions:

Assessment of the prevalence of unhealthy behaviors among youth population in Kuwait is the first step in the prevention and control of chronic diseases and deaths in Kuwait. Plan future health education programs in collaboration of other GCC countries

Key Words: Health; Risk; Behaviors

Funding Agency: International Medical Center- Saudi Arabia

Putting Medical Negligence on the Map: The Spectrum of available Information in Kuwait

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Introduction:

A recent Publication by Sir Liam Donaldson, Chief Medical Officer in England, "Making Amends", pointed to the fact that 10% of hospital in-patient admissions may result in some kind of adverse event. This type of information is unavailable in Kuwait. The objective of this study was to identify the spectrum of information on medical Negligence in the country.

Methods:

Medical negligence information was obtained through literature review, Internet search, telephone and personal interviews to identify the availability and accessibility of information, scope and nature of data (Administrative/legal/Clinical), and database system (Manual/Computerized).

Results:

There is currently no identified/accessible registration system in Kuwait. In addition, there was an atmosphere of secrecy surrounding the topic. The only available information came from the Department of Forensic Medicine - Ministry of Interior. The number of cases referred to this department from the Kuwaiti courts for opinion were 33 cases in the year 2000, 43 cases in 2002 and 73 cases in the year 2004 with more than two folds increase in that period.

Conclusions:

A major finding of this study was the absence of published administrative and clinical data about this issue from the Ministry of Health. There was lack of transparency and atmosphere of secrecy surrounding the issue. The number of claims is escalating with associated increase in cost and possible effect on an already demoralized profession. The present information and situation is one of a major concern to claimants and defendants alike.

Key Words: Medical Negligence; Reporting system; Spectrum of information
Funding Agency: None

Patterns and Symptoms of Menopause among Kuwaiti Women aged 45 to 65 years

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Introduction:

Objectives: To quantify the prevalence of menopause related symptoms experienced by Kuwaiti women aged 45 to 65 as well as to explore the association between menopausal symptoms with the socio-demographic characteristics, general health status and reproductive related factors. We also aimed to estimate the mean age of menopause in Kuwaiti women.

Methods:

We conducted a cross sectional study using a sample of 362 Kuwaiti women aged 45 to 65 years. A self-administered questionnaire that included a frequently used Menopausal Rating Scale (MRS) was used. We used bivariate logistic regression models to identify the factors associated with menopausal symptoms.

Results:

Prevalence of menopausal symptoms varied in our study population where almost 31% of the women complained of severe or very severe musculoskeletal discomfort. Peri-menopausal women had the highest prevalence of menopausal symptoms followed by post-menopausal women who had their menstruation ceased naturally. Women who were less educated and had lower income, had higher prevalence of menopausal symptoms. Presence of chronic illnesses were found to worsen the menopausal experience. We found the median age of menopause to be 49 years.

Conclusions:

This study was one of the first to quantify the menopausal symptoms among Kuwaiti women and to estimate the age of menopause. Overall level of menopausal symptoms as well as chronic illnesses such osteoporosis, were alarmingly high in the study population. Public health and educational interventions including consideration for appropriate screening programs should be evaluated in Kuwait.

Acknowledgements: Dr Hanan Badr for her generous help.

Key Words: Menopause; Symptoms; Age

Funding Agency: None

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Self-rated Health and Associated Factors among Faculty Members and Support Staff of Kuwait University

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Introduction:

Objectives: This study aimed to assess the prevalence of self-rated health and self-reported morbid conditions and to evaluate the association between self-rated health and socio-demographic, lifestyle variables and self-reported morbid conditions.

Methods:

A structured and pre-tested self-administered questionnaire was completed by 550 academics and support staff from eight randomly selected colleges of Kuwait University. The data regarding socio-demographic characteristics, lifestyle behaviors, self-reported morbid conditions and self-rated health were collected from 5th to 8th January 2009.

Results:

Among the 550 participants, the most common self-reported morbid conditions were vision problems (28.0%), chronic back problems (20.8%) and chronic bowel problems (19.5%). However, majority of these participants rated their health as very good (46.6%), good (30.0) or excellent (18.5) compared to 4.4% and 0.2% as fair or poor respectively. Final, multivariate logistic regression model showed significant, independent relationship between fair/poor self-rated health and home type, chronic back pain, chronic sleep problems and diabetes.

Conclusions:

In conclusion, this study showed that Kuwait University employees are generally healthy population in terms of self-rated health. Fair/poor self-rated health in this population was associated with house type, self-reported morbid conditions including diabetes, chronic back pain, and chronic sleep disorders. Future studies may focus on detailed epidemiological evaluations of these chronic conditions in this population.

Key Words: Self-rated health; Self-reported morbidities; Risk factors
Funding Agency: None

Knowledge and Awareness of Colorectal Cancer in Ministries Complex Employees in Kuwait

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Introduction:

Colorectal cancer, the second leading cause of cancer-related deaths in the Western world has increasing incidence in the Arab countries due to exposure to some prominent risk factors including inflammatory bowel disease.

Methods:

A cross-sectional survey was conducted on employees from Kuwait ministries complex. Data was collected through a self-administered questionnaire containing questions on level of knowledge and self evaluation of being at risk, for which scores were assigned.

Results:

Of the 414 subjects, 55% participants considered colorectal cancer as a major public health issue in Kuwait. Only 30% correctly identified the major risk factors (history of inflammatory bowel disease, polyps, age and male gender) and more than 50% identified the less important ones. The median knowledge score was 7 (Range 0 – 15) and females had a significantly lower knowledge score (OR = 1.109, 95% CI = 1.027 – 1.197). The median risk score was 1 (Range 0 – 3). Five of the 15 people who had been screened had had symptoms of colorectal cancer including changes in bowel habits (66.7%) and presence of blood in stool (40%). Association was found between high risk scores and family history of colorectal cancer (OR = 1.965, 95% CI = 1.587 - 2.433) and inflammatory bowel disease (OR = 2.217, 95% CI = 1.670 – 2.943). 133 (36%) were of the opinion that they were at risk of colorectal cancer and this opinion was significantly associated with the presence of symptoms (OR = 3.036, 95% CI = 1.907 – 4.834). 22 (36.7%) reported fear of finding out something is wrong as the reason behind not getting screened, despite medical advise.

Conclusions:

Overall the knowledge score and risk score were quite low indicating misinformation regarding significant risk factors and screening methods. In order to change public opinion favorably, benefits of screening methods and advantages of early detection need to be highlighted.

Key Words: Colorectal Cancer; Kuwait; Knowledge

Funding Agency: None

Community Medicine
Category: Graduate (Resident)

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Optimal Waist Circumference Cut-off Points to Predict the Risk of Diabetes Type 2 in Kuwaiti Adult Population

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Introduction:

To evaluate the value of the cut off points suggested by Adult Treatment Panel III (ATPIII) for waist circumference (WC) and to determine the optimal WC that predicts the subsequent diabetes risk, in the Kuwaiti adult population.

Methods:

A cross-sectional survey was conducted among Kuwaiti employees (20 years or older) in the ministry complex using gender stratified multi-stage cluster sampling (n=562). Receiver operating characteristic (ROC) curve analysis was used to identify optimal cut-off values of WC with sensitivity of 80% for detection of diabetes, and impaired fasting glucose IFG (Fasting glucose 6.1- 6.9 mmol/l).

Results:

The optimal cut-off points for WC were between 90.5 and 97.5 cm for men and 83.5 and 87.5 cm for women in predicting diabetes risk for Kuwaiti adult population.

Conclusions:

We found that the cut off suggested for waist circumference by ATPIII to have limited predictive value when applied Kuwaiti adult population, particularly for males. Thus, we developed new cut off for waist circumference to be used in any diabetes screening program in Kuwait.

Key Words: Wait circumference cut-off; Diabetes; Kuwait

Funding Agency: None

Chronic Illness and Functional Disability among Older Kuwaitis: how Strong is the Association?

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Introduction:

Functional disability is exacerbated by chronic illnesses as found internationally. Our objective was to measure the association between major chronic illnesses and self-reported prevalence of functional disability and severe disability, after controlling for relevant socio-demographic, lifestyle and psychosocial factors.

Methods:

Data from a cross-sectional interview survey of Kuwaiti households in Capital and Ahmadi governorates, held in 2005/6 were analyzed. Among 2605 eligible persons aged 50+, 2487 (95%) participated. Functional disability was measured as physical ability, ability for self care, and ability to perform daily routine activities. A score of 0-28, 0 representing no disability and 28 representing the highest level, was developed. Persons with a score of 20-28 were defined as severely disabled. Association of 5 chronic illness (hypertension, diabetes, heart disease, stroke, and arthritis) with disability was analyzed.

Results:

About a quarter of all respondents reported to suffer from at least some functional disability, slightly more women than men (25% and 24%, respectively, $p=0.485$). Logistic regression indicated that functional disability was significantly higher among the older, currently non-married, non-Bedouin, least educated and lowest income persons. Of the five chronic illnesses considered, all emerged as significant predictors of functional disability, except hypertension, with stroke representing the highest risk. Among 607 persons who reported any functional disability, 35% indicated it to be severe. Stroke and arthritis were significantly associated with severe disability, as were older age, unmarried status, non-Bedouin ethnicity, lower socioeconomic status, higher depression level and lack of co-resident children.

Conclusions:

Chronic illnesses, especially stroke, and several socio-demographic and psychosocial factors are significant correlates of disability that should be addressed.

Key Words: Functional ability; Chronic illness disability; Physical quality of life

Funding Agency: Kuwait Foundation for the Advancement of Sciences (KFAS 2003-1302-02)

Survival of Male Breast Cancer Patients: Population Based Cohort Study

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Introduction:

Little information is available on the survival of male breast cancer patients because the disease is extremely rare in men. Moreover, previous reports on the prognosis of male breast cancer have been conflicting.

Methods:

We took advantage of a number of large, nationwide registries in Sweden to evaluate the prognostic value of sex in breast cancer patients. A population-based cohort of 269 male and 30 011 female breast cancer patients born after 1935 and diagnosed with primary breast cancer between 1970 and 1997 was generated by linking a number of Swedish registries, including the Swedish Cancer Registry, the Cause of Death Registry, the Swedish Generation Registry, and the Registry of Population and Population Changes. We used this cohort to quantify the association between the gender of the patient and breast cancer-specific mortality, using the Cox proportional hazards.

Results:

The sex of the patient did not significantly influence the prognosis of breast cancer (crude OR =0.81; 95% CI 0.60, 1.08; female gender was taken as the reference). Adjusting for age at diagnosis and calendar period did not alter the results (Adjusted OR = 0.84 (95% CI: 0.63, 1.12). Nor did the results change when the analyses were repeated for all causes of mortality (Adjusted OR = 0.86 (95% CI: 0.65, 1.12). Our study, one of the largest to date, failed to find evidence to support the proposed association between the sex of breast cancer patients and survival.

Conclusions:

Given the previous reports, which advocated that male breast cancer patients have poorer survival and need aggressive treatment strategies, our findings are reassuring and clinically very important.

Key Words: Male breast cancer; Prognosis; Sex or gender
Funding Agency: Kuwait University

Dentist Awareness and Application of Current Guidelines for Antibiotic Prophylaxis Prescription

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Introduction:

Objective: Guidelines for antibiotic prophylaxis have been recently updated. The aims of this study were to examine dentist awareness of the current guidelines for antibiotic prophylaxis prescription, and to assess the reasons behind any conflicts with current guidelines, in addition to the contributing factors that influence the decision making process.

Methods:

A questionnaire was distributed to a sample of 300 dentists in Kuwait and a response rate of 70% was obtained. The survey examined demographic data, awareness of current guidelines regarding conditions and procedures that require antibiotic prophylaxis, and first line drug commonly prescribed with appropriate dose and factors affecting application of current guidelines. The 2007 AHA guidelines were used as the standard for results comparison. Data were analyzed using SPSS version 16.

Results:

A Knowledge score was calculated based on the correct answer of 15 questions regarding conditions and procedures that require antibiotic coverage. The mean knowledge score was 9.05. The correct antibiotic choice and dose were chosen by 74.3% and 72.9% of the sample, respectively. The responses, 66.7% considered infection more risky if antibiotic prophylaxis is not prescribed, while 28.6% considered microorganism resistance and anaphylactic shock more risky if the prophylaxis is over prescribed. In addition, 67.6% of the dentists stated that physician consultation is the primary source in decision making, 57.6% chose to follow the physician consultation even if they disagreed and 39% agreed that fear of serious consequences is the main factor behind malpractice. One-hundred and sixty dentists 76.2% stated that their practice is similar to recent guidelines and recommendations.

Conclusions:

Lack of uniformity between the literature recommendations and dental practice in Kuwait exists. Physician consultation and fear of serious consequences were the main factors in influencing dentists' decision making process.

Key Words: Guidelines; Antibiotic prophylaxis; Decision-making

Funding Agency: None

Dental and Medical Students Knowledge about Periodontal Disease and Diabetes

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Introduction:

Diabetes mellitus (DM) is a systemic disease with several complications affecting the general health. The available evidence supports a strong bidirectional relationship between DM and periodontal diseases (PD), which in turn suggests that knowledge of such relationship has clinically relevant therapeutic and preventive implications for the management of both diseases. The aim of this study was to evaluate the awareness of dental and medical students concerning the relationship between periodontal disease and diabetes mellitus.

Methods:

This was a cross-sectional study examining the awareness of dental and medical students at Kuwait University of the association between DM and PD. The students were requested to complete a questionnaire to record demographic information. In addition, subjects were asked specific questions regarding periodontal complications they thought DM patient are more susceptible to. Statistical significance was set at $p < 0.05$.

Results:

The study sample comprised 155 females and 57 males (age range 18-25 years). Dental students accounted for 65.6% and medical students accounted for 34.4% of the sample. The majority of the students (77.8%) were aware that diabetes mellitus has an effect on periodontal diseases. The most frequently reported periodontal complication was gingivitis. Factors significantly associated with student awareness of the effect of diabetes on periodontal conditions included gender, dental education and dental clinical training.

Conclusions:

Dental students were significantly more aware than medical students of the association between DM and periodontal complications. Efforts should be directed to increase the awareness regarding the oral complications associated with DM among both dental and medical students. Medical education may need to put more emphasis on delivering updated information about the relationship between DM and PD.

Key Words: Periodontal disease; Diabetes; Awareness
Funding Agency: None

Dentist and Physician Awareness of Periodontal Disease and Pregnancy Complications

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Introduction:

Gingival and periodontal changes during pregnancy are common, and several studies have also established a link between periodontal disease and pregnancy complications such as premature low birth weight (PLBW) infants. The aim of this study was to examine the awareness of dentists and physicians of periodontal changes during pregnancy and the association between periodontal disease and pregnancy complications.

Methods:

Physicians and dentists from all health districts were asked to complete a one-page questionnaire regarding periodontal and gingival changes seen during pregnancy, as well as their awareness of an association between periodontal diseases and pregnancy complications. A knowledge score was calculated for correct answers to 6 survey questions related to oral health effects during pregnancy and compared across physicians and dentists and with the awareness of periodontal disease and pregnancy complications.

Results:

Two - hundred dentists (RR= 80%) and 406 physicians (RR= 81.2%) completed the questionnaire. The mean knowledge score of periodontal/gingival changes during pregnancy was significantly higher for dentists than physicians (5.14 ± 0.90 vs. 3.41 ± 1.10 , $p < 0.001$), and more dentists than physicians reported there was an association between periodontal disease and pregnancy complications (42.3% vs. 31.8%, $p < 0.01$). The knowledge score was significantly higher for both dentists and physicians who reported an association between periodontal disease and PLBW infants (4.36 ± 1.36 vs. 3.83 ± 1.39 , $p < 0.001$).

Conclusions:

Although dentists were more aware of the periodontal changes during pregnancy and of the association between periodontal disease and pregnancy complications than physicians, the overall level of awareness was low. Efforts to increase this awareness may prove valuable in improving preventive care during pregnancy.

Key Words: Periodontal disease; Pregnancy complications; Inflammation

Funding Agency: None

The Effect of Cell Wall Components of Candida Albicans on the Adhesion to Poly (Methyl Methacrylate) Resin

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Introduction:

C. albicans is a yeast-like fungus. It can live commensally in the oral cavity without causing harm or can change to an aggressive form and invade tissue. The cell wall in *C. albicans* plays a role in the interactions with the human host and other surfaces. CPH1 and EFG1 are regulatory proteins, which have been associated with the cell morphology and virulence in *C. albicans*. Purpose: The aim of this study is to determine the role of cell wall regulatory proteins CPH1p and EFG1p in the adhesion of *C. albicans* to P. M. M. resins.

Methods:

Four *C. albicans* strains were used. *C. albicans* 14 (wild type), *C. albicans* 16 (cph1/cph1), *C. albicans* 33 (efg1/efg1) and *C. albicans* 34 (cph1/cph1 efg1/efg1). Sixteen resin blocks were fabricated. Each resin block was placed in a separate well, *C. albicans* with different strains were added to each well in addition to 4.5ml of Sabouraud dextrose broth. Adherent cells were fixed. A high powered light microscope in conjunction with an image analysis system was used at 20X magnification.

Results:

The Kruskal-Wallis test indicated that there were significant differences among the groups in the *C. albicans* counts (KW = 22.436, P value is < 0.0001). The Dunn's Multiple comparisons test indicated that *C. albicans* strain 14 differed significantly from *C. albicans* strain 16 (P value < 0.001), *C. albicans* strain 14 also differed significantly from *C. albicans* strain 33 (P value < 0.05). *C. albicans* strain 34 showed significant differences from *C. albicans* strain 14 P value < 0.001).

Conclusions:

There was an extremely significant reduction in *C. albicans* counts that adhered to the resin blocks in strain 16 (cph1/cph1-single mutant), strain 33 (efg1/efg1-single mutant) and strain 34 (cph1/cph1 efg1/efg1-double mutants) compared with strain 14 (wild-type).

Key Words: Candida Albican; Adhesion; Poly methyl methacrylate

Funding Agency: Harvard School of Dental Medicine

Dentistry

Category: Undergraduate

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Patient Information vs. Patient Satisfaction among Orthognathic Patients Treated in Ministry of Health Clinics in Kuwait

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Introduction:

Objectives: The purpose of this study were [1] to analyze the demographic profile of patients treated with orthognathic surgery in Kuwait MOH Dental Clinics; [2] to evaluate the type, amount and timing of preoperative patient information; [3] to determine the posttreatment patient satisfaction; and [4] to test whether patient satisfaction is associated with preoperative information.

Methods:

Of all patients who had completed combined orthodontic and surgical treatment at least 6 months previously, a total of 74 patients agreed to participate in a phone interview, which included questions on demographics, type and timing of general and specific information given to the patients prior to surgery, and patient satisfaction with the final outcome.

Results:

The majority of the patients were 20- to 30-year-old females with a middle socioeconomic status and a high education. The patients were least informed about the possibility of functional and social problems, while information regarding the importance of own compliance was well explained. The orthodontist was the most prominent source of information before treatment initiation. As the preoperative orthodontic treatment phase progressed, the roles of surgeon and orthodontist became more evenly distributed. A high proportion of the patients were satisfied with the final results. Overall satisfaction was related to the perception of thorough information regarding surgical risks. The more information given on adverse effects, discomfort, and surgical risks, the more likely the actual discomfort was as expected.

Conclusions:

The majority of patients in Kuwait undergoing orthognathic surgery are 20- to 30-year-old females with a middle socioeconomic status and a high education. The information received on surgical risks and social and functional discomfort after surgery is insufficient. Overall patient satisfaction is very high. An association exists between adequate information on surgical risks and overall patient satisfaction.

Key Words: Satisfaction; Orthognathic surgery orthodontics; Information

Funding Agency: None

Variability in Diagnosis and Treatment of Occlusal Caries among Dentists in Kuwait

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Introduction:

Objectives: The aims of this study were to assess the variability in the diagnosis and treatment of occlusal caries among dentists in Kuwait in comparison with a histological gold standard, to assess the dentist's knowledge of diagnostic methods, and to evaluate the rationale behind their treatment.

Methods:

A random sample of 156 dentists representing different oral health sectors in Kuwait was surveyed. Practitioners examined five separately mounted molars for probable occlusal caries according to a modified (ICDAS-II) visual criteria and were asked to answer questions. The teeth were then histologically sectioned and two independent investigators evaluated the depth of the caries. Descriptive statistics were used to analyze the data.

Results:

A large variability in the diagnosis of the occlusal surfaces of the mounted teeth was noted. 41% diagnosed tooth A as having discoloration only, 41.7% diagnosed tooth B as having a cavity in dentine, 43.6% diagnosed tooth C as having discoloration only, 32.7% diagnosed tooth D as having caries in dentine without cavitation and 94.9% believed that tooth E was sound. Whereas histological sectioning showed that teeth A and E have caries in enamel, teeth B and D have caries in outer dentine, and tooth C has caries in inner dentine. The majority of the dentists would use a dental probe or bitewing radiographs in the diagnosis of occlusal caries (42.9% and 39.1% respectively). Majority of dentists were not familiar with the use of the advanced diagnostic methods. 21.8% and 59.6% of the dentists believe that teeth A and E require no treatment respectively. 42.3% and 37.2% of the dentists choose composite restoration as a treatment option for teeth B and D respectively. 23.1% of the sample population decided to place fissure sealant on the occlusal surface of tooth C.

Conclusions:

There was an evident variability in the diagnosis, use of diagnostic methods and treatment choices of occlusal caries among dentists in Kuwait.

Key Words: Caries diagnosis; Visual criteria; Treatment choices

Funding Agency: None

Dentistry

Category: Undergraduate

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Child Oral Health Impact Profile (COHIP) for Preschool Children with Anterior Tooth Caries . (Caregiver's version)

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Introduction:

The aim of this study was to assess the quality of life of preschool children (3-6 years old) with anterior tooth caries in comparison to children without anterior tooth caries through the caregiver's report using the Child Oral Health Impact Profile (COHIP) measure.

Methods:

The study was conducted by interviewing the subjects and assessing the presence of caries in the anterior teeth by visual inspection and the caregiver responded by answering a questionnaire. The study was a case-control study. The sample size was 80 children, 40 in the study group and the other 40 in the control group. Subjects were recruited from Kuwait University Dental Center. The questionnaire was similar to the Child Oral Health Impact Profile (COHIP) form. It contained five domains; oral health well-being, functional well-being, social well-being, school environment, and self-image. The COHIP score of each subject was calculated and it reflected the quality of life of the child which is directly proportional to the COHIP score. A number of statistical tests including Chi-square test, ANOVA, and t-test were used in this study to examine the difference in COHIP scores between the study group and the control group.

Results:

The means and the standard deviations of the total score of COHIP for the study and control groups were 84.98 ± 20.24 and 105.25 ± 11.12 respectively. The results of t-test comparing the two groups showed that the difference between the study group and the control group was significant ($p < 0.001$). The effect of nationality, gender and age of child, age and educational level of the caregivers on the score of COHIP was studied. No association was found between these factors and the COHIP score in the study group or the control group.

Conclusions:

Preschool children with anterior caries have low Oral Health Related Quality of life in comparison with children from same age group who have no anterior tooth caries.

Key Words: Tooth caries; Children; Quality of life

Funding Agency: None

Dentistry

Category: Clinical

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Oral Hygiene Status of Kuwaiti Schoolchildren in Different Governorates

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Introduction:

The purpose of the present study was to determine the oral hygiene status among Kuwaiti schoolchildren in different governorates.

Methods:

A national epidemiological survey of 5-14 year old children (n = 3, 294) was conducted in the primary and intermediate schools in 5 governorates of Kuwait. Clinical examinations were carried out according to the WHO criteria. Oral hygiene status was assessed using the simplified oral hygiene index simplified (OHI-S) recommended by Green and Vermillion. The debris index simplified (DI-S) describing the soft deposits was used. Data was analysed using statistical soft ware SPSS, Windows version 14.0. Descriptive statistics including means and standard deviations were calculated for plaque indices. Differences in mean scores were tested using student's t-test for independent samples. An independent-samples t-test was used to test the differences in gender. Chi-square tests were used to test differences in frequencies between the governorates, gender and age with oral hygiene status. One way analysis of variance was used to test the differences in the mean oral hygiene index with governorate and age.

Results:

Of the 3,294 children examined, 3.9% had good oral hygiene, 67% fair and 29.1% poor oral hygiene. The overall level of oral hygiene in the schoolchildren surveyed was fair and the mean (DI-S) was 1.5. There was significant difference in the oral hygiene status between the governorates. The mean (DI-S) was highest in Ahmadi 1.9, and lowest in Hawally 1.3 (p<0.001). The overall mean (DI-S) scores were higher in boys 1.6 than in girls 1.5 (p<0.001). The cumulated plaque index for the index teeth was almost the same in the age groups and the mean DI-S did not vary much by age. The mean DI-S index was 1.5 for the 5-year-olds and 1.6 for the 14-year-olds.

Conclusions:

Oral hygiene must be strongly emphasized as a vital aspect of total health care and maintained on a daily basis. Tooth brushing with fluoridated toothpaste should be promoted at all levels with special emphasis on supervised tooth brushing in schools. Parents and teachers should jointly promote the use of fluoride toothpaste and encourage healthy food choices. Oral health education should form part of school curriculum. Oral hygiene therapeutic measures need to be reinforced for the schoolchildren in Kuwait.

Key Words: Oral hygiene; Schoolchildren; Kuwait

Funding Agency: Ministry of Health, Kuwait and the Forsyth Institute

Dentistry

Category: Clinical

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Randomized Clinical Trial of In-office Dental Bleaching with or Without Light Activation

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Introduction:

Dental bleaching became a common conservative treatment for discolored teeth. The aim of this clinical study was to evaluate the effect of four in-office dental bleaching methods on color change, color stability, patient satisfaction and postoperative sensitivity.

Methods:

Forty patients, selected according to predetermined criteria, were randomly divided into four groups (n=10): Group A- 35% Hydrogen Peroxide (HP); Group B- 35% HP Plus Brite smile blue Curing Light; Group C- 35% HP plus Quick smile LED Curing light; Group D- 35% HP plus Zoom 2 metal halide curing light. For all groups, there was only one session of bleaching with 3 applications of bleaching gel for 20 minutes each. Shade was evaluated before bleaching, immediately after, and one month after treatment using VITA Classical Shade Guide.

Results:

Immediately after bleaching there was a significant difference in color change between the four groups, where Group B showed the best results ($p < 0.05$). At 1 month there was no difference between the four groups ($p > 0.05$). Immediate postoperative sensitivity was least in Group A and highest for Group B ($p < 0.05$). Patients in Group B were the most satisfied in the procedure ($p < 0.05$).

Conclusions:

In general, using light activation with In-office bleaching seems to increase the efficacy of the treatment only for short period.

Key Words: In-office bleaching; Light activation; Sensitivity

Funding Agency: None

Dentistry
Category: Clinical

35

Profile of Antibiotic Prescriptions at a Dental Center

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Introduction:

To study profile of antibiotic prescription by emergency dental surgeons in a dental center.

Methods:

A retrospective study was designed, and data were collected for 14 dental surgeons over a period of 9 months (from January to September 2006), which included the number of antibiotic prescriptions, extractions, root canal treatments, casual patients seen and reason of visit. Pearson correlation analysis was performed to detect any significant correlation between the number of antibiotic prescriptions and the number of extractions done, root canal treatments done, number of casual patients seen and 11 categories for reason of visit. Statistical analysis was done using SPSS version 13 statistics software.

Results:

A total of 3192 antibiotic prescriptions were prescribed. This was significantly correlated with the number of casual patients seen (< 0.05). Number of antibiotic prescriptions was also significantly correlated with visiting the dental clinic because of an acute symptom (< 0.01) and also with visiting the dental clinic demanding scaling and polishing (< 0.05).

Conclusions:

The number of antibiotic prescriptions was significantly correlated with number of casual patients seen and specifically with patients complaining of acute symptom. The results of this study will be used to design a self study for all the dental surgeons in the dental center to improve the management of dental infections.

Key Words: Dental Services; Antibiotic; Correlation analysis

Funding Agency: None

Infant Oral Health Knowledge of Expectant Mothers in Kuwait

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Introduction:

Severe early childhood caries (sECC) is a virulent form of caries affecting children under the age of six. If left untreated, it can have a lasting and detrimental impact on affected children. Studies have linked the knowledge of Infant Oral Health (IOH) among expectant mothers to sECC experience in their off springs. Objective of the study was to assess the knowledge of IOH among expectant mothers in Kuwait.

Methods:

Questionnaires with 15 questions and multiple choice answers were distributed to 230 expectant mothers at some maternity clinics in Kuwait. Answers were structured so that some were consistent with the American Academy of Pediatric Dentistry recommendations on IOH, and with the general consensus in that regard. Responses were rated as either consistent or inconsistent with the referenced recommendations and consensus. Group knowledge was rated as very high when >95% of the answers were correct, as adequate when 75-95% were correct, and as inadequate when <75% of the answers were correct. Data were analyzed descriptively using SPSS.

Results:

The survey's return rate was 87%. Participants had adequate knowledge (88%) about the link between mother's oral health and IOH. However, the knowledge of the participants was inadequate regarding the long term effects of sECC on growing children (46%), regarding the appropriate age for the child's first dental visit (5%), and regarding the appropriate time to start brushing the child's teeth (18.3%).

Conclusions:

Participants knowledge was inadequate on most areas related to healthy IOH practices. Health care providers and health care related organizations in Kuwait should therefore put more effort in promoting IOH education among expectant mothers.

Key Words: Severe early childhood caries; Infant oral health; Prevention

Funding Agency: None

Knowledge of Traumatic Dental Injuries Management among Dentists in Kuwait

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Introduction:

Correct management of traumatic dental injuries in the emergency phase is important for the prognosis and dentists must therefore have updated knowledge in this field. The objective of the present study was to assess the knowledge of dentists in Kuwait according to the latest, 2007, published guidelines of the International Association of Dental Traumatology (IADT) on emergency management.

Methods:

Questionnaires with clinical scenarios and related questions with multiple answer options were distributed to 200 dentists in Kuwait. Graduation year, place of graduation, trauma experience and trauma education was registered. The clinical scenarios were related to various types of traumatic dental injuries in the permanent dentition (intrusion, extrusion, avulsion, crown fracture, and root fracture).

Results:

Responses were received from 106 dentists, of whom 57 (54%) were specialists. 52.3% had graduated more than 5 years ago and 52% had not attended any trauma course in the past 5 years. 87% of the dentists saw one or more trauma cases per week. Correct management according to IADT were registered for the following injuries (range%); intrusion (66-78), extrusion (69), avulsion (30-94), complicated crown fracture (51-52) root fracture (53-54).

Conclusions:

There is inadequate knowledge among dentists in Kuwait on managing several common traumatic dental injuries. There is an urgent need to improve the knowledge of management of dental injuries among practicing dentists in Kuwait.

Key Words: Dental Traumatology; Knowledge; Management

Funding Agency: None

Prevalence and Risk Indicators for Alveolar Bone Loss in Kuwait

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Introduction:

Alveolar bone loss as a result of periodontal disease is associated with several risk factors such as smoking and diabetes mellitus. Limited data is available on the prevalence and associated risk indicators for alveolar bone loss in dental patients in Kuwait. The aim of this study was to examine the prevalence of alveolar bone loss and the associated risk indicators in Kuwait.

Methods:

This was a retrospective pilot study of 513 patient records from the Kuwait University, Faculty of Dentistry's Clinics. All patients were 18 years of age or older. Alveolar bone loss was assessed from the panoramic radiographs and scored by sextant as mild (<15%), moderate (15-30%), or advanced (>30%) using principles of the Schie ruler. Association with demographic variables, smoking status, and medical history factors was examined with chi-square and the Student t-test.

Results:

The prevalence of moderate or advanced bone loss was 28.5%. Factors significantly associated with having one or more sextants with moderate or advanced bone loss included age (47.6 ± 9.5 vs. 31.5 ± 10.6 years, $p < 0.001$), male gender (36.9% vs. 19.6%, $p < 0.001$), and diabetes mellitus (55.3% vs. 26.5%, $p < 0.001$).

Conclusions:

Approximately one-third of examined subjects had signs of moderate to advanced periodontitis. Alveolar bone loss severity was significantly associated with older age, male gender, and patient history of diabetes mellitus. Further studies with larger sample sizes are indicated for the assessment of the prevalence of alveolar bone loss in dental patients in Kuwait.

Key Words: Risk factors; Periodontal disease; Bone loss

Funding Agency: None

Female Patient Awareness of Periodontal Disease and Adverse Pregnancy Outcomes

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Introduction:

An emerging strong line of evidence supports an association between periodontal disease during pregnancy and adverse pregnancy outcomes such as premature low birth weight (PLBW) infants. The aim of this study was to examine female patient awareness of the association between periodontal disease and PLBW infants and factors influencing this awareness.

Methods:

This was a cross-sectional survey of female dental patients from all 6 governorates of Kuwait. The study questionnaire recorded sociodemographic variables, dental visit history, oral hygiene habits, as well as awareness of the relationship between periodontal disease and pregnancy complications. Descriptive statistics and univariate analyses were used for data analysis.

Results:

Out of 1800 distributed questionnaires, 1367 were completed and used in the analysis (response rate = 75.9%). Currently pregnant females accounted for 45.6% of the sample, 32.2% had previous pregnancies, and 22.2% were never pregnant. Of subjects with a current or previous pregnancy, only 17.1% were aware there was an association between periodontal health and pregnancy outcomes. Factors significantly associated with awareness of this association included having a dental prophylaxis in the past 12 months, having a dental prophylaxis during pregnancy, and receiving information from the dentist or OB/GYN ($p < 0.05$). Only 11.7% of subjects were ever advised by their OB/GYN to have a dental visit during pregnancy, and those receiving this advice were twice as likely to be aware of the association between oral health and pregnancy outcomes (30.0% vs. 15.3%, $p < 0.001$).

Conclusions:

Awareness of the association between periodontal disease and adverse pregnancy outcomes in this sample of female patients was low. Dentist and physician provision of information was significantly associated with increased awareness, which emphasizes the importance of their role in educational and preventive care.

Key Words: Periodontal disease; Pregnancy complications; Awareness

Funding Agency: None

Cusp Deformation by Composite Resin Restorations in MOD Cavity Model.

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Introduction:

Light-cured composite resins have the advantage of good esthetics for posterior restorations. However, a major disadvantage of these restorations is polymerization shrinkage. This may induce mechanical stresses on the tooth structure via the bond to enamel and dentin resulting in strain of the tooth or marginal failure. **Objective:** To determine the effect of resin placement techniques and retainer tightness on cusp deformation caused by resin restorations in a tooth model.

Methods:

A large MOD slot cavity was prepared in a first maxillary premolar tooth. The tooth was impressed in vinyl polysiloxane and thirty replicas were made with Orthoresin. The teeth were divided into three groups according to resin placement techniques (bulk, horizontal and oblique increments). Each group was further divided into two subgroups; tight or loose matrix retainer. All cavities were restored with universal hybrid. The intercusp distance was determined by a measuring microscope before and five minutes after they were restored. Furthermore, micro hardness values were obtained to compare the degree of cure of the lower and upper surfaces. Mean cusp deformations were analyzed using two way ANOVA and Tukey test.

Results:

1) Teeth with tight matrix retainer had significantly higher deformation than loose retainer ($p < 0.05$), 2) Resin bulk placement with loose retainer showed the least amount of deformation ($p < 0.05$), however; hardness of the lower surface was at the most 27% of the maximum hardness, and 3) The oblique increments technique resulted in significantly lower deformation than the horizontal ($p < 0.05$), and also showed acceptable hardness values.

Conclusions:

1) in deep cavities ($>2\text{mm}$), resin bulk placement results in low cusp deformation due to inadequate polymerization, 2) oblique increments results in less cusp deformation than horizontal increments, and 3) tightness of the matrix band have a significant impact on cusp deformation.

Key Words: Resin composites; Shrinkage; Deformation

Funding Agency: None

Behavioral Risk Factors for Incisor Trauma Prior to Adolescence

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Introduction:

Regression analyses of data from large, representative samples of adolescents conclude that increasing intervals of overjet and male gender are significant risk factors for maxillary incisor trauma. The majority of the injuries are due to falls or blows during regular activity, personal interaction and play inside or outside the home, suggesting that behaviors associated with certain social conditions are risk factors. Our purpose was to test that hypothesis.

Methods:

We selected a population-based sample of 1583 13-14-year-old subjects, representing about 7% of that age stratum in private and public schools in Kuwait. Incisor trauma was scored according to the NIDR index, and overjet was measured to the nearest 0.5 mm, both in a classroom setting. Information on participation in physical activities, family income, and number of siblings was collected through subject and family interview. Body mass index (BMI) was calculated from standardized measurements of height and weight, as weight in kg/height in m². Obesity was scored if BMI exceeded 30.

Results:

Univariate logistic regression detected reduced trauma risk among subjects from families of higher income ($P < 0.01$) and among subjects attending private schools ($P < 0.05$), and increased trauma risks among subjects engaging in physical activities ($P < 0.01$). No effect was detected of increasing number of siblings ($P > 0.05$). Although trauma was more frequent among obese subjects, the effect was not significant ($P > 0.05$). Univariate analyses also detected increased trauma risk in boys and in subjects with increasing intervals of overjet. Following use of multiple regression with forward selection, only male gender, increased intervals of overjet, and high family income were included in the final prediction model.

Conclusions:

Our findings suggest that behaviors associated with high family income and private school attendance are likely to reduce the risk of incisor trauma in adolescent subjects, while participation in sports activities is likely to increase the risk.

Key Words: Incisor Trauma; Body Mass Index

Funding Agency: None

Esthetic Smile

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Introduction:

Creating the perfect smile and individual esthetics is a challenging procedure that requires a micro-esthetic approach and meticulous treatment planning. Many Scientific, Artistic and Mathematical principles, like the Golden proportions, considered collectively are useful in creating a beautiful smile. The evaluation and analysis of the face, lips, gingival tissues and teeth are all considered by mathematical rules of proportional smile design.

Methods:

A method for determining the ideal size and position of the anterior teeth and dimensions of upper and lower lips were analyzed in accordance to the golden proportions. Standardized Color photographs of posed smiles of various male and female subjects were evaluated. Various anatomic structures such as the Upper lip in relation to lower lip, size of the anterior teeth in relation to the adjacent teeth, measurement of the gingival show and the width of the smiling lips were analyzed.

Results:

A detailed esthetic analysis of the smile was obtained in an objective manner. This assessment reveals the variations or coincidence of anatomic parameters with the mathematical norms. Recognizing the ideal proportions as a goal provides a direction for diagnosis and treatment planning for smile correction or reconstruction.

Conclusions:

This article focuses on the basic dento-labial guidelines ruled by golden proportions that have been proposed to help clinicians in the process of creating esthetic appearance. This approach may serve as a foundation on which to base initial smile design. However, when one begins to understand the relationship between beauty & mathematics one begins to appreciate their interdependence and their clinical applications.

Key Words: Esthetic Smile; Golden Proportion

Funding Agency: None

Oral Carriage of Candida in Patients Attending the Kuwait University Dental Clinic: Preliminary Data.

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Introduction:

Candida species are members of the commensal microbial flora of the oral mucosa. Since they differ in virulence and antifungal susceptibilities, understanding the oral candidal flora will have an impact on designing treatment and prevention strategies against oral candidosis. Moreover, the distribution of oral Candida species among populations remains largely unknown. Hence, this study is an attempt to assess the oral candidal carriage of Kuwaiti population seeking dental treatment at the Kuwait University Dental Clinic (KUDC). Here we report preliminary data of the oral yeast flora of 62 patients attending the Admission Clinic (AD) of the KUDC.

Methods:

Sixty - two patients attending the AD of the KUDC were examined for yeast sampling. Oral mouth rinse technique using sterile distilled water was used. Germ tube test, CHROMAgar Candida medium and API 20C Aux kits were used for the identification of yeast isolates.

Results:

Of the 62 patients investigated, 31 were males (16 – 67 years) and 31 females (17 – 71 years). Twenty-nine patients (13 males and 16 females: 47%) yielded Candida in culture. The isolation rate of Candida was significantly higher in individuals who were smokers or were receiving medication / had some other underlying condition (67%). Among non-smokers who were not receiving any medication / had no underlying condition other than dental complaints, the isolation rate was only 28%. The yeast species isolated from the oral cavity included *C. albicans* (n = 19), *C. dubliniensis* (n = 4), *C. krusei* (n = 4), *C. glabrata* (n = 1) and *Zygosaccharomyces bailii* (n=1)

Conclusions:

The higher percentage of Candida isolation in patients associated with either smoking, usage of medication or medical condition compared to healthy individuals (67% vs 28%), suggests that Candida species are opportunistic organisms. As this information is based on preliminary data it is important to analyze data from a larger number of patients attending the KUDC before arriving at conclusions relevant to Kuwaiti population.

Key Words: Oral Candida; Carriage

Funding Agency: Kuwait University Research Grant No: DB01/07

Knowledge and Attitudes of HIV/AIDS among Kuwait University Dental Students

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Introduction:

The human immunodeficiency virus (HIV) and the acquired immunodeficiency syndrome (AIDS) have emerged as complex health threats to the world population. As future dentists, it is pertinent that the dental students have sufficient knowledge and a positive approach towards the disease. Accordingly, the aim of this study was to assess the HIV/AIDS related knowledge and attitudes of clinical dental students at Kuwait University.

Methods:

A cross-sectional survey was conducted among the fifth, sixth and final year dental students using a structured questionnaire with 60 questions to examine their knowledge (HIV virus and AIDS disease process, potential transmission routes, oral lesions associated with HIV, HIV risk groups, HIV transmission in the dental setting) and 13 questions to examine their attitudes towards the disease. The mean knowledge and attitude scores were calculated and compared among students from different years using one-way ANOVA with SPSS 16.0. Depending on the scores, the respondents were classified as having high, medium and low level of knowledge with either positive or negative attitudes.

Results:

The survey revealed that almost 58% of the respondents demonstrated a high level of knowledge (mean score: 45.0 ± 4.0). The majority of the students (63.6%) expressed negative attitude (mean score: 5.0 ± 3.0). A significant difference ($p = 0.022$) was noticed in mean knowledge scores about the virus and disease process among the three years. However, no significant difference was observed with respect to other categories.

Conclusions:

HIV/AIDS related knowledge was high among the clinical dental students indicating adequate HIV/AIDS education in the pre-clinical curriculum. Despite the high level of knowledge, the students displayed a negative attitude towards HIV/AIDS. Hence, the findings imply that there is a need to address, more clearly, the students' misconceptions and attitudes towards the disease.

Key Words: HIV/AIDS; Knowledge; Attitudes
Funding Agency: None

Determining The Superior Tempromandibular Joint Space In Centric Relation Using Lateral Tomogram In Edentulous Patients

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Introduction:

To determine the superior condylar-fossae space on both sides for edentulous patients while the mandible is in centric relation to the maxilla at the estimated vertical dimension of occlusion. Comparison of condylar position was planned to be achieved by two different methods of establishing the jaw relation; the wax interocclusal check bite method and graphical method.

Methods:

Forty edentulous patients were selected for this study. For each patient, two acrylic trial denture bases were prepared on the working casts with wax occlusal rims attached to them. Radiographic examination was done for each patient by using double Tomogram, Double TMJ program was used to produce 2 closed views for the left and right TMJ during occlusion on a bite blocks secured in centric relation by the wax interocclusal check bite record, and the other by the graphical method.

Results:

The difference between superior condylar space achieved by the Graphical method, and Wax inter-occlusal check bite method in both left and right side were found to be non-significant ($t < t_0$) at 5% level of significance.

Conclusions:

The superior space between the head of the condyle and the condylar fossa has no relation with the technique of centric relation registration.

Key Words: Centric Relation; Edentulous Patients; Condylar position

Funding Agency: None

Dentistry

Category: Clinical

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Assessment of Dental Surgeons' Referrals to the Orthodontic Clinic in a Dental Center

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Introduction:

The aim of this study is to assess the quality of referral and standards used by the dental surgeons to the orthodontic clinic.

Methods:

Seventy referred cases to the orthodontic clinic were randomly selected, referrals were categorized (Dental terminology, normal language or no description) A descriptive analysis was done; results were analyzed in relation to the studied group and in relation to each Dental surgeon, the indication for orthodontic treatment or no was also evaluated.

Results:

Most of the dental surgeons included in their referral the patient's main complaint, but others did not mention anything. Twenty seven cases (38.57%) were referred with normal language or no description at all. (Wants ortho, appointment for ortho., irregular teeth) Twenty seven cases (38.57%) dental/orthodontic terminology was used to describe the case and patient complaint. Sixteen cases (23%) used dental/orthodontic terminology to give the patient's main complaint. Sixty one cases (87.14%) were indicated for orthodontic treatment, four missed their appointment for orthodontic inspection (can not be judged), and three cases only were not indicated for orthodontic treatment. The analysis for each dental surgeon revealed two groups with almost a well defined profile; those who refer only without any description, and those who use terminology or at least the main patient's complaint.

Conclusions:

Almost 90% of the cases referred were indicated for treatment, but the quality of referral needs to be improved, especially with the group who does not mention any description of the case. It was noticed with the recent introduction of the new dental software DENTIMAX that the dental surgeons tend to click the referral icon only, without writing the reason for referral. In order to improve the standards of referral, it is highly recommended to increase the dental surgeons' knowledge with malocclusion and orthodontic terminology, to enforce the use of dental/orthodontic terminology rather than normal language.

Key Words: Orthodontic clinic; Referral; Dental surgeon

Funding Agency: None

Dentistry

Category: Undergraduate

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Knowledge and Attitudes of Dentists Practicing in Kuwait Towards Evidence Based Dentistry

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Introduction:

As health care providers, it is important that dentists offer the best possible care for their patients. In order to do so, dentists will require a good source of evidence that can justify their chosen treatment plan. This study was conducted to assess the current level of awareness, knowledge and practice of evidence based dentistry (EBD) among public sector dentists in Kuwait and to explore the association between the knowledge level and related factors.

Methods:

This was a cross sectional study that included 120 dentists from all 5 health districts across Kuwait. One hundred and fifty self-administered questionnaires were distributed and a response rate of 80% was obtained. The questionnaire examined the knowledge, awareness and level of practice of EBD, and possible barriers towards the implementation of EBD. In addition to descriptive statistics, appropriate inferential statistical methods were used to study any associations.

Results:

Although 60.8% of the dentists self reported that they practice EBD most of the time, adjusted analysis revealed that only about 18.3% of the sample had a reasonable understanding of EBD. It was found that most of the clinical practice in Kuwait was based on the clinician's own judgment (73.3%), rather than evidence based sources like the Cochrane library (6.7%) or PubMed (28%). In addition, the vast majority of dentists had neither internet connection at their work place (94%) nor access to international journals (91%).

Conclusions:

The overall level of awareness and knowledge of EBD among dentists practising in Kuwait was low, despite the fact that more than half of the dentists reported having evidence based practice. Training in the areas of EBD as well as assuring that Kuwaiti dental centers have access to evidence based sources is essential if dental practice in Kuwait is to become evidence based.

Key Words: Dentistry; Evidence Based Practice; Community Dentistry

Funding Agency: None

Oral Cancer Awareness Among Dentists in Kuwait.

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Introduction:

Oral cancer is the eighth most common cancer worldwide. Early detection makes them more amenable to treatment. However, lack of dentists' knowledge has been shown to contribute to delays in referral and treatment. Hence, the aim of this study was to assess oral cancer awareness among dentists in Kuwait.

Methods:

A cross-sectional survey was conducted among the dentists working in the various specialty centers and university dental center in Kuwait. Approximately 200 structured questionnaires were distributed which examined their knowledge of oral cancer risk factors, diagnostic concepts, current practice and opinions, preferred point of referral as well as interest in continuing education. Data management and statistical analysis was carried out on SPSS 16.0. A knowledge score was calculated based on the correct responses to 30 questions regarding risk factors (15) and diagnostic concepts (15) in oral cancer.

Results:

The mean knowledge score was 20.6 ± 3.99 out of 30. Only 22.9% of the dentists had consistently high knowledge scores for both risk factors and diagnostic concepts. Almost 63% of the respondents biopsied suspicious lesions and their preferred point of referral was the oral and maxillofacial surgical unit. Out of 153 dentists, who responded (response rate = 76.5%), only 38% felt confident to diagnose oral cancer from the clinical appearance. Almost 87% of the dentists were interested in obtaining further information, with majority preferring an information pack.

Conclusions:

Appropriate knowledge and information about risk factors and diagnostic procedures for oral cancer are absolute pre-requisites for dentists. The results of this survey suggest that dentists recognize certain gaps in their knowledge. Educational strategies should be aimed at providing current information on risk factors, oral examinations, adjunctive diagnostic aids, biopsy decisions and frequent patient referrals thus aiding in early detection.

Key Words: Oral cancer; Knowledge; Opinions

Funding Agency: None

Association Between Chronological Age and Third Molar Development in a Kuwaiti Population Using Panoramic Radiographs- a Pilot Study

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Introduction:

In the late adolescence and early adulthood third molar mineralization is one of few maturation events that are still taking place and it is widely used for chronological age estimation in that age group. Many researchers have attempted establishing some age reference standards for third molar development in populations of different ethnicities. Findings suggest that there is a correlation between age and developmental stages and that the maturation standards are varying between populations of different origin. To date, insufficient data are available on populations of Middle Eastern origin. The objectives of this pilot study were three folds:

- 1- To test the correlation between 3rd molar development stages and age in a Kuwaiti sample.
- 2- To establish preliminary age reference standards for third molar development in a smaller sample of Kuwaiti young adults.
- 3- To compare those preliminary age reference standards with populations of different ethnicities.

Methods:

One hundred ninety nine panoramic radiographs (100 males, 99 females) from the data base in KUDC were used in this pilot study. Inclusion criteria were patients of Kuwaiti origin, aged 9-24 years. Using Demirjian's eight stage for classification of tooth development, all mandibular third molars were assessed by one investigator (LK). Data were recorded and descriptively analyzed including linear regression using SPSS.

Results:

A significant correlation between the stages of development and the chronological age was found ($r=0.72$). Boys were about one year ahead of the girls for most stages of development. The mineralization of the third molar was found to start at the age of 9.5 years and it was fully formed at about 21.6 years for a boy. When compared with other different ethnical populations was the development of the third mandibular molar early in the Kuwaiti population.

Conclusions:

Using the development of the third molar as an indicator of age seems appropriate for the studied age group in Kuwait. A larger material is needed to establish Kuwaiti norms.

Key Words: Third molar; Chronological age; Age estimation

Funding Agency: None

Dentistry

Category: Graduate PhD (Basic Science)

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Comparing Two Designs of Mandibular Advancement Sleep Apnea Appliances

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Introduction:

The purpose of this study is to evaluate the patients' tolerance as well as the improvement of sleep apnea in patients suffering of sleeping apnea while they were using either the acrylic or the chrome-cobalt Mandibular Advancing Sleep apnea appliances.

Methods:

Twenty - four adult patients with apnea/hypopnea Index (AHI) 10/h were recruited. Patients underwent a sequence of treatment regimens and follow-up studies over a period of three consecutive weeks. The three regimens consisted of treatment with the Acrylic MAA (Mandibular Advancing Appliance) or Chrome cobalt MAA device or no treatment. At the end of each week, symptoms and side effects were evaluated with questionnaires referring to the regimen of the previous 7 d. Overnight oximetry was also performed.

Results:

All patients stated that treatment with IOA had positive effects on their well-being, and all wished to continue this treatment. The majority of patients (15 of 24) preferred treatment with the chrome cobalt appliance over that with the acrylic resin device, eight patients had no clear preference and only one patient preferred the acrylic device ($p < 0.008$ versus chrome cobalt).

Conclusions:

In conclusion, our findings show that IOAs that advance the mandible are an effective alternative for treatment of selected (Obstructive Sleep Apnea) OSA patients who are unwilling or unable to use nasal CPAP (Continuous Positive Airway Pressure).

Key Words: Sleep apnea; Mandibular Advancing appliance; Oxymetry

Funding Agency: None

Dentistry

Category: Clinical

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Age specific caries experience of Kuwaiti Kindergarten schoolchildren in different governorates

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Introduction:

The aim of this national dental survey was to determine the age specific caries experience of Kuwaiti kindergarten schoolchildren in different governorates.

Methods:

A national epidemiological survey of the 4- and 5-year-old kindergarten schoolchildren (n = 1, 277) was conducted in the five different governorates (Ahmadi, Farwaniya, Hawally, Jahra, Capital) in Kuwait. A stratified, multistage, probability sample of 2.5% of the target population was drawn from each census region. Five trained and calibrated dentists examined the children. Dental caries was scored using WHO criteria. The data were analysed using the statistical software SPSS, Windows version 14.0. Descriptive statistics including means and standard deviations were calculated for the caries indices. Kruskal Wallis test was used to test the differences in caries levels between the governorates. An independent-samples t-test was used to test the differences in gender and age. Chi-square test was used to assess the association between the caries-free children by age, gender and governorate.

Results:

The proportion of caries-free 4- and 5-year-old children was 32% and 24% respectively. Considerable variation was observed between the governorates. Amongst 4-year-olds, these percentages varied from 10% in Capital to 45% in Hawally (p<0.001) and in the 5-year-olds varied from 9% in Capital to 40% in Farwaniya (p<0.001). The mean dft/dfs for 4- and 5-year-olds were 3.7/6.9 and 4.8/9.6. The mean dft was 3.7 among 4-year-olds, and 4.8 among the 5-year-olds (p<0.001). In the 4-year-olds, the caries experience was highest in Capital (6.4/11.7) and lowest in Hawally (2.3/4.6) (p<0.001) and in the 5-year-olds it was highest in Capital (7.5/15.6) and lowest in Farwaniya (2.9/5.8) (p<0.001).

Conclusions:

Caries prevalence is high in Kuwaiti kindergarten children. There are variations in the caries experience of children between the governorates. An extensive prevention program in preschool and kindergarten children is needed to prevent caries.

Key Words: Dental caries; Kindergarten Schoolchildren; Kuwait

Funding Agency: Ministry of Health, Kuwait and the Forsyth Institute

An Intervention to Improve Adherence to Daily Flossing Regimen Among Patients in Kuwait University Dental Center

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Introduction:

Action control has been suggested as an important self regulatory strategy that can assist people who have decided to engage in a specific behavior to translate their intention into action. It is composed of the facets "self monitoring", "awareness of standards" and "self regulatory effort"; which are necessary to develop self control to act on an intended goal. The aim of the present study was to test the effectiveness of a stage matched intervention in improving adherence to dental flossing among patients in Kuwait University Dental Center.

Methods:

The sample population was drawn from the population of active patients receiving treatment in the center. Two groups received the intervention (a self monitoring tool for dental flossing in the form of a calendar) matched to the volitional group and mismatched to the motivational group. People in motivational stage are those that have not yet formed the intention to change behavior while those in volitional stage are those that have already decided to change but need to initiate or maintain the behavior. During recruitment dental floss were given free and plaque score and bleeding score were measured. Clinical measures were repeated after 4 weeks.

Results:

The intervention resulted in improved flossing frequency and clinical outcomes (plaque score and bleeding score) for all participants. A standard multiple regression model that adjusted by baseline score was used to test for differences in the frequency of flossing, plaque scores and bleedings scores at time 2 between motivational and volitional groups. There was no significant difference in flossing frequency between the motivational and volitional groups at time 2 (coef=-6.02, 95% ci; p=0.38). There was no significant difference in plaque scores between the motivational and volitional groups at time 2 (coef=-3.16, 95% ci; p=0.55). Also there was no significant difference in bleeding scores between the motivational and volitional groups at time 2 (coef=-1.29, 95% ci; p=0.63).

Conclusions:

The action control intervention improves oral hygiene behaviour but matching the intervention to the individual's stage in behaviour change (motivational or volitional) had no significant effect.

Key Words: Self monitoring; Awareness of standards; Self regulatory effort

Funding Agency: None

Genetic Diversity in Two Different Ethnic Groups (Arab and Persian) Using 15 STR Markers

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Introduction:

DNA variations have contributed enormously to the fields of medical and forensic science, especially through their use in studies on genes responsible or susceptible to various diseases and those on screening of chromosomal abnormalities in tumors. Herein we are investigating the genetic variation between two ethnic groups (Arabs and Persian) using 15 STR (short tandem repeat or microsatellite).

Methods:

DNA extracted from 140 and 240 randomly selected subjects from Kuwait and Tehran (IRAN) respectively was used in this study. Multiplex PCR using 7 and 8 sets of fluorescence labeled primers specific for 15 different STR markers per reaction was used followed by fragment analysis electrophoresis using ABI3100 genetic analyzer, LIZ600 molecular weight marker was added. Genepop Version 1.2 was used to determine Hardy Weinberg equilibrium and allele frequencies. ALFRED site was used to search for marker alleles details and frequencies in various populations.

Results:

No significant deviation from Hardy-Weinberg equilibrium ($p < 0.05$) was observed in both populations for all the studied markers meaning that both cohorts used were homogeneous. Some reported alleles were found missing in the Kuwaiti population however, some novel alleles were discovered. Markers D8S1779, D8S514, D8S1743, D11S1998, D12S96, D12S329, D16S2624 were not diverged from the Tehran population however, markers D8S1132, D11S1304, D11S934, D12S1632, D16S3096 showed some diversity among the two population.

Conclusions:

Our study can be of great use when applied in association with studies in clinical disorders in the Kuwaiti and Iranian population.

Key Words: Genetic diversity; STR; Multiplex PCR

Funding Agency: Kuwait University NM01/07

Do You Know Your Blood Type: It Can Save Your Life!

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Introduction:

It is essential that everyone know their own blood group and that of their family members. There are many occasions when knowing your blood group could be important, for example, if you or a member of your family, required an urgent blood transfusion it would be useful to know your blood group in advance. If you travel overseas carrying a blood group card could prove invaluable. Accidents and other emergencies can often be dealt with more efficiently knowing the blood group of the person or persons involved. The objectives of this study were firstly to assess the knowledge and awareness of medical students about their own blood types and secondly to identify any misreporting of blood types on governmental and official records.

Methods:

A survey of the registered blood donors who participated in the latest blood donation campaign organized by the Kuwait Medical Students Association in the Faculty of Medicine was conducted using a self-administered questionnaire and a brief interview to verify the information (related to blood type) in the governmental ID card.

Results:

A total of 36 donors (23 Males and 13 Female participants) participated in the study. Blood type was unknown prior to current donation in 30% and known in 70%. Of these 40% were informed of blood type after applying for driving license recently and 15% became aware of their blood type after donating blood last year in the first (KUMSA) campaign. Wrong blood type on governmental documentation was observed in 15% and 60% of Civil ID lacked blood type information. In 8% of cases one governmental document lacked blood type information, and another showed wrong information.

Conclusions:

We found inadequate knowledge about blood type in a random self selected group of medical students indicating the need to raise public awareness of the importance of being knowledgeable of one's blood in Kuwait. In addition, poor recording of blood types on governmental documents needs urgent review.

Key Words: Blood; Donation; Identification cards

Funding Agency: None

Improvement of Lesion Detection in Ga67 Imaging Using Two Energy Photopeaks in Patients with Lymphoma Disease

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Introduction:

Ga-67 has multiple energy emissions of different abundances and the quality of images are affected by this inhomogeneous energy distributions. Medical centers vary in their utilization for the number of energy windows. Thus, our objective was to investigate whether two or three energy windows will result in better image quality and patient diagnosis.

Methods:

The performance of the gamma camera using Ga67 was determined and characterized by the intrinsic uniformity and the spatial resolution in both dual and triple energy photopeaks. Seven patients were injected with 6 mCi of Ga67, in which planar and SPECT chest images were performed 5 days post injection. The data were acquired first with triple and then repeated with dual energy photopeaks. The contrast of the lesions was calculated and compared using Student paired t-test and the images were evaluated using McNemar test.

Results:

For dual energy photopeaks, the integral and differential uniformity were 2.26 and 1.39 respectively while for three photopeaks were 3.04 and 1.81 respectively. Better visualization of the bar phantom images has been noticed in dual window settings with a FWHM of 9.24 mm compared to 10.42 mm for triple energy acquisition. The mean contrast values in planar chest images acquired using dual and triple energy window was 0.55 ± 0.18 and 0.50 ± 0.18 respectively with 9% improvement in the contrast (p-value < 0.001). McNemar test showed that the physician is highly supporting planar and SPECT gallium images acquired with dual energy window (P=0.03).

Conclusions:

Our results showed that the detection system has better physical response to two energy peaks in Ga-67 rather three windows. Further, in patients' studies, better image contrast and interpretation confidence was obtained with two energy peaks. However, further research work is warranted to investigate the effect of the two choices on SPECT studies.

Key Words: Ga-67; Two photopeaks; Contrast

Funding Agency: None

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Scintigraphic Localization of Parathyroid Lesions in Patients with Chronic Renal Failure Using a Magnified Pinhole Technique

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Introduction:

Parathyroid scintigraphy using Tc-99m sestamibi dual phase scan is the study of choice for preoperative parathyroid localization. However, the imaging technique is not standard leading to difficulties in image interpretation. The study objective is to optimize image acquisition by using the pinhole collimator to magnify the area of interest thus improving the diagnostic accuracy of the procedure especially by reducing the false negative rate.

Methods:

Thirty five chronic renal failure patients referred for a parathyroid scan were included in this study. All patients had elevated serum parathyroid hormone levels. Imaging was performed at 10 minutes and 2 hours post injection of 925 MBq (25 mCi) Tc-99m sestamibi using both a pinhole and a parallel hole collimator fitted to a scintillation camera. Delayed SPECT imaging was also performed. The images were reviewed by 2 experienced nuclear medicine physicians blinded to clinical outcome and imaging technique (pinhole vs parallel hole). Scans were as scored as negative or positive. McNemar test was used for analysis of image interpretation data. In addition, contrast of visualized lesions was analyzed using student t-test.

Results:

There were 18 patients (51%) with abnormal scans. McNemar test revealed better detection of parathyroid lesions using the pinhole compared to parallel hole imaging ($p < 0.01$) but no significant difference between pinhole and SPECT imaging. Both observers showed good agreement in evaluating different imaging techniques (Kappa 0.71). Observers were in favor of pinhole imaging as SPECT imaging suffered from noise and false positive results. The lesion contrast was found to be significantly higher in pinhole imaging compared to parallel and SPECT imaging.

Conclusions:

Magnified pinhole imaging provides better visualization and contrast of lesions in parathyroid scintigraphy than parallel hole imaging. Physicians are more in favor of pinhole images compared to the more noisy SPECT slices.

Key Words: Parathyroid imaging; Dual phase; Pinhole collimator

Funding Agency: None

Radiosynovectomy: Another approach to treat inflamed Knee joint

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Introduction:

Radiosynovectomy (RSV) by intra-articular injection of Yttrium-90 (90Y) offers a local & minimally invasive therapy for treating recurrent inflamed synovium of the knee. 90Y causes necrosis of the villi in the synovium and subsequently decreasing fluid collection. In this study the effectiveness of RSV was assessed in patients with inflammatory knee joint conditions refractory to conventional treatment.

Methods:

Patients referred from different hospitals from May 2007 to Oct 2008. Twenty joints of 17 patients were injected, age 26 -59 years, 3 female, 14 male. All had chronic synovitis due to RA², psoriatic arthritis², villonodular synovitis², non-specific synovitis (4) and OA (10) and were refractory to conventional therapy (including intra-articular corticoids). X-ray, ultrasound (U/S) and 3-phase bone-scan (BS) are needed for preliminary assessment. Written consent is signed and total procedure along its complications explained to the patient by the doctor. Under aseptic conditions, the needle is inserted within the joint cavity under fluoroscopy guidance and 185 MBq of 90Y –colloid is injected followed by a steroid flush to reduce acute refractory synovitis. Follow-up with clinical parameters like pain, joint swelling and range of motion are assessed at 0, 2, 5 and 12 months post injection. 2 phase BS and U/S of the injected knee are repeated at 5 months to assess synovial response.

Results:

Out of 20 injected joints, 4 didn't complete follow up BS, the rest shows good clinical improvement. Baseline BS was compared to follow-up BS and showed mild, moderate, and marked improvement in blood pool images in 2, 7 and 6 knee joints respectively. One joint didn't shows any response, a 2nd injection after 6 months was repeated with marked improvement.

Conclusions:

RSV using 90Y is an effective alternative therapeutic approach in patients with chronic inflammatory knee joint conditions refractory to conventional treatment.

Key Words: Radiosynovectomy; Yttrium-90; Knee joint therapy

Funding Agency: None

Importance of Ischemia Detection by Gated Myocardial Perfusion Imaging in Chronic Renal Disease with Cardiac Dysfunction

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Introduction:

Chronic renal disease (CRD) patients often suffer from cardiac disease manifested with symptoms of failure such as dyspnea and peripheral edema. The cause of heart failure could be related to the uremia environment or to coronary artery disease (CAD) that could be caused by chronic diabetes, hypertension or other risk factors. The objective of the study is to evaluate patients with CRD who display signs of cardiac dysfunction by gated myocardial perfusion imaging (G-MPI) for presence of ischemia or CAD.

Methods:

Forty - three patients with CRD in whom abnormal cardiac function was reported by Tc-99m tetrofosmin dipyridamole stress and rest G-MPI are included in this study. The cardiac pump abnormalities are reported in terms of decreased left ventricular ejection fraction <50%, increased end diastolic or end systolic volume (>120 ml, >80 ml respectively), or abnormal regional wall motion of the left ventricle. The images were analyzed for presence of myocardial perfusion abnormalities in terms of reversible or non-reversible (fixed) defects of radiotracer uptake between the stress and rest components of the study. The data were analyzed using standard descriptive statistics.

Results:

Patients demographics: average age 58 y, gender: 29 male (67%). G-MPI studies with perfusion abnormalities: 38 (88%), The number and percentage of studies showing ischemia ie reversible defects: 35 (92%).

Conclusions:

Chronic renal disease patients with cardiac pump dysfunction have underlying coronary artery disease in the majority of cases. Only 12% are negative for CAD and are thought to be related to uremia. The evaluation for CAD, especially myocardial ischemia, is very important in the management strategy in CKD patients.

Key Words: Chronic renal disease; Heart failure coronary artery disease; Gated myocardial
Funding Agency: College of Graduate Studies, Kuwait University

Liver Function Evaluation Using Tc-99m Colloid and HIDA Imaging in Diabetic Rats. Experimental Model and Findings.

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Introduction:

Radionuclide imaging of liver function such as the phagocytic reticuloendothelial (RES) or hepatobiliary system can be done using Tc-99m sulfur colloid (SC) or Tc-99m HIDA (HIDA) respectively. Objectives: To evaluate changes in the kinetics of these tracers in experimentally-induced diabetes mellitus (DM) in the rat.

Methods:

Two groups of rats were studied: control and diabetic. DM was induced using streptozotocin (55mg/kg ip). Imaging SC or HIDA involved dynamic acquisition at 1sec/frame for 1 min followed by 1 min/frame for 1 h after injection of 37 MBq radiotracer (SC or HIDA). Cardiac blood pool clearance and hepatic uptake were determined. Differential distribution was determined by drawing region of interest (ROI) on heart, liver, spleen and whole body (WB) for SC and liver, liver parenchyma, bile, abdomen and WB for HIDA. The following ratios were obtained: heart or liver or spleen to WB for SC and liver, bile, liver parenchyma, abdomen to WB for HIDA for both control and diabetic rats.

Results:

The SC image in the control rat shows uptake in the liver and spleen. The image of HIDA in a control rat shows hepatic uptake and biliary excretion. Comparison of SC uptake (mean±SE) between controls and DM rats was: 1-heart ratio: 0.15±0.02 control and 0.19±0.02 diabetic rat (p<0.05), 2-liver ratio: 0.81±0.03 control and 0.75±0.02 diabetic rat (p<0.05) and 3-spleen ratio: 0.06±0.01 control and 0.07±0.02 diabetic rat (p=0.22). The data for HIDA uptake was: 1-liver ratio: 0.67±0.08 control and 0.69±0.07 diabetic rat (p=0.44), 2-bile ratio: 0.70±0.07 control and 0.72±0.02 diabetic rat (p=0.41), 3-liver parenchyma ratio: 0.13±0.004 control and 0.12±0.005 diabetic rat (p=0.42) and 4-abdomen ratio: 1.1±0.13 control and 1.1±0.09 diabetic rat (p=0.46).

Conclusions:

An experimental setting for study of liver function alterations in diabetes is being evaluated using non-invasive radionuclide methods for assessment of RES (SC) and hepatobiliary (HIDA) function. This study provides useful insight into diabetes-induced liver pathological changes.

Key Words: Liver function; Radionuclide; Diabetes Mellitus

Funding Agency: Kuwait University-Research Administration MN01/07.

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Influence of Frequent Vaso-Occlusive Crisis and Avascular Necrosis of the Femoral Head on Bone Mineral Density in Sickle Cell Disease Patients

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Introduction:

Kuwaiti sickle cell disease (SCD) patients have a relatively mild phenotype because of high Hb F levels. However some patients have frequent vaso-occlusive crisis (FVOC) and some have avascular necrosis of the femoral head (AVNFH). The present study was designed to evaluate the influence of FVOC and AVNFH on bone mineral density (BMD) in Kuwaiti SCD patients.

Methods:

SCD patients were recruited from hematology clinics of Mubarak Hospital. BMD was measured using dual X-ray absorptiometry (DEXA, Hologic) at the lumbar spine and the hip (left femoral neck). T-scores were used to classify the adults while Z scores were used to identify children with low BMD (which was also expressed as g/cm²). Patients with signs of AVNFH on MRI were identified. Patients who were hospitalized with ≥ 4 VOC episodes in the year preceding the study were classified as having FVOC.

Results:

Eighty - one SCD patients were studied. When those with FVOC (n = 44) were compared to those without FVOC, the lumbar spine mean BMD was significantly (p<0.001) lower in the former (0.907±0.178 vs 1.031±0.115 g/cm²). There was no significant difference in the hip BMD in the 2 groups (0.976±0.196 vs 0.946±0.147 g/cm²). There were 42 SCD patients with previous MRI of the hips of whom 18 (42.9%) had evidence of AVNFH. The mean lumbar spine BMD (0.892 ± 0.228 gm/cm²) in this group was significantly higher (p< 0.001) than the mean (0.668 ± 0.172 g/cm²) among those without AVNFH. Similarly the mean BMD values in the hip (0.940 ± 0.181 vs.0.724 ± 0.117 g/cm² respectively) were significantly different (p<0.001).

Conclusions:

SCD patients with FVOC had significantly lower mean BMD especially in the lumbar spine, but those with AVNFH were more likely to have normal or osteosclerotic BMD.

Key Words: Bone mineral density; Sickle cell disease; Osteoporosis

Funding Agency: None

Imaging of Peripheral Nerve Entrapment

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Introduction:

With the advancement in the imaging techniques, it has now become possible to image the peripheral nerves reliably for a variety of lesions like tumors, compressive neuropathies, neuritis, nerve trauma and denervation. Apart from the anatomical localization and characterization of the lesion, it is also possible to assess the severity of nerve injury, for determination of the cause of nerve entrapment, and to predict which patients may benefit from surgical repair. The aim of this study is to evaluate the role of different imaging modalities in detection and diagnosis of the commonly encountered entrapment peripheral nerve lesions of the upper and lower limbs.

Methods:

Sixteen patients suffering from upper or lower limb pain and/or swelling with variable degrees of neuropathy and dysfunction were included in this study, where clinical suspicion of peripheral nerve entrapment was raised in most of them. They were examined by Ultrasound, Magnetic resonance imaging or Computed Tomography as indicated. The choice of the imaging modality depended on the site of the lesion, the provisional diagnosis and the radiologists experience.

Results:

Out of the 16 patients included in the study, 10 patients (62.5%) showed nerve entrapment in the lower limb and were further subdivided into: 4 cases (25%) of sciatic nerve entrapment, 4 cases (25%) of Morton neuroma, and 2 cases (12.5%) of tarsal tunnel syndrome. The remaining 6 cases (37.5%) were in the upper limb and included 3 cases (18.75%) of carpal tunnel syndrome, and 3 cases (18.75%) of ulnar nerve entrapment in the cubital tunnel after supracondylar fracture of the humerus.

Conclusions:

Imaging modalities play a fundamental role in the diagnosis of peripheral nerve entrapment lesions. It displays detailed topographical anatomy of the scanned area leading to precise localization, characterization and treatment planning.

Key Words: Peripheral nerves; Entrapment; Imaging

Funding Agency: None

MRI Evaluation of ACL Graft Complications: Correlation with Clinical Assessment and Arthroscopic Findings

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Introduction:

ACL reconstruction has become one of the most common arthroscopic procedures performed on the knee. The complications from this procedure, however, can be devastating to the overall function of the knee. MRI plays a major role in the assessment of these complications. The aim of this study is to evaluate the accuracy of MRI in the assessment of symptomatic patients after ACL reconstruction and to identify to which extent the MRI findings can be correlated with the clinical assessment and the arthroscopic findings.

Methods:

MRI scan of the knee was performed in 19 symptomatic patients at different periods of time (6 months to 5 years) after ACL reconstruction using a 0.7T dedicated system. Images were reviewed for ACL graft integrity and for presence of other complications and then compared to the clinical assessment and arthroscopic findings.

Results:

Out of the 19 scanned cases, 8 had clinically stable ACL reconstruction and 11 were clinically unstable. In 8 out of the 11 cases, the MRI studies were reported as complete ACL re-tear, this was confirmed by arthroscopy in 5 cases while in one patient there was a partial re-tear. In the remaining 3 cases, the ACL was reported by MRI as partially torn, which was confirmed by arthroscopy.

Conclusions:

MRI can play a major role in the assessment of complications after ACL reconstruction. We found an excellent correlation between clinical assessment, MRI evaluation, and arthroscopic findings in ACL tears. The Fallacies of MRI are mostly encountered in the early postoperative period during which the ACL graft normally shows high signal intensity.

Key Words: ACL reconstruction; Complication; MRI peripheral nerves

Funding Agency: None

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Echocardiographic Correlation of Four Quantitative Gated SPECT Methods in the Estimation of the Left Ventricular Ejection Fraction.

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Introduction:

QGS, ECTb, LMC, and LVGTF are four different methods designed to estimate the left ventricular EF. The third method is relatively newly and achieved good results in preliminary investigations. Thus, The objective of the study was to further assess the performance of the LMC versus 2D echocardiography in the estimation of the LVEF in comparison to other methods.

Methods:

Thirty - eight patients were retrospectively collected for the study (27 males) with a mean age of 51+10 y. All patients underwent myocardial perfusion gated SPECT and 2D echocardiography. EF estimated by the four methods and echocardiography were recorded and statistically analyzed with paired t-test, Pearson correlation coefficient, ANOVA, and Bland- Altman plot.

Results:

The mean EF by echo was significantly higher than QGS and LMC ($p < 0.0001$ and $p = 0.003$ respectively) whereas it was significantly lower than ECTb and LVGTF methods ($p = 0.02$ and $p = 0.001$ respectively). QGS, ECTb, and LMC correlated well in the measurements of the EF with echo ($r = 0.844, 0.825,$ and 0.700), however, fair correlation was found between LVGTF and echo ($r = 0.595$). Pair-wise comparison has shown that the EF calculated by QGS was significantly lower than ECTb ($p = 0.009$) and LVGTF ($p < 0.0001$) whereas it was not different from LMC ($p = 0.928$). For ECTb, the EF was significantly higher than LMC ($p = 0.011$) but was not different from LVGTF method ($p = 0.173$). Further, the EF by LMC was significantly lower LVGTF method ($p < 0.0001$).

Conclusions:

The quantitative gated SPECT methods showed a significant correlation with echocardiography in the calculation of the EF. LMC method showed close results to that obtained by QGS and ECTb with similar variability when compared to echo. This study has investigated the utility of using LMC method in clinical practice, however, it will be more feasible when it becomes an independent and extensively validated in a variety of patient conditions.

Key Words: Ejection Fraction; Gated SPECT; Echocardiography

Funding Agency: None

Use of ⁹⁹Tcm MIBI Spect for Diagnosis of Silent Myocardial Ischemia in Diabetic Patients

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Introduction:

Patients having diabetes mellitus are known to suffer from consequences of silent myocardial ischaemia due to autonomic neuropathy. This study was designed to detect the presence of myocardial ischaemia in diabetic patients referred to CENAR Hospital, Quetta for assessment of coronary artery disease.

Methods:

Fifty - four diabetic patients (37 Male, 17 Female, mean age 56 years) were included in this study. These patients were divided into two groups. Those having signs and symptoms of ischemia (Group A, N=33) and those without any typical signs and symptoms of myocardial ischemia (Group B, N=21). All these patients underwent exercise tolerance test by using modified Bruce protocol. ⁹⁹Tcm stress/rest myocardial perfusion imaging was done at sophy gamma camera on two separate days. All patients with perfusion deficits and all symptomatic patients with normal scan findings were referred for angiography and results of perfusion scan were compared with angiographic findings. Sensitivity, specificity, positive & negative predicted values were calculated by comparing the scan results with angiography as gold standard.

Results:

⁹⁹Tcm MIBI Scan was positive for ischemia in 69.6% (23 out of 33 symptomatic patients) and 47.6% of the cases (10 out of 21 asymptomatic patients) in Groups A and B, respectively. When we compared these results with findings of angiography, ⁹⁹Tcm MIBI Scan was found to be 93% sensitive and 83% specific for assessment of coronary artery disease. Moreover, it showed a negative predictive value of 83% and positive predictive value of 91% for diagnosis of coronary artery disease in our clinical settings.

Conclusions:

This study showed that a definite percentage of diabetic patients suffer from silent myocardial ischemia. Use of ⁹⁹Tcm MIBI perfusion scan for diagnosis of silent ischemia was found to be a reliable non-invasive diagnostic tool. Results of our study support the use of myocardial perfusion imaging for screening of silent ischaemia.

Key Words: Silent ischemia

Funding Agency: None

Partially-Reversible Myocardial Perfusion Defects: Clinical and Electrocardiographic Correlates

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Introduction:

Myocardial perfusion imaging (MPI) using radionuclide methods is an established procedure for evaluation of coronary artery disease. The presence of defects of myocardial uptake of the radiotracer and their reversibility between the stress and rest components of the study denotes ischemia, while defect non-reversibility (fixed) indicates scar after myocardial infarction. The degree of defect reversibility is however variable; partially-reversible (PR) defects are frequently observed. The objective of this study is to look for particular clinical or electrocardiographic (ECG) findings associated with this pattern of myocardial perfusion abnormalities in an attempt to define its pathophysiologic and clinical significance.

Methods:

Sixty - six MPI studies with a report of at least one PR defect were identified by a computer search of MPI study reports performed over a 1 year period (2008). All patients had treadmill exercise for stress and Tc-99m tetrofosmin (Myoview) gated-SPECT for imaging. Patient age and gender were recorded as well as a history of previous myocardial infarction (MI), chest pain (CP), hypertension (HTN) and diabetes mellitus (DM). The treadmill ECG stress test was scored as positive, negative or non-diagnostic. Data were analyzed using standard descriptive statistical methods.

Results:

Patient demographics: average age: 51.6 y, gender: 54 male (88%). Clinical correlates: MI: 23 (36%), CP: 18 (28%), HTN: 26 (41%), DM: 25 (39%). ECG data: Positive: 12 (19%), Negative: 45 (70%), Non-diagnostic: 7 (11%).

Conclusions:

PR defects are associated with a previous MI in a third of the patients studied. A large proportion of these patients, about 40%, suffer from HTN and DM. Most ECG stress test data are negative in these patients. Residual ischemia post MI identified as PR defects is an important consideration that would require specific intervention in these patients.

Key Words: Myocardial perfusion imaging; Partial reversibility; Ischemia

Funding Agency: None

Success Rate Of 131i Ablation In Patients With And Without Preliminary Diagnostic Whole Body Scan

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Introduction:

Thyroid stunning is a phenomenon of impaired thyroid tissue function after administration of a therapeutic dose of 131I subsequent to a diagnostic dose of 111- MBq (3 mCi) or greater. The impact of stunning on the clinical outcomes is still not well documented. Aim: The purpose of this study was to investigate the clinical effects of stunning.

Methods:

Four to six weeks after total or near-total thyroidectomy forty patients with nonmetastatic papillary or follicular carcinoma of the thyroid were evaluated. TSH level should be above 30 mU/L. They were divided prospectively into 2 groups. Group 1: 20 patients underwent 131I ablative therapy without a preliminary 131I diagnostic whole body scan. Group 2: 20 patients underwent 131I ablative therapy after preliminary 131I diagnostic whole body scan. Comparisons of the postablation outcomes were evaluated by chi 2 analysis. Successful ablation required a negative follow-up thyroid scan 6 months after ablation and also thyroglobulin level < 1.5 µg/L.

Results:

Only 30% of patients in the scanned group had the thyroid gland ablated after a single 131I dose, compared with 85% in the non scanned group ($P < 0.005$). 30% of patients in scanned group versus 15% in non-scanned group required second therapeutic dose. 40% of patients in scanned group required third therapeutic dose. In contrast no patients received third dose in the non-scanned group. Patients in the scanned group required higher total 131I therapeutic activity (199mCi or 7.36GBq) to ablate the thyroid gland compared to those in the non- scanned group (132 mCi or 4.8 GBq). In analysis of the relation between TSH level and number of patients required single 131I dose, to achieved thyroid remnant ablation, there are 5 patients in the range from 30 to 40 mU/l, 8 patients in the range of 41 to 50 mU/l and 10 patients in the range of 51 to 61 mU/l. The difference in outcome between the scanned and the non- scanned groups demonstrates that the efficacy of 131I ablation is reduced subsequent to the use of 185 MBq (5 mCi) of 131I for diagnostic imaging.

Conclusions:

This study confirms that thyroid stunning after diagnostic 131I whole body scan affect the clinical outcomes of 131I ablation. We also concluded that the higher the TSH level the greater the number of ablated thyroid remnant after single 131I therapeutic dose.

Key Words: Thyroid Cancer; Stunning; I-131

Funding Agency: None

Accuracy of 64-Multidetector Row CT in the Diagnosis of Coronary Artery Disease.

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Introduction:

Coronary artery disease continues to be one of the leading causes of morbidity and mortality worldwide. Hence a reliable and reproducible non-invasive diagnostic test for the diagnosis and grading of coronary stenosis is highly desirable. The aim of the present prospective study was to assess the accuracy of 64-multidetector row computed tomography (CTA) in the diagnosis of coronary artery disease (CAD).

Methods:

Ninety - two patients suspected of having CAD underwent CTA using 64 slice CT scanner before a scheduled conventional coronary angiogram (CCA). Blinded assessment of CTA to detect CAD was performed. The accuracy of CTA was compared to CCA to detect significant stenoses (>50%).

Results:

Final analysis was performed in 73 cases. For the patient based analysis CTA had 95% sensitivity, 96% specificity, 98% PPV and 90% NPV. For the whole vessel the sensitivity of CTA was 60% or above for all vessels and the specificity was 82% or above. Pooled sensitivity was 92% and pooled specificity was 98%. For the segments the sensitivity of CTA was 64% or above for all vessels except distal LAD (40%), mid circumflex (50%) and PDA (60%) and the pooled sensitivity was 79%. The specificity for the segments was 82% or above for all vessels and pooled specificity was 94%.

Conclusions:

The sensitivity and specificity for patient based analysis and for the main coronary vessels was high whereas for the segment the sensitivity was moderately good but the specificity again was high confirming that a negative CTA is useful to rule out significant CAD. A co-ordinated classification system between the radiologists and the cardiologists is required to eliminate errors in classification of the segments.

Key Words: 64- slice, Multidetector CT; Coronary artery disease; Coronary angiography
Funding Agency: Kuwait University Grant No: MT 01/06

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Intraoperative Gamma Probe Localization of Parathyroid Using Tc-99m MIBI in Patients with Primary Hyperparathyroidism

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Introduction:

The classic operation for hyperparathyroidism involves identification of the pathological gland after exploring all parathyroid tissue. The use of new procedures such as unilateral invasive technique using gamma probe is becoming more common as they appear to reduce operation time hospital stay and perioperative complication with improved cosmetic results. The aim of this study is to evaluate the usefulness of Tc 99m MIBI scintigraphy and gamma probe localization of parathyroid glands in patients with primary hyperparathyroidism.

Methods:

Thirteen patients with primary hyperparathyroidism (mean age, 49±14yrs; median age 46yrs; age range, 29-68 yrs) were evaluated. The diagnosis of hyperparathyroidism was established by elevated serum calcium and parathormone levels. The patient that included in the study has normal thyroid gland (no nodular goiter), no history of familial hyperparathyroidism or MEN, and no history of previous neck irradiation. All patients underwent Tc99m MIBI Scintigraphy and gamma probe localization before radioguided minimally invasive parathyroidectomy.

Results:

The preoperative localization of the affected gland was successful in all cases, using gamma probe and Tc 99m MIBI scintigraphy. The pathological parathyroid tissue was localized and successfully removed with the aid of gamma probe. The histopathological diagnosis was parathyroid adenoma in 12 cases and hyperplasia in one.

Conclusions:

Our initial experience intraoperative use of gamma probe is useful to determine the side of the parathyroid lesion. The intraoperative use of gamma probe helps the surgeon to detect parathyroid lesion more easily. Radioguided minimally invasive parathyroidectomy is an attractive, easy, safe surgical approach to treat patient with primary hyperparathyroidism

Key Words: Tc 99m MIBI scintigraphy; Primary hyperparathyroidism; Gamma prob
Funding Agency: None

Kuwait University Medical Students do Benefit from Printed Topics for their Learning

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Introduction:

Printed learning Topics were introduced to support the New Curriculum and encourage independent student study. It is the first time we have been able to follow student achievement based on study from written texts. It has long been held that our students are orate learners and much less able to take advantage of textbooks or other written resources. We have surveyed students and staff as well as collated evidence from assessments for the first student cohort of 2005.

Methods:

The printed learning topic (LT) materials used in the first five modules (A-E) studied in Phase II were used for analysis. Student achievement on assessment items aligned with objectives specifically related to materials presented in LTs and those aligned with face-to-face teaching were compared. An eighteen item inventory survey was administered to student cohort 2005 and all staff members who had contributed with at least one LT. Finally, Module evaluations were consulted for information related to LTs.

Results:

Increasing dissatisfaction was encountered with LTs in successive modules A-C, after which uniform formatting was introduced. This resulted in an immediate improvement. LTs proved to be superior as a source of knowledge that was tested in 3/5 module examinations ($p < 0.05$). Students believe that LT allow them to study at their own pace and time. Staff believed lectures should deliver concepts, principles and mechanisms; not just curricular content.

Conclusions:

This is an example of a successful strategy introduced in the New Curriculum, however, not before students had expressed their dissent.

Key Words: Learning; Lecture; Printed topic
Funding Agency: None

Some of what we do may not be Necessary: Writing Five Option Multiple-Choice Questions

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Introduction:

Decisions about new strategies, formats and resources introduced by curricular change are seldom pre-tested by any school before they are implemented. Although the MCQ A-type assessment item is not new, it is the first time its performance has been closely evaluated in Faculty of Medicine exams, Kuwait University. We investigated whether writing five-option multiple-choice questions is justified by the evidence.

Methods:

Eight MCQ examinations administered to the same 2005 student cohort were available for analysis. Functional distractor frequency (FDF), Kuder Richardson test reliability (KR-20) and mean test scores (MTS) were determined for the whole class and three ability groups. The least performing distractor was removed using item analysis and selections were randomly re-assigned to the remaining four options. Using two standards of 50% and 60%, the added number of passes was determined.

Results:

A sigmoid curve was the best fit to explain the correlation between MTS and FDF, $r^2=0.95$. Three abilities of examinee MTSs were substantially different, $p<0.001$. After removing the least performing distractor 1.9 (standard set at 60%) and 2.4 (50%) more examinees passed. The KR-20s and mean item discrimination remained unchanged.

Conclusions:

Lord F, 1970, in a theoretical study asserted high ability examinees never guess and only consider one or two options, while low ability examinees frequently guess. We endorse this, but believe that in medical school assessments asking Faculty staff to write five-option MCQs is probably not justified. Following test scores of low ability examinees is important evidence to decide whether to retain five options MCQs.

Key Words: Assessment; Multiple-choice questions; Options

Funding Agency: None

Perceived Preparedness for the Smoking Cessation Role among Students of Health Professions in Kuwait

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Introduction:

The prevalence of smoking outside the U. S. and Western Europe remains high even among health professionals and students. Interventions targeting the health professional are needed; starting early in professional schools. We developed a 4-hour training seminar for the third year pharmacy students in Kuwait. Two years later, we wanted to compare their attitudes toward the smoking cessation professional role with a cohort of medical and dentistry students.

Methods:

A questionnaire was administered to students in medicine, dentistry and pharmacy who had experienced direct patient contact. The questionnaire elicited demographics, smoking status, perceptions related to the curriculum and to the professional role in smoking-cessation.

Results:

Of the 313 students invited to participate, 292 responded. Thirty five (12%) were current smokers. The prevalence of smoking was 2.6% in females and 29.7% in males. Non-smoking medical students were more likely to agree that it's their professional responsibility to help smoking patients quit (82.2%) than smoking medical students (48.5%). In one-way ANOVA analysis pharmacy students had significantly higher perceptions of curricular smoking cessation content ($M = 4.13$) than both medicine ($M = 2.89$, $p < 0.001$) and dentistry ($M = 2.90$, $p < 0.001$). Pharmacy students perceived competency to help smoking patient was significantly higher ($M = 3.54$) than both medicine ($M = 2.46$, $p < 0.001$) and dentistry ($M = 2.82$, $p = 0.006$). The perceived responsibility was also significantly higher for pharmacy ($M = 4.43$) than dentistry ($M = 3.83$, $p = 0.002$), but not significantly higher than medicine ($M = 4.25$, $p = 0.37$).

Conclusions:

Smoking cessation training program similar to the one used here could improve the preparedness of health sciences students to take an intervention role. The smoking status of medical students may influence their readiness to help their future patients quit; therefore, smoking cessation interventions targeting students are warranted.

Key Words: Students; Attitudes; Smoking cessation
Funding Agency: None

Medicine

Category: Clinical

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Oscillations on Osteocalcin Levels in Uremic Patients Maintained on Regular Hemodialysis

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Introduction:

Osteocalcin (OC) is the most abundant non-collageous protein synthesized by osteoblasts. OC is considered a marker for bone formation and has been used to assess bone turnover in postmenopausal women. In patients with chronic kidney disease the use of OC to predict the nature of their metabolic bone disease is hampered by the retention of OC fragments of unknown function in the plasma of uremic patients. Nevertheless, good correlations is established between plasma OC and bone histomorphometry in these patients. Measurement of bone markers, such as osteocalcin, in patients with CKD can be important because it can diagnose the nature of the underlying bone disease without having to perform bone biopsy the gold standard test for diagnosis of renal osteodystrophy. As uremic patients on regular dialysis suffer various degrees of changes in bone mineral density and exact levels of osteocalcin and its relationship to dialysis is not clearly established, this study aimed to examine the effect of hemodialysis session on plasma OC levels.

Methods:

In order to evaluate the influence of hemodialysis on osteocalcin (OC) levels, we have studied OC levels in 72 (28 Males and 44 females) uremic patients who were on maintenance hemodialysis. In the morning, prior to dialysis, all patients had blood drawn under fasting conditions. Then, again on the same day blood was drawn at noon time after the end of first session of dialysis. Levels of osteocalcin prior (Pre-OC) and after hemodialysis (Post-OC) were measured by ELISA.

Results:

Subjects were on regular hemodialysis ranging from 3 months to 11 years. All were eucalcemic under adequate conservative medical therapy. Their baseline osteocalcin level Pre-OC dropped significantly from (Mean \pm SEM) 317 \pm 40 ng/ml to Post-OC: 259 \pm 40 ng/ml after hemodialysis, P=0.02. Baseline (Pre-OC) did not correlate with patients' metabolic mineral variables.

Conclusions:

Levels of osteocalcin are influenced quickly by hemodialysis resulting in a significant drop. It is essential to assess the impact of such drop and the correlations of OC levels with bone mineral density and mass.

Key Words: Osteocalcin; Uremia; Hemodialysis

Funding Agency: None

Renal Biopsies in Mubarak Al Kabeer Hospital Indications and Clinical Significance

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Introduction:

Renal biopsy is an important diagnostic tool in nephrology. In this study all biopsies done in Mubarak al kabeer Hospital, Nephrology department from January 2007 to December 2008 were studied.

Methods:

Data from patients who underwent renal biopsy were analyzed.

Results:

Nine hundred and twenty nine patients were admitted to the nephrology department in the study period. 186 (20.02%) required renal biopsy. Indications for biopsy were: nephrotic syndrome in 61 (32.8%) cases; non nephrotic range proteinuria in 20 (10.7%); isolated hematuria in 8 (4.3%); unexplained acute renal failure in 24 (12.9%); unexplained chronic renal failure in 14 (7.5%); transplant dysfunction in 10 (5.4%); and renal manifestation of a systemic diseases as systemic lupus erythematosus (SLE) in 20 (10.7%), diabetes mellitus in 18 (9.68%), and other systemic vasculitis in 6 (3.2%) cases. Regarding the histopathology results: minimal change lesion was detected in 19 (10.2%), focal segmental glomerulosclerosis in 26 (13.98%), membranous glomerulonephritis in 24 (12.9%), membranoproliferative glomerulonephritis in 3 (1.6%), IgA nephropathy in 24 (12.9%), post infection glomerulonephritis in 5 (0.03%), tubulointerstitial disease as well as acute tubular necrosis in 6 (3.2%), diabetic glomerulosclerosis in 11 (5.9%), crescentic glomerulonephritis in 9 (4.8%), SLE in 21 (11.3%), end stage renal disease in 10 (5.4%), multiple myeloma in 3 (1.6%), thin glomerular basement membrane disease in 2 (1%), only one case (0.54%) of each of acute pyelonephritis, granulomatous interstitial disease, and normal kidney tissue. Biopsy failed in 7 (3.7%) cases. The clinical diagnosis coincides with the tissue diagnosis in 128 (68.8%) cases. Complications were reported in 6 (3.2%) cases.

Conclusions:

Percutaneous renal biopsy is a method of diagnosis in renal diseases that is not associated with a high complication rate and provides an accurate tissue diagnosis that helps to guide treatment and predict prognosis.

Key Words: Renal biopsy; Proteinuria; Renal failure

Funding Agency: None

Bacterial Spectrum of Permcath Catheter Related Infection Among Hemodialysis Patients

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Introduction:

Dual-lumen cuffed central venous catheter (permcath) is an alternative vascular access in maintenance of haemodialysis. Infection however is a major problem associated with long-term central venous catheters. This study assesses the spectrum of catheter related bacterial infection among haemodialysis patients.

Methods:

Charts of 174 patients were reviewed during the period between January 2007 and December 2008. Quantitative blood culture was obtained simultaneously from the catheter and from a peripheral vein when catheter related infection is suspected. Episodes of catheter related infection were registered including the causative bacteria.

Results:

Seventy - six permcath double-lumen catheters rooted were inserted in 76 (43.7%) haemodialysis patients. 79 episodes of catheter related bacteria infection in 45 (59%) patients were analysed. 6 (13.33%) patients had more than one episode of catheter related infection. The causative bacteria included Gram-positive organisms in 51 (64.6%). Methicillin Resistant Staph Aureus (MRSA) was detected in 25 (31.6%) episodes, staph epidermidis in 9 (11.4%) episodes, staph aureus in 8 (10%) episodes, enterococci in 6 (7.5%) episodes. Gram-negative bacteria were the cause of infection in 28 (35.4%) episodes. Pseudomonas was isolated in 6 (7.5%) episodes, Acintobacter in 5 (6.3%) episodes, and E-coli in 5 (6.3%) episodes. Other bacteria were the cause of infection in 15 (18.9%) episodes. Bacteraemia was reported in 47 (59.5%) episodes. 75 (95%) episodes were cured with proper antibiotics without catheter removal. 4 episodes (5%) required catheter removal. Exit site infection was reported in 32 (40.5%) episodes. Concomitant exit site infection and septicaemia was reported in 6 (7.5%) episodes

Conclusions:

This study clearly demonstrated that MRSA is the most common cause of permcath infection in haemodialysis patients. Early treatment and or catheter removal reduces patients' morbidity. Exit site infection should be treated punctually.

Key Words: Hemodialysis; Permcath; Infection

Funding Agency: None

Gender has Significant Impact on Obesity-Related Metabolic Abnormalities and Phenotypic Traits in Healthy First-degree Relatives of Type 2 Diabetes Patients

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Introduction:

The aims of this study were to determine the impact of gender and family history of Type 2 diabetes (T2DM) on adipokines, beta-cell function (%B), insulin sensitivity (% S) and resistance (HOMA-R).

Methods:

Fasting adiponectin, leptin, leptin receptor (sOB-R), insulin, glucose, and full lipid profile were determined in 229 normoglycemic first-degree relatives (FDR) of 115 T2DM probands and 41 healthy nondiabetic control subjects without a family history of diabetes matched for age, sex, and BMI. Variables were compared between T2DM, FDR and controls and between males and females.

Results:

Gender dimorphisms were noted with female patients having significantly higher mean insulin (21 vs 8 uIU/mL) and HOMA-R (10 vs 2.5) compared to male patients. 83% of female patients and 32% of female FDR had HOMA-R > 2 compared to 33% of male patients and 24% of male FDR. Male patients and male FDR had significantly lower mean%B (45 and 113% respectively) compared to female patients (57 and 136% respectively). Female patients also had significantly higher leptin, HbA1c and significantly lower adiponectin and sOB-R than male patients. However, in the FDR and control subjects, gender dimorphism was noted with only leptin with females having significantly higher leptin than males. FDR of the T2DM probands had significantly higher insulin and leptin and lower sOB-R and adiponectin compared with control subjects.

Conclusions:

Our results suggest that some of the obesity-related metabolic parameters in T2DM are genetic/heritable but gender and environmental factors may influence the clinical and metabolic phenotypes.

Key Words: Gender; First degree relatives; Type 2 diabetes

Funding Agency: Supported by KFAS grant 2004-1302-03

Evaluation of Adiponectin as a Potential Component of the Criteria for the Metabolic Syndrome

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Introduction:

First-degree relatives (FDR) of patients with type 2 diabetes (T2DM) have increased risk of developing diabetes because of aggregation of cardiometabolic risk factors. This study explores the potential use of adiponectin as a marker of the metabolic syndrome (MS) in normoglycemic FDR of T2DM patients.

Methods:

Fasting adiponectin, insulin, glucose, and full lipid profile were determined in 423 and 53 healthy control subjects without family history of diabetes. Clinical and anthropometric data were recorded and subjects were classified on the basis of the degree of adiposity, insulin resistance (IR) (HOMA-IR) and the number of criteria of the MS (International Diabetes Federation).

Results:

Adiponectin concentration was higher in females than males (mean 9.7 vs. 6.9 ug/ml) despite similar waist circumference (WC). In both FDR and controls, adiponectin was inversely correlated with WC and HOMA-IR and positively correlated with HDL-cholesterol (HDLC). Adiponectin showed stepwise decrease with increasing number of MS criteria. Binary logistic regression showed that the odds ratio of MS as predicted by adiponectin was 0.55 [95% confidence interval 0.41-0.73; $p < 0.0001$]. At cut-off points of 7.5 ug/ml, the diagnostic sensitivity and specificity of adiponectin for the MS were 90% and 70% respectively compared to 42% and 95% for triglycerides and 80% and 54% for HDLC at standard cut-off points. Receiver Operating Characteristic analysis showed that adiponectin (0.859) had significantly higher area under the curve compared with HDLC (0.745) and triglycerides (0.823) for detection of MS.

Conclusions:

Adiponectin should be an additional and useful criterion for identification of the MS.

Key Words: Obesity; Adiponectin; Metabolic Syndrome

Funding Agency: Supported by KFAS grant 2004-1302-03

Comparison between Familial and Sporadic Systemic Lupus Erythematosus in Kuwaiti Patients

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Introduction:

In order to validate the use of multiplex case families in studying the pathogenesis of SLE, we investigated the pattern of familial systemic lupus erythematosus (SLE) in relation to sporadic SLE in the highly consanguineous Kuwaiti population. We sought to determine if familial and sporadic SLE has the same clinical and serological features.

Methods:

We compared 21 cases of familial SLE in 21 families with 42 non-familial SLE controls matched for age, sex, and duration of disease. Twenty-one families, in which the diagnosis of SLE was verified in at least two relatives, were included in the study. The diagnosis was made according to the revised 1982 American College of Rheumatology (ACR) criteria.

Results:

There were no significant differences in clinical features or serological manifestations between familial SLE cases and their matched controls. However, our results showed that the frequency of anti-La antibodies was higher in the sporadic group ($p=0.048$), although this was not significant after application of Bonferroni's correction for the number of comparisons. Familial cases of SLE were more likely to present at younger age of 20 years, and sporadic cases at 26 years ($p = 0.006$). The prevalence of familial SLE was 27.4%.

Conclusions:

We have found that familial and sporadic cases of SLE are broadly similar, and it is justified to include multiple case families in genetic studies.

Key Words: Systemic lupus erythematosus; Familial; Sporadic

Funding Agency: None

Medicine

Category: Clinical

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Putative Roles of Circulating Resistin In Patients With Asthma, COPD and Cigarette Smokers.

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Introduction:

Resistin has been linked to several inflammation-related diseases like atherosclerosis, arthritis and recently to inflammatory lung diseases. The main aim of this study was to explore the associations and putative roles of resistin in patients with acute and stable inflammatory obstructive airway diseases and cigarette smokers.

Methods:

We determined fasting resistin, complements C3, C4, insulin, glucose and lipid profile; calculated insulin resistance (homeostasis model assessment (HOMA)) in patients with acute asthma exacerbation (n=34); stable asthma (n=26) and stable chronic obstructive pulmonary disease (COPD; n=26), cigarette smokers (n = 81), and healthy control subjects (n = 42). Uni- and multivariate regression analyses were used to find the associations between these variables and pulmonary function tests.

Results:

Patients with COPD, acute and stable asthma had significantly higher resistin and insulin than control subjects. Resistin (p = 0.019), insulin (p = 0.03), HOMA-IR (p = 0.02), FEV1% (p = .002) and FEV1/FVC (p < 0.0001) were significantly different when patients with acute asthma were compared with stable asthma and COPD; smokers had similar levels of resistin, C3 and C4 as patients with asthma and COPD that were significantly higher than in control subjects. In smokers and patients with asthma or COPD, resistin showed significant inverse correlations with FEV1%; FEV1/FVC% and positive significant correlations with BMI and HOMA-IR. Logistic regression analyses showed that resistin is associated with inflammatory obstructive airways disease – odds ratio (OR) = 1.22 (p = 0.001) and smoking OR = 1.18 (p<0.0001).

Conclusions:

Smoking and conditions with pulmonary inflammation are accompanied by higher resistin which contributes to an insulin resistant state. The higher resistin in smokers is independent of the BMI and degree of insulin resistance and may be a key player linking smoking, insulin resistance and cardiovascular disease.

Key Words: Inflammatory Lung Diseases; Resistin; Smoking

Funding Agency: None

Medicine

Category: Undergraduate

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A Case-control Study of the Risk Factors for Developing Diabetic Foot in Type 2 Diabetes Patients in Kuwait

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Introduction:

Diabetic foot is an increasing problem among diabetic patients and an important public health problem. The aim of this study is to evaluate several potential risk factors that may contribute in the development of diabetic foot complications in Kuwait.

Methods:

One hundred-thirty-one type 2 diabetic patients who had received a diagnosis of diabetic foot at Al-Amiri and Al-Farwaniya diabetic foot clinics were recruited as cases patients and 245 controls, who were type 2 diabetic patient and did not have foot deformity, ulcer, gangrene, or amputation, were selected from Al-Nuzha and Al-Rabiya diabetes clinics. Data was collected between 9th and 13th of December 2007. The research tool included a questionnaire that was either self-administered or the patients were interviewed. The questionnaire consisted of sociodemographic factors, patient's history of diabetes and its complications, and diabetes knowledge questions. Binary logistic regression was used to estimate the odds ratios. Age, gender, nationality, educational level, smoking, and monthly household income were included as covariates in the model to calculate the adjusted odds ratios (aOR).

Results:

Cases were significantly more likely to be male (aOR=2.1) and non-Kuwaiti Arabs (aOR= 2.6). Cases had significantly lower compliance to diabetes treatment (aOR= 2.2) and more diabetes complications as compared to controls. Diabetic neuropathy was very highly associated to diabetic foot (aOR=16). Cases were more likely to be on insulin injections (aOR= 5) and having above normal weight.

Conclusions:

Gender, nationality, compliance to diabetes treatment and diabetes complications were found to be significantly associated with the development of diabetic foot complications. The knowledge of the risk factors for this condition will lead to a better care for diabetic patients.

Key Words: Diabetic foot; Risk factors; Kuwait

Funding Agency: None

Medicine

Category: Clinical

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Safety and efficacy of novel dose regimen of cinacalcet in the treatment of hyperparathyroidism in hemodialysis patients

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Introduction:

Cinacalcet has improved the management of hyperparathyroidism in hemodialysis. To the best of our knowledge there are no specific studies addressing the dose regimen of Cinacalcet. The aim of the present study was to evaluate the efficacy of twice weekly Cinacalcet on the treatment of hyperparathyroidism.

Methods:

Twenty - seven hemodialysis patients with intact parathyroid hormone, $d 88 \text{ pmol/L}$ were divided into two groups. Group 1 received oral Cinacalcet which was given with the main meal in a single daily start dose of 30 mg and titrated thereafter monthly. Group 2 received oral Cinacalcet which was given with the main meal in a twice weekly start dose of 90 mg at the 1st day of the week, 120 mg at midweek and titrated thereafter monthly.

Results:

Intact parathyroid hormone reduced significantly ($p=0.0001$) from $124.00 \pm 44.77 \text{ pmol/L}$ to $37.78 \pm 12.49 \text{ pmol/L}$ and from $109.61 \pm 53.13 \text{ pmol/L}$ to $33.93 \pm 12.03 \text{ pmol/L}$ after 12 weeks in group 1 and 2 respectively. After 12 weeks alkaline phosphatase declined significantly ($p=0.0001$) from $143.42 \pm 75.20 \text{ IU/l}$ to $87.42 \pm 14.46 \text{ IU/l}$ in group 1 ($p=0.013$) and from $148.00 \pm 108.49 \text{ IU/l}$ to $101.61 \pm 46.62 \text{ IU/l}$ in group 2 ($p=0.05$). There were no significant differences between the reductions of iPTH, calcium phosphate product and alkaline phosphatase levels in both groups in the vertical comparison at the end of the study

Conclusions:

These results indicate that Cinacalcet twice weekly has been reasonably safe and effective in suppressing high parathyroid hormone in hemodialysis patients.

Key Words: Hyperparathyroidism; Cinacalcet; Hemodialysis

Funding Agency: None

Medicine

Category: Clinical

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Clinical Spectrum and Management of Cutaneous Leishmaniasis in Kuwait

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Introduction:

Cutaneous leishmaniasis (CL), is a major public health problem. The currently available therapies are expensive, freely unavailable, toxic and not always curative. Simple, effective, non-invasive, treatment approach is required for treating CL.

Aims

To find out the clinical patterns of CL, in addition to our experience in managing CL

Methods:

One hundred and ten patients of CL seen from January 2005 to December 2007 were included in this study. The diagnosis was based on clinical features, parasitological diagnosis, histopathology and culture. Each patient was treated according to the disease severity with either topical (cryotherapy or imiquimod) or systemic (itraconazole or dapson) monotherapy or a combination of these modalities.

Results:

CL was found to be more common in adult, expatriate males; affecting the upper limbs most commonly. Nodulo-ulcerative CL was the most common presentation (84.6%). Atypical CL was found in 18 patients. Skin biopsy was the most common diagnostic technique (66.6%). Monotherapy showed an overall success rate 56.41%, whereas combination therapy was successful in 69.56% cases. However, cryotherapy alone was successful in 68.18% cases. Imiquimod alone was not effective at all.

Conclusions:

A step-ladder approach is a rational and practical way of confirming CL. Combination of itraconazole/dapsone & topically applied imiquimod is safe, simple and effective in treating CL. More studies are needed to establish the role of such an approach. However, cryotherapy is a safe, simple and effective method of treating CL.

Key Words: Leishmaniasis; Kuwait; Imiquimod

Funding Agency: None

Medicine

Category: Clinical

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Comparative Study on the Efficacy, Safety and Acceptability of Imiquimod 5% Cream versus Cryotherapy for Molluscum Contagiosum in Children.

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Introduction:

To compare the efficacy, safety and acceptability of imiquimod 5% cream with cryotherapy for the treatment of Molluscum Contagiosum (MC) in children.

Methods:

A total of 74 children, with MC were divided randomly to receive treatment with either imiquimod 5% cream 5 days per week or cryotherapy once a week until clinical cure or up to a maximum of 16 weeks. The patients were followed up for 6 months after the treatment to look for the relapse.

Results:

In imiquimod group, the overall complete cure rate was 91.8% (34 of 37), 22 of the 37 patients cleared by the end of 6 weeks and 12 more patients cleared by the end of 12 weeks while the remaining 3 patients (8.1%) did not clear even after 16 weeks. Whereas in the cryotherapy group; all patients (37) achieved complete cure, 26 of 37(70.27%) cleared after 3 weekly applications and another 11(29.72%) cleared by the end of 6 weeks. Pain, bullae formation, pigmentary changes, and superficial scarring were significantly more common in cryotherapy group compared to imiquimod group.

Conclusions:

Imiquimod 5% cream seems to be slow acting but effective agent for the treatment of MC in children. Imiquimod appears to be practically painless and more cosmetically accepted procedure when compared to cryotherapy, and may be the preferred treatment of MC in children especially with numerous small lesions.

Key Words: Imiquimod; Molluscum contagiosum; Children

Funding Agency: None

JAK2 V617F Mutation in Polycythemia Vera in Kuwait: Molecular versus Conventional Diagnosis.

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Introduction:

Polycythemia vera (PV), a malignant myeloproliferative disorder, is conventionally diagnosed using combinations of several clinical and laboratory investigations. Recently, a point mutation in the JAK2 gene (V617F) was found to be associated with more than 95% of PV cases. Therefore, detection of JAK2 V617F mutation is now considered as a diagnostic test for PV. At present, most PV cases in Kuwait are diagnosed based on conventional methods without testing for JAK2 V617F mutation. This study, the first in Kuwait, was conducted to determine the number of cases having JAK2 V617F mutation among the total number of cases diagnosed as PV by conventional methods. This may reflect the accuracy of the currently used conventional diagnostic method when molecular techniques are used.

Methods:

DNA was extracted from blood samples of 76 cases diagnosed conventionally with PV in Kuwaiti hospitals. PCR using appropriate primers, followed by RFLP technique using BsaXI restriction enzyme, were performed to detect JAK2 V617F mutation. The percentage of cases having the mutation among the total cases was calculated.

Results:

Only 25 out of the 76 cases (32.9%) were found to have the mutation. Of these 25 positive cases, 16 cases were heterozygous and 9 were homozygous.

Conclusions:

Unlike other reports, only one third of cases diagnosed with PV in Kuwait had the JAK2 V617F mutation. This means that a large number of cases were wrongly suspected to be PV by conventional clinical and laboratory methods. This emphasizes the need to introduce molecular techniques in correctly diagnosing PV in Kuwait.

Key Words: Myeloproliferative; Jak2 mutation; Diagnosis

Funding Agency: None

Trends in the Left Ventricular Structure before and after Spironolactone Treatment in Peritoneal Dialysis Patients

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Introduction:

Blockade of aldosterone effect with spironolactone is an approach that is being used more frequently in the treatment of hypertension and congestive heart failure. Objectives: The aims of our study were to prospectively describe trends in the left ventricular structure and function before and after spironolactone use, and to assess the safety of spironolactone use in peritoneal dialysis.

Methods:

Thirty - eight patients on continuous ambulatory peritoneal dialysis were selected for the study. All patients are adequately dialysed with serum potassium less than 5.6 mmol/l. Eligible patients received spironolactone tablets 25 mg daily. Spironolactone tablets decreased to 25 mg three times weekly according to serum potassium. Echocardiography was performed at inclusion, at 6 and at 12 months. Biochemical, blood pressure and medication data were collected.

Results:

Controlled blood pressure was achieved after 6 months ($p<0.001$) and 12 months ($p<0.001$) compared to baseline. There were significant regression of interventricular septal thickness (from 1.20 ± 0.25 to 1.03 ± 0.10), left ventricular internal diameter (from 6.06 ± 0.68 to 5.04 ± 0.58) and left ventricular wall thickness (from 1.27 ± 0.22 to 1.02 ± 0.12) at the end of the study ($p<0.0001$). The mean potassium level was 4.34 ± 0.63 mmol/l at baseline and 4.66 ± 0.62 mmol/l at study completion ($p=0.24$). Gynecomastia was noted in one patient. No significant rise of serum potassium levels was noted.

Conclusions:

Spironolactone can be safely considered as a treatment option to control blood pressure and improve the cardiac structures in continuous ambulatory peritoneal dialysis patient

Key Words: Spironolactone; Left ventricle; Peritoneal dialysis

Funding Agency: None

Assessment of LPS Induced Monoarthritis in Mice Using the Catwalk Video based Gait Analysis System.

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Introduction:

Arthritis is a group of common inflammatory joint disorders with significant socioeconomic costs. Lipopolysaccharide (LPS)-induced arthritis animal models show synovial hyperplasia and inflammatory cell infiltration similar to what is observed in rheumatoid arthritis or septic arthritis.

Methods:

C57BL/6 mice were anaesthetized with halothane and LPS (10 µg/20 µL PBS was injected intra-articularly into the hind limb right ankle joint through the Achilles tendon using a 29-gauge needle. PBS (20 µl), was administered in the same way to control mice. The video based Catwalk gait analysis system was used to assess changes in gait and pain behavior in the mice. The changes in light intensity on the glass panel (which served as the floor where mice freely walked) were used to measure changes in paw pressure.

Results:

The mice which were inoculated with LPS exerted reduced paw pressure on the glass panel with the right hind limb whilst walking, whereas they exerted more pressure with the left hind limb, showing a clear transfer of weight bearing from the right to the left hind limb, which was significant (** p < 0.01, two way ANOVA) at 2 and 3 days post LPS inoculation. There were no differences between the left and right front limbs. No changes were observed in the PBS injected controls.

Conclusions:

Our results show that the Catwalk gait analysis system can be used to evaluate movement-related pain and weight-bearing changes in freely moving mice models of arthritis.

Key Words: Arthritis; Gait analysis; Catwalk

Funding Agency: None

Medicine

Category: Clinical

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Does Vitamin D have a Role in Patients with Musculoskeletal Pain?

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Introduction:

Several studies recently have shown that vitamin D (vit D) deficiency is common in musculoskeletal (MSK) diseases. The objective of the study is to determine if vitamin D has a role in patients with wide spread MSK pain in our patients.

Methods:

Patients who were referred to the rheumatology clinics in four major hospitals for musculoskeletal pain during the last 6 months were evaluated by certified rheumatologists. We did clinical evaluation and investigations including determination of 25 hydroxy vitamin D level, parathyroid hormone (PTH), calcium, alkaline phosphatase (ALK) and albumin levels.

Results:

Fifty - two patients were evaluated with mean age 41.92 years and duration of symptoms 21.64 months. 81% were Kuwaitis. 69% had wide spread pain, 8% low back pain and 23% hand /wrist pain. 81% wore long garments and 48% wore veils. 78% had less than one hour of sunlight exposure. Diet was poor in calcium in 36.5%. Mean vitamin D level was 24.32 ± 1.6 n mol/L, PTH 10.72 ± 1.7 p mol/L, Calcium 2.28 ± 0.16 m mol/L, ALK 89.9 ± 1.8 IU/L and albumin 35.86 ± 4.6 g/L respectively. 94% of our patients were deficient in vit D.

Conclusions:

Our results show that vitamin D deficiency is common among patients with musculoskeletal pain in our population. Significance of this preliminary observation in relation to clinical and laboratory outcome after treatment with vitamin D has to be further evaluated by longitudinal studies.

Key Words: Vitamin D; Musculoskeletal pain; Kuwait

Funding Agency: None

Medicine

Category: Clinical

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Chronic Antibody Mediated Rejection (CAMR) in Renal Transplants

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Introduction:

Chronic renal allograft injury and dysfunction is a multifactorial process in which immunological and non immunological factors contribute. Recent data showing the association of circulating antiHLA antibodies and C4d deposits in peritubular capillaries (PTC) in chronically failing renal allografts indicate a pathogenic role of humoral mechanisms leading to CAMR in a subset of patients with chronic allograft dysfunction. Our aim is to conduct a pilot study on 5 patients with CAMR and to treat them with our specific protocol and follow prospectively the progression of renal function after treatment.

Methods:

Five renal transplant recipients fulfilling the diagnostic criteria of CAMR were recruited for the study and were given the following treatment- increase in basic immunosuppression, daily plasma exchange (PE) for 5 days, intravenous immunoglobulin 25 gms per day for 5 days and Rituximab 1gm IV for 2 doses at 14 days interval. These patients were followed up prospectively for a period of 6 months to 1 year from the time of starting treatment and monitored for the changes in renal function.

Results:

All the five patients on follow up were found to have stable or no significant deterioration of their graft function in terms of serum creatinine and estimated GFR. The mean pretreatment serum creatinine and estimated GFR were 208.8 umol/L and 42.3 ml/mnt and mean posttreatment serum creatinine and estimated GFR were 221.8umol/L and 41.8ml/mnt respectively.

Conclusions:

We conclude that our protocol is an effective way of treating CAMR

Key Words: Chronic antibody mediated rejection; Renal transplant; Immunosuppression

Funding Agency: None

Medicine

Category: Clinical

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Combination of Split Skin Grafting and Excimer Laser for the Treatment of Chronic Stable Localized Vitiligo in Children

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Introduction:

Refractory and stable lesions of vitiligo may be unresponsive to medical treatment. Treatment of children with vitiligo is often difficult. Surgical treatment can quickly restore normal pigmentation in selected patients. However, residual achromic areas may be seen even after surgical correction.

Objective: To evaluate the efficacy of excimer laser treatment after split skin grafting for correction of stable vitiligo in children.

Methods:

Thirteen patients (age < 15 years) with chronic stable localized vitiligo not responding to topical treatments were treated with split skin grafting. Two weeks after the surgery the treated area was exposed to excimer laser twice a week to treat the achromic areas left after the grafting.

Results:

Depigmentation was 100% restored in all thirteen patients within 16 weeks after grafting and after 6-16 sessions of excimer laser. The patients have been under follow up without treatment for 1-2.5 years without any relapse.

Conclusions:

Surgical methods followed by excimer laser may be helpful in restoring complete repigmentation of depigmented defects at a much faster rate. It may be of great help in children because of non-compliance with topical medicines.

Key Words: Vitiligo; Excimer laser; Children

Funding Agency: None

Impact of Gender on Treatment and Clinical Outcomes in Acute Coronary Syndrome Patients in the Middle East

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Introduction:

Several western studies demonstrated significant disparities in presentation and outcome between men and women. We aimed to evaluate acute coronary syndrome (ACS) in Middle-Eastern women with emphasis on gender differences in presentation, management and hospital outcome.

Methods:

We used data from the Gulf Registry of Acute Coronary Events (GulfRace) which is a prospective, multinational multicenter survey of 8187 consecutive patients hospitalized with ACS at 65 hospitals in the Gulf countries.

Results:

When compared to men, Middle-Eastern women presenting with ACS were 9 years older (62.1± versus 53.1 ±years; P<0.001) and more often had diabetes (54.6% versus 35.9%, p < 0.001), hypertension (70% versus 43%, p < 0.001), dyslipidemia (44% versus 28%, p<0.001) and obesity (BMI 28.3 versus 26.3p=). Women were also more likely to have other co-morbidities including chronic lung disease, renal and peripheral vascular disease. On the other hand, men were more likely to be smokers (46%versus 5.1%, p < 0.001). Presentations with atypical symptoms including dyspnea and atypical chest pain were more common in women than men (15.1% vs 8.1%; p=.001 and 8.0% vs 6.1% p=0.02, respectively). Women were less likely to be appropriately treated with thrombolytic therapy use (83.6% vs 79.9), B-blockers (64% vs 57%), clopidogrel (60% vs 54%), and glycoprotein IIb/III inhibitor use (9.5% vs 2.2%) than men. Moreover, the door to needle time was more prolonged in women (median, IQR: 40, 50 vs 35, 41 minutes). Women had worse in-hospital outcomes compared to men and overall mortality in women was 1.7 times greater than in men (4.9% vs 3%, p=0.001).

Conclusions:

Similar to western studies, despite presenting with higher risk characteristics and having higher in-hospital risk, Middle-Eastern women with ACS are treated less aggressively than men.

Key Words: Gender; Acute coronary syndrome; Management

Funding Agency: Gulf Heart Association

Nerve Conduction Studies in Diabetic Patients- A Single Centre Experience

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Introduction:

Nerve conduction study (NCS) is used to evaluate the integrity of peripheral nervous system. Many symptomatic diabetic patients referred to EMG lab in Mubarak Hospital had normal conduction parameters, irrespective of duration of disease and poor diabetic control. This study was designed to compare the pattern of nerve conduction abnormalities in diabetics with normal subjects in our population.

Methods:

We compared NCS in 139 type II-diabetics (40 M and 98 F, mean age 54 years) with 79 normal subjects (29 M and 50 F, mean age 36 years). 50% patients were referred to rule out carpal tunnel syndrome (CTS) and 40% for peripheral neuropathy (PN). Mean duration of diabetes was 12.9 years. Study period was two years, 2007-2008.

Results:

Significant prolongation of onset latency (motor 74% vs. 10%, $p=0.010$ and sensory 54% vs.0%, $p =0.000$), slowing of conduction velocity (CV) (motor 26% vs.0%, $p =0.000$ and sensory 67% vs. 16%, $p= 0.000$) and comparable sensory amplitudes were noticed in median nerve in upper limb in diabetics vs. normal subjects. Ulnar conduction parameters were similar in both study groups. In lower limb, there was a significant decrease in amplitudes (peroneal 36% vs. 10%, $p =0.002$, tibial 37% vs. 4%, $p =.000$ and sural 9% vs.0%, $p = .031$) and slowing of CV (peroneal 30% vs. 0%, $p =0.000$, tibial 38% vs. 2%, $p =0.000$ and sural 24% vs. 2%, $p =0.001$) in diabetics, vs. normal population. 16 diabetic patients (11.5%) had absent sensory action potentials. Tibial amplitude showed a significant negative correlation with duration of diabetics, Pearson correlation coefficient, -0.317 , $p =0.04$.

Conclusions:

It was concluded that PN (proved by decrease in amplitudes and CV) was prevalent only in 35-37% in our diabetics in contrast to ~ 50% in other populations. Median entrapment neuropathy, CTS was the common diabetic manifestation in upper limb. This is the first data that shows the electrophysiological patterns of diabetic polyneuropathy in Kuwait.

Key Words: Diabetic Polyneuropathy; Nerve Conduction Study; Kuwait

Funding Agency: None

Medicine

Category: Clinical

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Singapore General Hospital Heart Failure Registry

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Introduction:

Increasing longevity and high incidence of diabetes mellitus (DM) account partly for the high rate of cardiovascular diseases in Singaporeans. A Heart Failure (CCF) Registry is necessary to highlight patterns of care, improve knowledge of CCF and to define better treatment strategies.

Methods:

All patients with CCF admitted to medical wards from December 2006 to December 2007 were included. The parameters recorded were: age, sex, ethnic group, clinical and biochemical data. The clinical diagnosis, medication prescribed, clinical progress, electrocardiogram and 2D-Echo, education given and outcome, were noted.

Results:

Total number of patients=737, F=49.9%, M=50.1%, Chinese=69.6%, Malay=16.6%, Indian=12.5%, Others=1.3%. Median age=74 (SD=8.5) years. Hypertension=80.3%, IHD=68.0%, dyslipidaemia=60.7%, DM=57.3%, prior heart failure=46.7%, repeated admissions=46.7%. Initial assessment: bilateral basal crackles=89.1%, peripheral oedema=78.34%, NYHA Grade IV=16.7%, III=46.5%, II=17.5%. ECG: NSR=74.5%, AF/Flutter=14.4%. Chest radiograph: congestion=79.7%. Median PRO-BNP=3395 pcmg/ml, elevated Troponin-T=2.7%. Procedures: dialysis=0.4%, mechanical ventilation=0.7%, defibrillation=0.3%, cardiac catheterisation=0.1% and CPR=0.9%. Asymptomatic on discharge=73.1%. Medicines prescribed on discharge: diuretics=82.5%, beta-blockers=42.6%, ace-inhibitors/ARBs=72.1%, lipid lowering agents=52.1% and aspirin=43.2%. Mean length of stay=4 days, death=1.5%.

Conclusions:

Younger patients were usually channelled to cardiac wards explaining the high mean age of cohort admitted to medical wards. This may also explain partly the high rates of hypertension, DM and dyslipidaemia noted. The percentage of repeated admissions of patients indicated that CCF has still increased morbidity leading to increased healthcare costs even though intervention was low. Comprehensive CCF management led to decreased length of stay and costs.

Key Words: Congestive Cardiac Failure; Registry; Singapore

Funding Agency: Partly funded by Janssen-Cilag

Baseline Characteristics, Management Practices and Inhospital Outcome of Patients Hospitalized with Acute Coronary Syndromes in the Gulf (Gulf Registry of Acute Coronary Events)

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Introduction:

Acute coronary syndrome (ACS) is a leading cause of morbidity and mortality in Gulf countries. Our aim was to describe the epidemiology, treatments and in-hospital outcomes of patients with ACS in this region

Methods:

The Gulf Registry of Acute Coronary Events (Gulf RACE) is a prospective, multinational, multi-center survey of consecutive patients hospitalized with the final diagnosis of ACS over a period of 5 months from February to June 2007.

Results:

A total of 6706 ACS patients were recruited. The mean age was 56 years and 76% were men. Half of the patients had a history of hypertension while 41% were diabetics and 41% were smokers. The majority (78%) were Killip class 1 at presentation. The final diagnosis was ST elevation myocardial infarction (STEMI) in 39%, non-ST- segment elevation myocardial infarction in 32% and unstable angina in 29%. Among patients with STEMI, reperfusion therapy was administered to 63%. Primary Percutaneous coronary intervention (PCI) was performed in 6% of these patients. The median door to needle time was 40 minutes and the median door to balloon time was 79 minutes. Coronary angiography during hospitalization, other than for primary PCI, was performed in 19% of the patients. At discharge, aspirin was prescribed in 97% of patients, clopidogrel in 51%, beta blockers in 78%, Angiotensin converting enzyme inhibitors/Angiotensin receptor blockers in 79% and statins in 83%. The in-hospital mortality rate was 3.8%.

Conclusions:

This is one of very few ACS registries relating to patients from the Middle East. It provides an insight into a different patient population and practice patterns compared to those of Europe and North America. Our patients are about a decade younger and have more diabetes as a risk factor. The reperfusion strategy used in the majority of patients is thrombolytic therapy and the use of in-hospital cardiac catheterization is low.

Key Words: Acute coronary syndrome; Registry; Management

Funding Agency: Gulf Heart Association

Medicine

Category: Clinical

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Characteristics of Young Acute Coronary Syndromes Patients in the Gulf Registry of Acute Coronary Syndrome (Gulf RACE)

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Introduction:

The Gulf Region of the Middle East has a young population structure, yet has a high prevalence of acute coronary syndrome (ACS). We wanted to compare the characteristics of ACS patients ≤ 40 years old with those over 40 in this study.

Methods:

The Gulf Registry of Acute Coronary Events (Gulf RACE) is a prospective, multinational, multi-center survey of consecutive patients hospitalized with the final diagnosis of ACS over a period of 5 months from February to June 2007.

Results:

Of recruited patients, 9% were ≤ 40 years. The mean age of this group of patients was 36 years and 90% were males. They were less likely to have a previous history of cardiac disease and other comorbidities than older patients. The main risk factors in these patients were diabetes and smoking (81% and 60%, respectively). The most common ACS in this group was ST elevation myocardial infarction. The great majority presented with Killip class I and had an uncomplicated hospital course and a low rate of in-hospital mortality.

Conclusions:

Diabetes and smoking are the major risk factors in younger patients with ACS. This should be taken in consideration in patient education and ACS prevention programs in the Gulf region.

Table:

Variable	Patients ≤ 40 n=627 No. (%)	Patients ≥ 40 n=6070 No. (%)	P value
mean age	36.1	58.4	<0.001
male	565 (90)	4501 (74)	<0.001
Smokers	392 (67)	2517 (34)	<0.001
Diabetes	509 (81)	3443 (57)	<0.001
HTN	150 (24)	3211 (51)	<0.001
Lipid	94 (15)	5052 (34)	<0.001
F. H.	133 (21)	778 (13)	<0.001
Killip I	575 (92)	4638 (76)	<0.001
STEMI	308 (49)	2308 (38)	<0.001
NSTEMI	179 (29)	1979 (33)	0.038
UA	139 (22)	1780 (29)	<0.001
Mortality	3 (0.5)	248 (4.1)	<0.001

Key Words: Acute coronary syndrome; Registry; Age

Funding Agency: Gulf Heart Association

Microbiology of Urinary Tract Infections in Renal Transplant Patients: A 5 year Study Period

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Introduction:

Urinary tract infection (UTI) is considered to be the commonest type of infection in renal transplant patients. This retrospective study was done to evaluate the prevalence, microbial etiology of urinary tract infections and their antimicrobial susceptibility pattern over a 5 year study period in renal transplant patients. In addition, the study aimed to determine the prevalence and antimicrobial susceptibility pattern of ESBL- producing Enterobacteriaceae causing these UTIs.

Methods:

This study was done at Ibn- Sina Microbiology Laboratory on all culture positive urine samples received from renal transplant patients in the Organ Transplant Center from January 2004 to December 2008. The microbial etiology of UTIs and their antimicrobial susceptibility pattern was determined using Vitek 2 (bioMerieux, France). All the ESBL- producing Enterobacteriaceae were identified and their antimicrobial susceptibility pattern to a range of antibiotics were determined using E-test method (AB biodisk, Solna, Sweden).

Results:

Out of a total of 4129 positive urine cultures evaluated over the study period, 3656 (89%) were caused by Gram-negative organisms. Escherichia coli and Klebsiella spp. accounted for 2214 (61%) and 942 (26%) episodes of UTI respectively. Gram-positive bacteria accounted for 314 (8%) of which Streptococcus agalactiae 232 (74%) was the commonest. Yeasts accounted for 149 (3%) of the episodes of which Candida albicans accounted for 70(47%). Gram-negative isolates showed uniform susceptibility to carbapenems except Pseudomonas aeruginosa which showed 37% resistance to meropenem. Out of all the Enterobacteriaceae isolates, 45% were ESBL producers. The ESBL-producing Enterobacteriaceae showed 100, 50, 69 and 16% resistance to cephalosporins, gentamicin, ciprofloxacin and piperacillin/tazobactam respectively, compared to 0, 12, 15, & 0% in non ESBL producing Enterobacteriaceae.

Conclusions:

In the renal transplant patients, the prevalence of UTIs was found to increase steadily over the five year study period. Gram-negative isolates accounted for most of the episodes.

Key Words: UTI; Renal Transplant; Microbiology

Funding Agency: None

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Nested PCR for Detection of *Fusarium Solani* DNA and its Evaluation in the Diagnosis of Invasive *Fusarium Infection* using an Experimental Mouse Model

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Introduction:

The *Fusarium* species are common environmental fungi that enter the body through the lungs or through a cutaneous source and disseminate through the bloodstream in immunosuppressed/immunocompromised patients. Fusariosis is now the second most common mould infection in immunocompromised patients and *Fusarium solani* accounts for nearly half of these infections. The aim of this study was to develop a specific nested PCR (nPCR) assay for the detection of *F. solani* DNA in culture and in clinical specimens.

Methods:

The nPCR assay was developed by using genomic DNA isolated from *Fusarium* species and from other common pathogenic and environmental fungi. The nPCR assay was evaluated by using DNA isolated from bronchoalveolar lavage (BAL) and serum samples from mice infected intravenously with *F. solani* conidia and sacrificed on day 1 and then on every third day up to 25 days post-infection. The lung homogenate, BAL and blood samples were also cultured for *F. solani*.

Results:

The nPCR assay was specific for *F. solani* and the lower limit of detection was 450 fg of template DNA corresponding roughly to 11 *F. solani* cells. Cultures of lung homogenate of infected animals up to day 16 yielded *F. solani* with decreasing fungal load and were negative thereafter. The nPCR positivity in BAL was 100% concordant with lung tissue culture results. Although detection of *F. solani* DNA in serum was less sensitive than in BAL, it could be detected for longer duration, i.e. up to 22 days.

Conclusions:

The nPCR assay developed in this study is sensitive and specific for the detection of *F. solani* DNA. Our data from experimental mouse model further show that detection of DNA in BAL and to a lesser extent in serum by nPCR offers a sensitive and specific diagnostic approach for invasive *F. solani* infection.

Key Words: Fusarium solani; Nested PCR; Experimental Fusarium infection

Funding Agency: Kuwait University Research Grant MI 04/02.

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The Distribution of Bla_{CTX-M} genes amongst Clinically Significant *Escherichia coli* Isolates in 8 Major Hospitals in Kuwait

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Introduction:

Dissemination of CTX-M extended-spectrum β -lactamases (ESBL) is pandemic. The production of this enzyme is mediated by the bla_{CTX-M} gene which confers resistance to the third-generation cephalosporins mainly in *Escherichia coli* and *Klebsiella* spp. This study was designed to investigate the distribution of bla_{CTX-M} amongst *E. coli* isolated from 8 Kuwait government hospitals.

Methods:

A total of 876 consecutive isolates were collected from these hospitals; at least 100 per hospital. Production of ESBL was detected by the ESBL Etest method and confirmed by PCR. DNA extracts of ESBL-positive isolates were screened for the presence of bla_{CTX-M} gene using the following primers: MA-1- 5'-SCS ATG TGC AGY ACC AGT AA-3' and MA-2 5'-CCG CRA TAT GRT TGG TGG TG-3'. Strains with PCR amplicons positive for bla_{CTX-M} were sequenced using Bigdye Terminator®. The nucleotides were then analyzed with software available at website <http://www.ncbi.nlm.nih.gov/blast>. The CTX-M-15 positive strains were evaluated for genetic relatedness using PFGE with XbaI digestion of the genomic DNA.

Results:

Of the 876 isolates, 113 (12.9%) were ESBL producers, 88 (78%) of which produced CTX-M ESBL. Among these, CTX-M-15 accounted for 84%, followed by CTX-M-14 (7%), CTX-M-14b (6%) and TOHO-1 (3%). The highest number of *E. coli* carrying the bla_{CTX-M} gene was in Ibn Sina hospital (26%), a specialist hospital for immunocompromized patients, and the least in Maternity hospital (6%). CTX-M-15 was the predominant CTX-M type in all hospitals, representing 74 (84%) of the CTX-M ESBLs. Of these, 66 (89%) were found in isolates from Kuwaitis, Egyptians and Indians. PFGE pattern of the CTX-M-15-positive isolates was heterogeneous.

Conclusions:

Our data show an explosive emergence of CTX-M-15 type ESBL that appears to be evenly distributed in *E. coli* strains in patients belonging to the predominant nationalities in Kuwait and demonstrates no evidence of clonal spread.

Key Words: Distribution; bla_{CTX-M}; *Escherichia coli*

Funding Agency: Kuwait University Research Grant no YM06

**In Vitro Activity of 13 Antibiotics against CTX-M ESBL-Positive and -
Negative Clinically Significant *Escherichia coli* Isolates from 8 Major Hospitals
in Kuwait.**

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Introduction:

Background: Antibiotic-resistant *Escherichia coli* is becoming a complex therapeutic problem. Surveillance programs are valuable tools and offer important information on bacterial resistance trends. As an important community and hospital pathogen, its susceptibility in 8 Kuwait hospitals was evaluated.

Methods:

A total of 846 consecutive clinically significant strains of *E. coli*, collected between November 2006 and October 2007, were studied. In vitro activity of 13 antibiotics against the isolates was determined by Etest. ESBL-production was assessed by ESBL-Etest method and confirmed by PCR technique. PCR amplicons positive for blaCTX-M were sequenced.

Results:

About 69% of the *E. coli* isolates were highly non-susceptible to ampicillin with MIC₉₀ of 256 µg/ml. Resistance to the 3rd generation cephalosporins ranged from 7.5% in Maternity hospital (MH) to 29% in Ibn Sina hospital (ISH); ciprofloxacin resistance rates ranged from 14% and 40%, respectively. Carbapenems and amikacin demonstrated excellent activities. Prevalence of ESBL-producing *E. coli* varied from hospital to hospital, with highest rate (32%) from ISH and lowest (4%) from Mubarak hospital and MH. MIC₉₀ of cefotaxime, ceftazidime, cefepime and ciprofloxacin were >256, 64, >256 and >32 µg/ml, respectively for CTX-M-positive isolates versus 0.5, 1, 0.25 and 0.125 µg/ml for CTX-M-negative strains. Frequencies of CTX-M-positive isolates in cefotaxime MIC range of 1-2, 3-8, 9-16 and >16 µg/ml were 0, 4, 15 and 81%, respectively.

Conclusions:

The prevalence of *E. coli* resistant to the 3rd generation cephalosporins and ciprofloxacin is at an unacceptably high level. This is compounded by a high incidence of CTX-M ESBL-producing strains in almost all hospitals in Kuwait.

Key Words: Antibiotic activity; Escherichia coli; Kuwait Hospitals
Funding Agency: Kuwait University Research Grant no. YM06

Phylogenetic Relationship of *Helicobacter pylori* Isolated from Kuwaitis with Isolates from other Ethnic World Populations

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Introduction:

Helicobacter pylori (HP) causes gastritis, peptic ulcer and adenocarcinoma of the stomach throughout the world including Kuwait. Cytotoxin-associated gene (Cag) A antigen is the product of *cagA* gene in the *cag* pathogenicity island of HP and is an important marker of pathogenicity. Considerable polymorphism exists at the 5' end of the *cagA* gene. This has been exploited to study the evolutionary relationship of HP isolates in different populations and between populations. No data exist on the phylogeny of HP isolates from the Arab population including the native Kuwaiti population. This study defined the phylogeny of the isolates from the native Kuwaiti population.

Methods:

Single isolates obtained from the gastric biopsies of seven Kuwaiti patients with dyspepsia were studied. The 5'-end of the *cagA* gene (219-bp) was amplified by specific primers and the amplicons were sequenced by the dideoxynucleotide chain termination method. The sequences were compared with those in the public data base for different ethnic population groups with the PHYLIP programme and the phylogenetic trees visualised using the Treeview programme.

Results:

The seven isolates were distributed into five branches; 3 branches were closely related to one another; 2 other branches were closely related to each other, but somewhat distant from the other 3; 5 isolates in 3 branches closely clustered with isolates from India, Europe, USA, UK, Australia, Peru and the Gambia; all 7 isolates were distinct from those from the Far East including China, Hong Kong, Japan and Thailand.

Conclusions:

The genetic branches of the HP from the native Kuwaiti population were closely related to those from India, Europe, USA, UK, Peru and the Gambia, but distinct from those of the Mongoloid isolates. The close genetic clustering may indicate common ancestry and evolution of isolates.

Key Words: Helicobacter pylori; Phylogeny; CagA

Funding Agency: None

Antibiotic Resistance Pattern of Acinetobacter Species in Kuwait Hospitals

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Introduction:

As high and increasing resistance of Acinetobacter spp to many potential therapeutic agents limit the choice of appropriate therapy, this study was carried out to determine the resistance pattern of strains causing clinically proven infections and those associated with mere colonization.

Methods:

A total of 250 consecutive isolates were collected from infected and colonized patients in 8 major hospitals in Kuwait. They were identified by VITEK-2 and their susceptibility to 18 antibiotics determined by Etest method. Susceptibility and resistance were assessed according to the recommended criteria of the CLSI and FDA for tigecycline. Metallo-beta-lactamase (MBL) production was detected by the MBL Etest method.

Results:

Resistance to many of the tested antibiotics were very high, in particular to amikacin (82.8%), gentamicin (68.4%), cefepime (69.6%), ciprofloxacin (73.2%) and piperacillin-tazobactam (71.2%). It is note-worthy that, in this study, resistance to tigecycline was as high as 13.6%. Similarly, of clinical importance were the resistance rates of 25.2, 37.3 and 12% to imipenem, meropenem and colistin, respectively. The overall prevalence of MBL was 37.2%. Both MIC₅₀ and MIC₉₀ of amikacin, cefotaxime, ceftazidime, cefepime and piperacillin-tazobactam were each 256 ug/ml, while MIC₅₀ and MIC₉₀ of imipenem, meropenem, tigecycline and colistin were 1.5 and 32, 3 and 32, 0.38 and 3, 1 and 3, respectively. Interestingly, only 36% of MBL-positive strains were from infected patients, with the highest rate (48.3%) from Mubarak hospital followed by 44.9% from Al-Jahra hospital.

Conclusions:

Multi-resistant Acinetobacter spp is highly prevalent in our hospitals and has reached an alarming level which justifies continuous surveillance and stringent infection control measures to control its spread,

Key Words: Acinetabacter spp; Multi-resistant; MBL prevalence

Funding Agency: Kuwait University YM01/08

Amino Acid Substitutions within YMDD Motif of the Hepatitis B Virus Polymerase Gene Associated with Resistance to Lamivudine Therapy and Deterioration of Liver Histology

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Introduction:

Substantial inhibition of HBV replication can be achieved by lamivudine (LAM) therapy in patients with chronic HBV (CHB) in the short-term. However; prolonged LAM therapy induces the emergence of drug-resistant strains leading to relapses of hepatitis. LAM-resistance is characterized by amino acid substitutions in the methionine residue of the conserved catalytic YMDD motif of the HBV polymerase (Pol) gene. The aim of this study was to identify these substitutions associated with resistance to LAM and to determine their subsequent clinical deterioration in HBV-infected patients in Kuwait.

Methods:

Eighty sera samples were collected; 40 samples from therapy-naïve asymptomatic (ASC) carriers and 40 LAM-treated CHB infected patients. Catalytic domains B and C of the HBV Pol gene were amplified and sequenced. Amino acid substitutions within and upstream the YMDD motif were identified. Virological and biochemical breakthrough associated with worsening liver histology were also recorded.

Results:

YMDD mutants were detected in 15% of CHB patients during prolonged LAM-therapy and in 7.5% therapy-naïve ASC carriers. Among which, 78% patients were observed with virological and biochemical breakthrough accompanied with ongoing necroinflammatory disease. Six genotypic patterns were identified: 3 commonly recognized as LAM-resistance associated mutations (rtL180M + YVDD, rtL180M + YIDD, YIDD); while the other 3 were rare polymerase mutations (rtL180M + YLDD, YLDD, YMDN).

Conclusions:

YMDD mutants were detected in therapy-naïve ASC carriers indicating their role as naturally-occurring HBV mutants. Of interest, new YMDD mutant (YLDD+rtL180M) was identified conferred resistance to LAM in vivo and caused virological and biochemical breakthrough.

Key Words: LAM-resistance; YMDD mutants; Virological and biochemical breakthrough
Funding Agency: Research Administration project grant YM 02/03, Kuwait University.

Comparison of Performance of Two DNA Line Probe Assays for Rapid Detection of Multidrug-Resistant Isolates of Mycobacterium Tuberculosis

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Introduction:

Infections with multidrug-resistant (resistant at least to rifampin, RIF and isoniazid, INH) strains of Mycobacterium tuberculosis (MDR-TB) are associated with high case fatality rate. Resistance of M. tuberculosis strains to RIF is a surrogate marker for MDR-TB. Rapid identification of MDR-TB strains is crucial for institution of appropriate therapy and to arrest further transmission. This study evaluated the performance of two simple DNA line probe assays, GenoType MTBDR (GT-MTBDR) and INNO-LiPA Rif. TB (INNO-LiPA) for the detection of resistance to RIF and INH in clinical M. tuberculosis isolates.

Methods:

Fifty MDR-TB and 30 pansusceptible M. tuberculosis strains isolated in Kuwait and Dubai and characterized by phenotypic drug susceptibility testing (DST) were analyzed. Mutations in hot-spot region of rpoB and/or katG codon 315 (katG315) were detected by GT-MTBDR and INNO-LiPA tests. Results were compared to those obtained by conventional DST, DNA sequencing and/or PCR-restriction fragment length polymorphism (RFLP) analysis of regions of interest of M. tuberculosis genome. Strain relatedness was determined by double-repetitive-element PCR and by polymorphism at katG463 and gyrA95.

Results:

Compared to phenotypic DST and katG315 PCR-RFLP results, GT-MTBDR test results were concordant for INH resistance for 63 of 80 (78.7%) isolates. For RIF resistance, GT-MTBDR and INNO-LiPA test results were concordant with DST for 74 of 80 (92.5%) and 76 of 80 (95%) strains, respectively. Results of GT-MTBDR correlated with sequencing results for 77 of 80 (96.2%) and with INNO-LiPA results for 79 of 80 (98.7%) isolates. Majority of MDR-TB isolates in Kuwait and Dubai were genotypically distinct strains.

Conclusions:

Both, the GT-MTBDR and INNO-LiPA tests are useful for rapid detection of MDR-TB strains, however, GT-MTBDR assay offers the advantage of detecting the resistance of M. tuberculosis isolates to both INH and RIF simultaneously when MDR-TB is suspected.

Key Words: Mycobacterium tuberculosis; GenoType MTBDR assay; Multidrug resistance

Funding Agency: College of Graduate Studies and grant YM03/06, Kuwait University

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Expression and Secretion of Mitogillin in *Aspergillus Fumigatus* Culture Filtrate Detected by Anti-mitogillin Antibodies Raised against Purified Recombinant Protein

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Introduction:

Mitogillin (MIT), a low molecular weight secretory protein of *Aspergillus fumigatus* is found in urine of patients with invasive aspergillosis (IA). The availability of MIT and anti-MIT antibodies may help in non-invasive early diagnosis of IA. The aim of this study was to generate anti-MIT antibodies against recombinant pure MIT protein and to study the expression and secretion of MIT in cultures of *A. fumigatus* grown under various conditions.

Methods:

The pure MIT protein was obtained by affinity chromatography and specific cleavage of fusion partner from recombinantly expressed MIT fusion protein in *Escherichia coli* and its identity was confirmed by sequencing. Anti-MIT antibodies were raised in rabbits and were used for studying the expression and secretion of MIT protein in culture filtrate of *A. fumigatus* under various growth conditions.

Results:

The pure MIT protein was nearly homogeneous (>99% pure) and was verified by its N-terminal amino acid sequence. Pure MIT protein reacted with anti-MIT antibodies from immunized rabbit sera while no reactivity was detected with serum samples obtained from rabbits before immunization. The MIT protein was not detected in culture filtrates upto 36 hours of growth and thereafter its concentration increased progressively.

Conclusions:

Specific anti-MIT antibodies were raised in rabbits that reacted with pure MIT protein in Western blots. The in vitro grown *A. fumigatus* exhibited delayed expression and secretion of MIT protein in the culture medium. The MIT protein may also be expressed during in vivo growth and elicit an immune response in patients with IA. The availability of pure antigen and specific anti-MIT antibody probes should be useful for the non-invasive diagnosis of IA.

Key Words: Aspergillus fumigatus; Mitogillin; Culture filtrate detection

Funding Agency: College of Graduate Studies and KURA grant YM 07/07

Prevalence of Azole Resistance among *Candida Glabrata* Isolates in Kuwait

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Introduction:

Candida glabrata has emerged as an important yeast pathogen because of its propensity to develop acquired resistance to azoles. The minimum inhibitory concentrations (MICs) of triazoles tend to be higher for *C. glabrata* than *C. albicans*. In Kuwait, although *C. glabrata* is associated with about 5% bloodstream infections, only scant information is available on its resistance to azoles. Here, we present fluconazole and voriconazole susceptibility data on *C. glabrata* isolates recovered over a three-year period from various clinical specimens.

Methods:

All the *C. glabrata* isolates were identified by microscopic morphology, and development of characteristic pinkish colonies on CHROMagar *Candida*, and/or by Vitek2 profile. The in vitro susceptibility to fluconazole and voriconazole was determined by the Etest on RPMI 1640 agar medium supplemented with 2% glucose. The plates were incubated at 35°C and readings were taken at 24 h. The isolates were considered susceptible, susceptible dose-dependent and resistant with MIC values of <8, 16-32, and >64 µg/ml for fluconazole and <1, 2, and >4 µg/ml for voriconazole, respectively.

Results:

Of 256 *C. glabrata* tested with fluconazole, 145 (57%) were susceptible, 41 (16%) susceptible dose-dependent, and 24 (9.3%) resistant. In contrast, of 199 isolates tested with voriconazole, 180 (90%) were susceptible, 5 (2.5%) susceptible dose-dependent and 14 (7%) resistant. The MIC₉₀s and MIC ranges for fluconazole and voriconazole were 48 µg/ml and 0.012 - >256 µg/ml, and 1 µg/ml and 0.006 - >32 µg/ml, respectively. Of 24 isolates resistant to fluconazole, 15 (63%) were also resistant to voriconazole suggesting occurrence of cross-resistance between the two drugs.

Conclusions:

The in vitro antifungal susceptibility data suggest that about 9% and 7% *C. glabrata* isolates were resistant to fluconazole and voriconazole, respectively, and 63% of the isolates resistant to fluconazole were also resistant to voriconazole.

Key Words: Candida glabrata; Azole resistance; Fluconazole and Voriconazole

Funding Agency: None

Pattern of Resistance and Serotype Distribution among Group B Streptococcus in Kuwait

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Introduction:

Penicillin is the first line agent used in the treatment and prevention of Streptococcus agalactiae (group B β -hemolytic streptococci; GBS) infections. The long-term impact of widespread use of intrapartum penicillin prophylaxis on the serotype distribution of GBS has not been explored. In the mean time, resistance to second-line antimicrobials, clindamycin and erythromycin, is increasing worldwide. The objective of study was to assess the serotype distribution and the differences in susceptibility profiles of invasive, non-invasive and colonizing GBS isolates obtained from patients in our hospitals in Kuwait.

Methods:

A total of 534 GBS isolates obtained from patients in various Kuwait hospitals were studied. They were 59 invasive isolates from blood and CSF, 378 non-invasive isolates from urine and wound swabs, and 97 colonizing isolates from the vagina and neonatal body swabs. Antibiotic susceptibility of the isolates was performed by determining the minimum inhibitory concentrations (MICs) of penicillin, erythromycin, clindamycin, tetracycline and gentamicin using the Etest method. The isolates were serotyped by latex agglutination technique.

Results:

Of the 59 invasive isolates, 24 (40.7%) belonged to serotype III which was the most common serotype in this group while 160 (42.3%) of the non-invasive isolates and 36 (37.3%) of colonizing isolates were of serotype V. Serotypes VI, VII and VIII were present only in the non-invasive and colonizing sets. Penicillin was the most active of all the antibiotics tested. All isolates were sensitive to penicillin although the invasive strains were killed at lower penicillin MIC than the others. High MIC ($>0.064\mu\text{g/ml}$) of penicillin occurred in 11 and 35.4% of the 2004 and 2007 and serotype VIII, NT and Ia isolates were less sensitive than other serotypes. Overall resistance rates to erythromycin, clindamycin, tetracycline, and gentamicin were 11.8%, 8.7%, 93.6% and 100%, respectively.

Conclusions:

GBS remains susceptible to penicillin over time, although the MIC of penicillin is increasing. Resistance to viable alternative drugs, erythromycin and clindamycin, is at unacceptably high levels. These observations call for continuous monitoring to identify potentially resistant isolates.

Key Words: GBS; Antibiotic resistance; Serotype distribution

Funding Agency: None

Genotypic Heterogeneity within Candida Orthopsilosis Strains Identified among Clinical Candida Parapsilosis-Complex Isolates in Kuwait

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Introduction:

Candida parapsilosis has now emerged as the second most common *Candida* species associated with invasive candidiasis. Recent molecular studies have shown that phenotypically identified *C. parapsilosis* isolates represent a complex of three species, namely, *C. parapsilosis*, *C. orthopsilosis* and *C. metapsilosis*. The aim of this study was to determine genotypic heterogeneity among 81 *C. parapsilosis* and five *C. orthopsilosis* strains identified by conventional and molecular methods.

Methods:

The species-specific identification of strains of *C. parapsilosis* and *C. orthopsilosis* was carried out by PCR amplification of internally transcribed spacer (ITS) region of rDNA using species-specific primers. The genotypic heterogeneity among *C. parapsilosis* and *C. orthopsilosis* strains was determined by PCR amplification of intergenic region sequences between 28S rRNA gene and 5S rRNA gene (IGS1), followed by digestion of amplicons with frequently cutting restriction enzymes to generate RFLPs and DNA sequencing of ITS region of rDNA.

Results:

All the 81 *C. parapsilosis* and five *C. orthopsilosis* strains were accurately identified by species-specific amplification of ITS region of rDNA. Two distinct genotypes among five *C. orthopsilosis* strains were identified based on DNA sequences of ITS region and PCR-RFLP of IGS1 region. Genotype I included all three strains isolated from blood while genotype II included the two strains isolated from other body sites. Only two genotypes were apparent among 81 *C. parapsilosis* strains.

Conclusions:

The association of one of the two distinct genotypes of *C. orthopsilosis* strains with candidemia cases is noteworthy. The presence of only two genotypes among 81 *C. parapsilosis* strains points towards limited genotypic heterogeneity among strains of this recently evolved species.

Key Words: Candida parapsilosis; Candida orthopsilosis; Genotypic heterogeneity
Funding Agency: College of Graduate studies and KURA grant YM04/06

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Prevalence and Characterization of High-Level Kanamycin Resistant- Group B Streptococcus from Patients In A Kuwait Hospital

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Introduction:

To determine the prevalence of, and characterize, high- level kanamycin-resistant (Group B Streptococcus) GBS isolated at the Maternity hospital, Kuwait using antibiogram, serotyping, pulse-field gel electrophoresis (PFGE) and DNA sequencing.

Methods:

In total, 154 GBS isolates were collected between July-September 2007 from mothers (149 isolates) and neonates (5 isolates). GBS serotypes were determined using latex agglutination test. High-level resistance to kanamycin was detected by the disk diffusion method with disks containing 200microg kanamycin. MIC was determined by agar dilution. PCR was used to investigate the presence of Kanamycin resistance genes (aph3 and ant4). PFGE was used to determine strains relatedness. DNA sequencing of the kanamycin-resistance gene was performed using the BigDye terminator method.

Results:

A total of 115 (74.7%) of the 154 isolates expressed high-level kanamycin resistance (≥ 1000 $\mu\text{g/ml}$). They were also resistant to erythromycin (12.2%), clindamycin (7.8%) and tetracycline (88.7%). PCR revealed the presence of a 299 kb amplified product corresponding to presence of aph3 in all 115 isolates. DNA sequencing of the aph3 gene product revealed a 99% similarity to aph3 present in genomic DNA of Enterococcus faecium and on a plasmid in Staphylococcus epidermidis. PFGE revealed 12 patterns with 40.8%, 12.2%, 11.3% and 10.4% of them belonging to PFGE patterns 1, 8, 2, 3 and 4 respectively. They belonged to eight serotypes with serotype V (40.8%) and serotype III (20.0%) dominating.

Conclusions:

The demonstration of aph3- mediated high-level kanamycin resistance in GBS isolates of different serotypes and genetic backgrounds, and its high degree of similarity to aph3 found in E. faecium, and S. epidermidis suggest interspecies acquisition of the aph3 from other Gram positive cocci.

Key Words: Group B Streptococcus; High-level kanamycin resistance
Funding Agency: Supported by Kuwait University Research Administration

Response to Antiviral Therapy Predicts the Development of Glucose Abnormalities in Patients with Chronic Hepatitis C Genotype 4 Infection

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Introduction:

An association of chronic hepatitis C virus (HCV) infection with high occurrence of type 2 diabetes has been reported in Kuwait and other countries. However, HCV genotype 4 has been underrepresented in all previous studies. Our aim was to investigate whether or not high viral load and non-sustained virological response to antiviral therapy were associated with increased incidence of glucose abnormalities in patients with chronic hepatitis C genotype 4 infection.

Methods:

The study population consisted of 220 patients with HCV genotype 4 infection. Patients completing antiviral therapy were followed-up, and the fasting plasma glucose levels were determined in patients with and without sustained virological response to antiviral therapy. HCV RNA concentrations in serum were determined using the COBAS AMPLICOR HCV Monitor v2.0 test. Sustained virological response to antiviral therapy was defined as undetectable viral load 6 months after completion of therapy. The association of the response to antiviral therapy with the development of glucose abnormalities was assessed by Kaplan-Meier survival analysis and the two-sided log-rank test.

Results:

The prevalence of HCV-patients with glucose abnormalities was 41%. There was no significant association of glucose abnormalities with HCV viral load ($p=0.36$). After achievement of sustained virological response, a decrease of the median fasting plasma glucose value was observed in our patients with chronic hepatitis C ($p<0.001$). In the group of HCV-patients with normal fasting plasma glucose levels, an association of non-sustained virological response with the development of impaired fasting glucose was observed ($p<0.001$).

Conclusions:

Our results suggest that clearance of hepatitis C virus may improve glucose metabolism in chronic HCV genotype 4 infection.

Key Words: Hepatitis C; Diabetes; Glucose abnormalities

Funding Agency: KFAS Grant No.2006-1302-03

Use of Molecular Methods for Identification of Atypical Brucella Isolates from Humans

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Introduction:

Brucellosis, a zoonotic disease, can cause serious disease in humans. It is endemic in Arabian Gulf region with most cases seen during spring & summer months. Using limited biochemical reactions a rapid identification of Brucella isolates is possible leading to prompt & appropriate chemotherapy. We compared the ability of traditional & molecular methods to accurately identify atypical Brucella isolates.

Methods:

During a period of 5 months, May to October 2008, 5 Brucella strains were isolated from blood cultures of equal number of patients. Using traditional methods 2 isolates were identified by colonial morphology, staining and positive oxidase & urease reactions. Since 3 of the strains were urease-negative after 24 h, automated (Vitek 2 & Phoenix) & molecular methods (PCR & DNA sequencing) were applied to confirm their identification. PCR was performed using genus - and species - specific primers. Genomic DNA was isolated from culture grown organisms using standard techniques. The genus Brucella - and species B. melitensis (Bm)-specific targets were amplified in a LightCycler equipment and the PCR products were analyzed by melting curve analysis & confirmed by agarose gel electrophoresis. For DNA sequencing, the isolates were identified using the Microseq500 16S ribosomal DNA (rDNA) based bacterial identification system. Chromosomal DNA isolation using Easy PrepmanTM Ultra sample preparation reagents, PCR amplification and DNA sequencing using Big dye terminator kit on 3130 xL genetic Analyser(Applied Biosystems) were performed according to protocols provided by the manufacturer. In vitro antimicrobial activities of rifampicin, tetracycline, ciprofloxacin, amikacin, gentamicin & tigecycline were determined by E test on chocolate agar.

Results:

All 5 strains appeared gram-negative cocco-bacilli on Gram stain & were oxidase-positive. However, 3 of the isolates were urease-negative after 24 h. Only one strain was identified as Bm by Vitek 2 & None by Phoenix. Four of them were identified as Bm by PCR & DNA sequencing. All strains presented antimicrobial susceptibility pattern compatible with Bm.

Conclusions:

When automated biochemical tests fail to identify unusual strains of Bm, molecular methods can be used to confirm their identification.

Key Words: Brucella; Identification; Molecular methods

Funding Agency: None

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The Expression of mRNA and Proteins of *Mycobacterium Tuberculosis* RD-Encoded Proteins PE35, PPE68, ESXA, ESXB and ESXV in *M. Tuberculosis*, *M. bovis* BCG, *M. avium* and *M. vaccae*

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Introduction:

We have previously shown that *Mycobacterium tuberculosis* RD-encoded proteins PE35, PPE68, ESXA, ESXB, and ESXV are Th1 cell antigens in healthy subjects. To determine if these reactivities were due to infection with *M. tuberculosis*, vaccination with *M. bovis* BCG or exposure to environmental mycobacterial, we studied the expression of above proteins in *M. tuberculosis*, *M. bovis* BCG, and environmental mycobacterial species of *M. avium* and *M. vaccae*.

Methods:

The expression of the above rd genes at mRNA level was determined using mycobacterial RNA in reverse transcriptase-polymerase chain reaction (RT-PCR). The expression of proteins was studied by Western immunoblotting of mycobacterial sonicates with antibodies raised in rabbits against pure recombinant proteins. The natural expression of each protein in various compartments of *M. tuberculosis* was determined by Western immunoblotting using cell walls, culture filtrates and sonicates of *M. tuberculosis*. The breadth of antibody-reactivity was determined using synthetic peptides and anti-protein rabbit-anti sera in ELISA.

Results:

The results of RT-PCR and Western immunoblotting showed that mRNA and proteins of PE35, PPE68, ESXA, ESXB and ESXV were expressed in *M. tuberculosis*, ESXV was expressed in *M. bovis* BCG, and None of them were expressed in *M. avium* and *M. vaccae*. Furthermore, analysis of cell walls, culture filtrates and sonicates of *M. tuberculosis* by Western immunoblotting showed that PE35, PPE68, ESXA, ESXB and ESXV proteins were present in various sub-cellular fractions of *M. tuberculosis*. Analysis of humoral responses with synthetic peptides suggested induction of broad responses to each protein in immunized rabbits.

Conclusions:

The RD proteins PE35, PPE68, ESXA, ESXB and ESXV are expressed in *M. tuberculosis* and None of them are expressed in other mycobacteria studied, except ESXV in *M. bovis* BCG. Thus, the positive Th1 cell responses in healthy humans are primarily due to infection with *M. tuberculosis*.

Key Words: Expression; mRNA, proteins; Mycobacterium Tuberculosis

Funding Agency: Supported by the College of Graduate Studies Grant No. YM01/03

Extra-hepatic Cystic Hydatid Disease: A Diagnostic Dilemma

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Introduction:

Cystic hydatid disease (CHD), a zoonosis due to the metacestode of the canine tapeworm *Echinococcus granulosus*, is endemic in sheep-rearing areas of the Middle East, including Kuwait. CHD of the liver is well documented but as man is an aberrant host, a variable proportion of the cysts develop extra-hepatically giving rise to non-specific symptoms, resulting in delayed or misdiagnosis. The magnitude of the problem and the consequent difficulties in diagnosis has yet to be defined and may be an underestimate, even in Kuwait.

Methods:

We first present 4 patients with extra-hepatic CHD. We then analysed the requests for diagnosis for CHD over a 2-year period and determined hepatic from extra-hepatic cyst patients. Diagnosis was by serology, presence of scolices and hooklets from cyst fluid and/or histopathology of sectioned cysts.

Results:

We describe extra-hepatic cysts in the lung in a Saudi female; in the posterior triangle of the neck in a female Kuwaiti and in the breast in another; in the brain and heart in a Syrian male and in the pelvis in a Bangladeshi male to show the variety of unusual presentations and discuss the difficulties in laboratory diagnosis. Of a total of 1201 patient requests, CHD was diagnosed in 198 (16.5%); 155 (78.3%) had cysts in the liver but in 39(19.7%) they were extra-hepatic. In 4 patients (2%), cysts were both in the liver and extra-hepatic too. The number of patients with extra-hepatic cysts will vary in each endemic zone depending on the phenotypic and genotypic variability of the parasite. Indeed our data may not reflect the true magnitude of the problem as a whole body scan was not performed either on those with hepatic or extra-hepatic cysts.

Conclusions:

Such data are essential for the attending physician to make an informed judgment and to differentiate CHD from masses like tumors, congenital, simple and other cystic lesions which we encountered from this geographic locale.

Key Words: Cystic hydatid disease; Extra-hepatic; Diagnosis
Funding Agency: Kuwait University Grant No. MI 113

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**Evaluation of PorA, the Major Outer Membrane Protein (MOMP) of
Campylobacter Jejuni, as a Potential Vaccine Candidate against
C. Jejuni Infection**

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Introduction:

Campylobacter jejuni is a leading cause of gastroenteritis. It encodes a 45kDa major outer membrane protein known as PorA, which may mediate in vivo adhesion of *C. jejuni* to the mucosal surface of the gut. Therefore, immunization with PorA may confer protection against the infection. The aim of this study was to evaluate a recombinant PorA fusion protein, (GST-PorA) for protective efficacy against challenge by a homologous strain, *C. jejuni* C31, in an adult mouse intestinal model.

Methods:

A recombinant plasmid, pGSTP7RIL expressed PorA gene from *C. jejuni* C31 as a fusion protein with glutathione S transferase (GST). The GST-PorA fusion protein was solubilised in urea and purified by GST purification module. The purified fusion protein was used for immunization in adult (6-8 weeks) BALB/c mice. Mice were orally immunized with two doses of 50 micro. gm. GST-PorA together with a mucosal adjuvant (5 µ.gm. LT R192G), given a week apart. Control mice received 0.5 ml PBS in a similar fashion. Three weeks after immunization, the mice were orally challenged with 1×10^9 *C. jejuni* C31 in 0.5 ml volume. Faecal shedding of the bacterium was monitored over a period of nine days by culturing faeces. Passive hemagglutination was done to identify the O antigen (Penner serotype) of *C. jejuni* C31.

Results:

Passive hemagglutination revealed that *C. jejuni* C31 has a Penner serotype of 6, 7. Purification of GST-PorA showed a 78kDa band in SDS PAGE and in Western blotting when probed with anti-GST Ab. The CFU/mg bacteria in faeces was found to be much lower in immunized mice as compared to the control mice.

Conclusions:

Our results showed that PorA induced protection against colonization of *Campylobacter jejuni* in the mice intestinal tract, suggesting that PorA may be an effective target for vaccine development against the pathogen.

Key Words: Campylobacter jejuni; Major outer membrane protein; PorA

Funding Agency: Kuwait University Grant No.YM 06/07

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Minor Contribution of Mutations at EmbC-embA Intergenic Region and iniA Codon 501 in Ethambutol-resistant Clinical *Mycobacterium Tuberculosis* Isolates in Kuwait

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Introduction:

Resistance to ethambutol (EMB), a first-line anti-tubercular drug, in *Mycobacterium tuberculosis* strains is mediated by mutations in genes involved in arabinan synthesis notably three emb (arabinosyl transferase) and iniA (isoniazid-inducible) genes. Most epidemiologically unrelated EMB-resistant *M. tuberculosis* strains contain mutations at embB codons 306, 406 and 497, embC-embA intergenic region (IGR) and iniA codon 501 (iniA501). This study aimed to develop a more comprehensive screen for EMB-resistance detection among epidemiologically unrelated EMB-resistant *M. tuberculosis* strains previously analyzed for embB codon 306, 406 and 497 mutations by including analysis of mutations at iniA501 and in embC-embA IGR.

Methods:

Fifty EMB-resistant and 25 pansusceptible *M. tuberculosis* strains isolated from 75 TB patients in Kuwait and characterized by phenotypic drug susceptibility testing were analyzed. Mutations at iniA501 were detected by Hpy 99 I-generated restriction fragment length polymorphism (RFLP) patterns of PCR amplified fragments. Direct DNA sequencing was used to confirm RFLP results and for detecting mutations in embC-embA IGR.

Results:

Nearly same number of *M. tuberculosis* strains were resistant to EMB alone and EMB together with additional resistance to rifampicin and isoniazid (9 of 50, 18% and 11 of 50, 22%, respectively). All the 25 pansusceptible strains contained wild-type sequences at iniA501 and in embC-embA IGR. The analysis of 50 EMB-resistant *M. tuberculosis* isolates showed that only one strain contained a mutated iniA501 while a mutation was not detected in any isolate in embC-embA IGR.

Conclusions:

Analysis of iniA501 and embC-embA IGR in epidemiologically unrelated EMB-resistant *M. tuberculosis* isolates in Kuwait indicate that mutations at these locations occur infrequently and their inclusion for the development of a comprehensive molecular screen will make only minor contribution towards rapid EMB resistance detection.

Key Words: Mycobacterium tuberculosis; Ethambutol resistance; Molecular detection
Funding Agency: College of Graduate Studies and grant MI 06/02, Kuwait University

Antimicrobial Resistance among Clinical Isolates of *Streptococcus Pneumoniae* in Kuwait, 1997-2007: Implications for Empirical Therapy

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Introduction:

Increasing antibiotic resistance of *Streptococcus pneumoniae* (pneumococci) raises concern about therapeutic options available for common and life threatening infections. Monitoring of drug resistance of local isolates of *S. pneumoniae* is important, since most pneumococcal infections are treated on an empirical basis. This study was conducted to evaluate resistance trends in *S. pneumoniae* isolated at a tertiary hospital in Kuwait and its implications for empiric therapy.

Methods:

Antimicrobial susceptibility of 1353 strains of *S. pneumoniae* isolated from clinical specimens during 1997-2007 was performed by disk diffusion method. Minimum inhibitory concentration (MIC) was determined by E test. The results were compared for 1997-2001, 2002-2005 and 2006-2007.

Results:

The prevalence of resistance for the respective periods were as follows: Penicillin 51.3%, 61.3% and 54.5%; erythromycin 31.2%, 36.7% and 37.7%; tetracycline 30.8%, 45.3% and 41.3%; co-trimoxazole 49.5%, 58.5% and 62.8%; clindamycin 20.4%, 20.6% and 24.5% and chloramphenicol 8.1%, 8.9% and 3.7%. All isolates were susceptible to vancomycin and rifampicin. The MIC results for penicillin-resistant isolates showed increasing rates of fully resistant isolates (by meningeal breakpoints) for penicillin 0.06%, 5.7% and 28.7%, cefotaxime 0%, 5.3% and 16.5%, and ceftriaxone 0%, 1.8% and 7%. For meropenem, resistance increased from 1.7% intermediate resistant (I) to 22.4% I and 0.8% resistant. Multiple drug resistance increased from 22.4% to 37.8%.

Conclusions:

Antimicrobial resistance of *S. pneumoniae* is increasing in Kuwait. The MIC studies indicate that the effect of the present level of beta-lactam resistance affects mainly the therapy of pneumococcal meningitis and not that of non meningeal infections such as pneumonia, encouraging the continued use of these agents. Resistance to erythromycin is high and therapy of pneumonia with a macrolide alone may result in failure in many cases.

Key Words: Streptococcus pneumoniae; Antibiotic resistance; E test

Funding Agency: None

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Bacteriology of Meningitis: A Three Year Study at RNMLC, YIACO Adan

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Introduction:

Meningitis is broadly grouped into purulent and aseptic meningitis. While aseptic meningitis is generally viral and self limiting, purulent meningitis has a bacterial etiology with an exudative inflammation. Specific bacterial diagnosis and prompt treatment is vital in reducing morbidity and mortality. Neonates have the highest prevalence probably largely due to immature immune system. Meningitis due to multi- drug resistant bacteria particularly extended spectrum beta-lactamase (ESBL) producers presents a serious challenge in the management. A three year study from clinically suspected cases of meningitis from Adan Hospital is presented here.

Methods:

Standard culture media and procedures were used for culture of CSF. Isolates were subjected to gram smear, catalase and oxidase tests. While most of isolates were processed using MicroScan panels (NUC35, NBPC34 and PC21), others were subjected to conventional methods of identification and susceptibility tests. Wellcogen kit was used for bacterial antigen detection. ESBL strains were confirmed in MicroScan or by E-test AB BIODISK.

Results:

A total of 42 non-repetitive isolates (41 bacterial and 1 yeast) included 9 Coagulase negative Staph, 8 *K. pneumoniae*, 7 *S. pneumoniae*, 3 *P. aeruginosa*, 2 each of *N. meningitidis*, *S. aureus*, *S. marcescens* and *S. viridans* and 1 each of *H. influenzae*, *S. agalactiae*, *A. bauman/haem*, *E. coli*, *S. faecalis*, *C. meningosepticum* and *C. albicans*. Antigen detection was informative in some but with false positivity in others. One third (33.33%) infections were found in neonates, with nearly half (47.62%) in children under one year. ESBL strains (7 *K. pneumoniae* and 1 *E. coli*) were isolated from about one fifth (19.05%) of patients.

Conclusions:

Etiological agents responsible for meningitis should be periodically reviewed in a given health care setting to serve as guide lines for institution of antimicrobial therapy. Detection of ESBL strains is crucial in the management of meningitis.

Key Words: Meningitis; CSF; ESBL

Funding Agency: None

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Salmonellosis and Shigellosis: Experience at RNMLC, YIACO Adan

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Introduction:

Salmonella and shigella are major agents in the bacterial etiology of diarrhoea. These infections occur either as sporadic cases or in endemic/epidemic forms. Such infections are usually food and water borne and are more common in developing countries. While shigellosis is invariably a non-invasive disease, some salmonella species are invasive as well and produce septicemia. The salmonellae may be isolated not only from stool but also from other specimens including blood and urine. We present a three year study at Yiaco, Adan.

Methods:

Standard culture media and procedures were used for processing specimens. Blood culture was done in BacT/ALERT and BACTEC. The bacterial identification and susceptibility testing was done using MicroScan panels (NUC35 and NBPC34). Serotyping was done using Mast Assure antisera. Isolates were sent for reconfirmation to Public Health lab.

Results:

Out of the 179 patients, 154 (86.03%) were positive for salmonella and 25 (13.97%) for shigella. Repeat isolates were excluded from the study. Whereas, out of confirmed salmonella serotypes, group B, D, C, E, G and A were 35.71%, 30.00%, 21.43%, 5.71%, 4.29% and 2.86% respectively, the confirmed shigella serotypes were Sh. sonnei (66.67%), Sh. flexneri (26.67%) and Sh. boydii (6.67%). Most of salmonella and shigella isolates were from stool. While thirty salmonellae were isolated from blood and three from urine culture, shigella was isolated from blood of only one fatal case. Eight (six salmonella & two shigella) strains were multi drug resistant (MDR) of which two salmonella and one shigella were resistant to ciprofloxacin.

Conclusions:

Salmonellosis was found to be more common than Shigellosis in this environment. Although very few MDR strains were encountered in the present study but the bugs at the door certainly sound an alarm.

Key Words: Salmonellosis; Shigellosis; diarrhea

Funding Agency: None

Trends in the Susceptibility Pattern of *E-coli* and *Klebseilla pneumoniae* Isolated From Neonates in the Maternity Hospital, Kuwait.

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Introduction:

Antimicrobial resistance substantially affects the morbidity and mortality of infected patients and the early and accurate recognition of resistant bacteria significantly aids in the optimal management of patients. The goal of this study was to detect resistance so as to provide a valuable data that can be used to optimize therapy. Additionally, to provide data to track resistance trends among clinically relevant bacteria.

Methods:

Four hundred thirty isolates of E-coli and 471 isolates of K. pneumoniae isolated from different samples in the neonates during the period of 2003-2007 were evaluated for antimicrobial susceptibility pattern. MIC for antibiotics like cefotaxime, ceftazidime, amikacin, tazocin and meropenam was tested by using E-test.

Results:

MIC was interpreted according to CLSI guidelines. Among the strains of E-coli and K. pneumoniae more than 50% of the isolates were susceptible to cefotaxime. 144 (35.5%) isolates of E-coli and 136 (30.22%) isolates of K. pneumoniae had MIC of 0.094-0.125 for ceftazidime respectively. MIC of amikacin for 221(56.2%) of E-coli and 166 (35.7%) of K. pneumoniae was in the range of (1.5-2). 17 (4.07%) of E-coli and 53 (11.37%) of K. pneumoniae were having MIC of 24-64 for tazocin and were intermediately resistant. 3(0.7%) isolates of E-coli were highly resistant to tazocin as compared to 14 (3%) K. pneumoniae isolates. 36 (7.74%) isolates of K. pneumoniae were intermediately resistant to amikacin having an MIC of 24-32.5 (1.13%) isolates of K. pneumoniae and one isolate of E-coli were resistant to meropenam.

Conclusions:

E. coli and K. pneumonia isolated from neonates are highly resistant to third generation cephalosporins. Rise in the MIC of tazocin is worrying since it is the drug of first choice for treating health-care associated infections in neonates and limited number of antibiotics is available to treat such infections. Continuous surveillance and infection control measures are mandated to watch the resistance.

Key Words: Multi-resistance; Gram negative; Neonatal infections

Funding Agency: None

Antifungal Activity of Toothpastes against Candida Species Isolated from Clinical Specimens

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Introduction:

Candida species which forms part of the normal flora of oral cavity are the main etiologic species associated with Candida colonization and subsequent infection. Although many types of toothpaste have been formulated with the aim of either preventing or reducing plaque, gingival inflammation or dental caries, only scant information is available on their antifungal activities. In this study, we report anti-candidal activity of nine different brands of toothpastes available in Kuwait.

Methods:

The antifungal activity was determined by agar diffusion test. The common ingredients incorporated in the toothpastes included sodium lauryl sulfate, sodium monofluorophosphate, triclosan, and strontium chloride hexahydrate. The herbal toothpastes contained miswak extract. Uniform quantities of toothpaste were filled in 6 mm diameter wells punched into Sabouraud dextrose agar medium (60 ml/plate) already inoculated with 0.5 McFarland suspension of the test isolate. One hundred thirty-four isolates representing *C. albicans* (n = 65), *C. tropicalis* (n = 37), *C. dubliniensis* (n = 21), and *C. glabrata* (n = 11) were tested. The plates were incubated at 35°C and read after 24 h for inhibition zone diameters.

Results:

All the nine toothpastes showed varying inhibitory activity against Candida species. The mean inhibition zone diameters of different toothpastes varied between 12.4 to 23.5 mm for *C. albicans*, 11.4 to 19.5 mm for *C. tropicalis*, 11.8 to 27.1 mm for *C. dubliniensis*, and 10.0 to 20.5 mm for *C. glabrata*. The herbal toothpaste preparation was found to be the most active against all four Candida species tested.

Conclusions:

This study reports variable anti-candidal activity of nine different brands of toothpaste preparations available in Kuwait. This information may be used as a guide in prescribing the most therapeutically active toothpaste for patients with oral Candida infection.

Key Words: Candida species; Toothpastes; Antifungal activity

Funding Agency: None

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Distribution of Coagulase Serotypes in Methicillin-Susceptible and Methicillin-Resistant *Staphylococcus aureus* in Kuwaiti hospitals

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Introduction:

Staphylococcus aureus is defined by its production of the coagulase enzyme (Staphylocoagulase). Coagulase serotypes are used as an epidemiological marker to distinguish *S. aureus* strains. Ten coagulase serotypes (serotypes I-X) have been described in *S. aureus*. Reports from the literature indicate that there is a geographical bias in the distribution of coagulase serotypes. The objective of this study was to determine the distribution of coagulase serotypes in clinical isolates of *S. aureus* obtained in Kuwait hospitals.

Methods:

A total of 888 *S. aureus* isolates consisting of 310 methicillin-susceptible (MSSA) and 578 methicillin-resistant (MRSA) isolates were obtained from 11 hospitals between March and October 2005. Coagulase serotyping was performed using the Coagulase typing antisera (Denka-Seiken Co. Ltd, Japan).

Results:

Overall, coagulase serotype IV was the dominant serotype in both MSSA and MRSA isolates. Two serotypes consisting of serotype IV (98.4%) and serotype III (1.6%) were detected in MRSA isolates. Four serotypes were detected in MSSA isolates. This consisted of serotype IV (51.0%), serotype III (48.1%), serotype II (0.3%) and serotype VII (0.3%). The coagulase serotype of one MSSA isolate was not determined.

Conclusions:

The study revealed that two coagulase serotypes, serotypes III and IV are common in Kuwait *S. aureus* isolates with the MRSA predominantly belonging to serotype IV.

Key Words: MRSA; Coagulase serotyping; *S. aureus*

Funding Agency: Kuwait University Grant MI 03/01

Comparative Evaluation of Galactomannan, (1-3)-beta-D-Glucan and Species-Specific DNA in the Diagnosis of Invasive Aspergillosis

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Introduction:

Invasive aspergillosis (IA) is a serious disease of patients with hematological malignancies and is associated with high mortality largely due to delayed diagnosis. Although demonstration of the fungus in infected tissues is the gold standard for definitive diagnosis, the procurement of biopsy material may not be feasible due to extremely poor or thrombocytopenic state of these patients. To overcome these limitations, alternative approaches, such as detection of (1-3)- β -D-glucan (BDG), galactomannan (GM) or DNA in serum or bronchoalveolar lavage specimens have been developed. The proposed study aims to evaluate usefulness of these surrogate markers in the early diagnosis of IA.

Methods:

Serum samples (n=238) from 161 patients suspected of Aspergillus infection were tested. The DNA from serum specimens was extracted by using standard procedure. The presence of GM was detected by ELISA, DNA specific for Aspergillus fumigatus, A. terreus and A. flavus by Nested PCR (nPCR) and BDG by colorimetric assay. The cut-off values for GM and BDG were 0.5 ng/ml and 80 pg/ml; respectively. The sensitivity and specificity were determined using the results obtained from control sera.

Results:

Of the 238 serum samples tested, the positivity for GM, Aspergillus DNA and BDG was 71 (30%), 77 (32%) and 75 (32%) respectively. The A. fumigatus DNA was detected in 70, A. terreus in 6 and A. flavus in one sample. Twenty-five sera samples from 21 patients were positive for all the three markers and of these only five patients yielded Aspergillus spp in culture of respiratory specimens. Additionally, 45 sera samples from 37 patients were positive for two markers, and only two of 37 patients yielded Aspergillus spp. in culture of respiratory specimens.

Conclusions:

The findings suggest that culture of respiratory specimens lacks sensitivity and detection of GM, Aspergillus species-specific DNA and BDG may be useful adjunct to early diagnosis of IA.

Key Words: Invasive aspergillosis; Surrogate markers; Diagnosis

Funding Agency: KFAS grant No.2005-130-205

Real-Time PCR for Detection, Identification and Quantitation of Nine Species of Pathogenic Candida

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Introduction:

Early identification of *Candida* species and quantification of fungal load should improve the outcome of invasive candidiasis as well as guide physicians to rationalize the use of anti-*Candida* agents. In this work, we report PCR assays for sensitive detection, quantification and identification of nine pathogenic *Candida* species.

Methods:

Standard strains (n=8) and clinical isolates(n=31) of nine *Candida* species were obtained from American Type Culture Collection and local patients, respectively. The organisms were cultured in vitro and genomic DNA were isolated using standard procedures. The PCR assays (end-point PCR in a Thermal Cycler and real-time PCR in a LightCycler System) were performed using pan-*Candida* primers. The real-time PCR process was monitored by fluorescent quantification of SYBR Green and melting temperature (T_m) analysis was performed to obtain characteristic melting profiles for each species. The amplicon size was determined by agarose gel electrophoresis and the sequence of amplified DNA was obtained by automated DNA sequencing.

Results:

The detection limit for *Candida* cells by using pan-*Candida* PCR assays ranged from 2 to 200 cells per PCR reaction. The T_m analysis of products obtained with real-time PCR using DNA from standard species of *Candida* showed a specific peak for each species tested, with lowest T_m for *C. haemulonii* (83.12°C) and the highest T_m for *C. krusei* (89.94°C). The sequence analysis of PCR products confirmed their individual identities and the experimental T_m values correlated with the theoretical T_m values calculated from DNA sequence. In addition, T_m values of clinical isolates of various *Candida* species correlated with the T_m values of the respective standard strains.

Conclusions:

Real-time PCR coupled with T_m analysis is a simple and specific method for identification and quantitation of pathogenic *Candida* species.

Key Words: Candida; Real-time PCR; T_m analysis, Species identification

Funding Agency: KFAS Grant No. 2005-130-205

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HLA-DR Binding Analysis and Mapping of Th1-cell Epitope Regions for Identification of Promiscuous Peptides of *Mycobacterium Tuberculosis* Antigen Rv1980c

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Introduction:

Rv1980c is a major antigen of *M. tuberculosis*. The aim of this study was to identify its promiscuous peptides by HLA-DR binding analysis and recognition by T helper 1(Th1)-cells.

Methods:

The sequence of mature Rv1980c protein (205 aa) and 20 synthetic peptides (20-mers overlapping with neighboring peptides by 10 aa) covering the sequence of mature protein were analyzed for HLA-DR binding prediction to 51 HLA-DR alleles by using a prediction program (ProPred). In addition, the synthetic peptides were evaluated for recognition by T-cells in antigen-induced proliferation assays using Rv1980c-reactive T-cell lines established from the peripheral blood mononuclear cells of 12 HLA-DR heterogeneous healthy subjects. Furthermore, T-cell lines from five and three HLA-DR heterogeneous subjects were also tested for peptide-induced IFN-gamma secretion and cytotoxic activity, and one T cell line was investigated for HLA-restriction using anti-HLA antibodies and HLA-DR typed autologous and allogeneic antigen presenting cells (APCs).

Results:

The ProPred analysis predicted the binding of Rv1980c to all (51/51, 100%) HLA-DR alleles. Furthermore, six of its peptides (P3, P7, P9, P17, P18 and P20) were predicted to bind HLA-DR molecules promiscuously, i. e. binding to >10 alleles of >3 HLA-DR specificities. Testing of the peptides with T cell lines showed that Th1-cell epitopes were scattered throughout the protein sequence, and 18 of the 20 peptides yielded positive responses with one or more T-cell lines in one or more of the assays used. The comparison of HLA-DR binding data and recognition in Th1-cell assays showed that four of the six HLA-promiscuous peptides were recognized by >50% donors in Th1-cell assays. Furthermore, both autologous and allogeneic APCs presented a tested peptide to the responding T-cell line.

Conclusions:

The ProPred analysis was useful in predicting the promiscuous HLA-DR binding regions of Rv1980c, which stimulated Th1-cell responses among T-cell lines obtained from HLA-heterogeneous donors.

Key Words: Rv1980c; HLA-DR binding; Th1-cell reactivity

Funding Agency: Kuwait University Research Administration Grant No. MI03/05

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***Mycobacterium Tuberculosis* Genomic Regions of Difference Encode Antigens
with Protective and Pathological Consequences**

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Introduction:

The protective and pathologic immune responses in tuberculosis are mediated by a complex network of pro-inflammatory, T helper (Th)1 and Th2 cytokines. In this work, we have evaluated the secretion of these cytokines by peripheral blood mononuclear cells (PBMCs) from pulmonary tuberculosis patients in response to complex antigens of *M. tuberculosis* and its peptides corresponding to proteins encoded by the regions of difference (RD) genes, which are absent in the vaccine strains of *M. bovis* BCG.

Methods:

A total of 1648 peptides corresponding to 89 proteins predicted in 11 RDs of *M. tuberculosis* were designed and synthesized. PBMCs were isolated from the blood of 17 pulmonary tuberculosis patients and cultured in vitro in the absence and presence of complex mycobacterial antigens (whole cells, culture filtrate and cell walls) and peptide pools of various RDs. On day 6, culture supernatants were collected and assayed for concentrations of pro-inflammatory (TNF- α , IL-6, IL-8 and IL-1 β), protective Th1 (IFN- γ , IL-2, and TNF-beta) and pathologic Th2 (IL-4, IL-5 and IL-10) cytokines using flowcytomix assay.

Results:

PBMCs from the majority of tuberculosis patients (53-100%) spontaneously secreted detectable concentrations of all cytokines, except for IL2 and IL-10. The secretions of proinflammatory cytokines were similar when PBMCs were cultured with various complex mycobacterial antigens and peptide pools of RDs. However, with respect to Th1 and Th2 cytokines, the complex antigens and the RDs could be divided into two major groups; one group with Th1 bias (culture filtrate and RD1, RD5, RD7, RD9 and RD10) and the other group with Th2 bias (whole cells, cell walls, RD12, RD13 and RD15).

Conclusions:

The results suggest that *M. tuberculosis* RDs encode antigens that may play roles in protection and pathogenesis of tuberculosis by differential secretion of Th1 and Th2 cytokines.

Key Words: Tuberculosis; RD peptides; Cytokines

Funding Agency: KFAS Grant No. 2002-1302-04

Enterobacter Bacteremia in a Teaching Hospital in Kuwait -an Analysis of 27 Episodes

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Introduction:

Enterobacter species is emerging as an important nosocomial pathogen causing serious infections like bacteremia. This study was conducted in a teaching hospital in Kuwait during the period 2004 - 2006 to evaluate the antimicrobial susceptibility pattern, therapeutic factors with special reference to third generation cephalosporins and clinical factors associated with bacteremia caused by this organism.

Methods:

Twenty - seven cases of bacteremia caused by Enterobacter species were detected by blood culture (BACTEC). and identified by commercial identification systems (API20E, Vitek 2). Antimicrobial susceptibility was determined by disc diffusion method. Double disc antagonism method was used for the detection of AmpC beta lactamase and disc approximation method and E- test for the detection of extended spectrum beta lactamases (ESBL).

Results:

Enterobacter bacteremia accounted for 2.4% of all bacteremias during this period of study, *E. cloacae* being the leading species (77.8%). Twenty - one episodes (77.8%) were hospital acquired. The most common portal of entry (decided by the site other than blood from which the same organism with similar antimicrobial susceptibility pattern was isolated) was the urinary tract (25.9%). The most common underlying disease detected was renal disease (40.7%). The prevalence of antimicrobial resistance was as follows : piperacillin - tazobactam 8%, cotrimoxazole 5%; all were susceptible to carbapenems, aminoglycosides and ciprofloxacin; resistance to third generation cephalosporins was 30%, 9.5% of these being ESBL producers. AmpC beta lactamase production was observed in 90.5% of the isolates. 88.98% patients responded to therapy with the appropriate antibiotic.

Conclusions:

Nosocomial bacteremia due to Enterobacter species is common in patients with underlying disease. AmpC beta lactamase production is a major factor in deciding therapy with cephalosporins. In serious infections, carbapenems, aminoglycosides and ciprofloxacin may be the antibiotics of choice.

Key Words: Bacteremia; Enterobacter; Nosocomial

Funding Agency: None

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Identification and Characterization of Streptococcus Agalactiae Isolates Using 16S rRNA Sequencing and Cellular Fatty Acid (CFA) Composition Analysis.

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Introduction:

The traditional identification of bacteria on the basis of phenotypic characteristics is generally not accurate as identification based on genotypic methods. Comparison of the bacterial 16S rRNA gene sequence has emerged as a preferred genetic technique. 16S rRNA gene sequence analysis and cellular fatty acid (CFA) composition analysis can better identify poorly described, rarely isolated, or phenotypically aberrant strains

Methods:

This study was undertaken to identify and characterize Streptococcus agalactiae isolates obtained from seven fish samples using 16SrRNA and CFA analysis techniques. All samples were cultured on Brain Heart Infusion agar. All the seven isolates were Gram positive and were identified as Streptococcus spp. 16S rRNA gene sequencing and CFA analysis were used to confirm the species for all isolates.

Results:

16S rRNA sequencing method yielded about 1500 bps for each strain where upon the sequence was compared to 16S data in Gene Bank using BLASTN, NCBI, USA. 16S rRNA Sequence alignment using BLASTN 2. 2.1 from NCBI for the comparison up to 1500 bp of the 16SrRNA gene sequence gave a 99% similarity to plus, plus strand with Streptococcus agalactiae ATCC 13813, ATCC 27956. (accession number AB023574). All strains appeared to be nearly identical to each other after CFA analysis using Library Generation System (LGS) software (MIDI) and were consistent to that of S. agalactiae ATCC 12386 (reference strain used in these studies).

Conclusions:

CFA and DNA based techniques are invaluable in identifying and characterizing bacteria associated with disease spread in human, animal and environment. Despite there accuracy, 16S rRNA gene sequence analysis and CFA analysis lacks widespread use beyond the large and reference laboratories because of technical and cost considerations.

Key Words: Streptococcus agalactiae; 16S rRNA; CFA

Funding Agency: KISR

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Application of a Simple Uniplex Polymerase Chain Reaction Assay for the Detection of Atypical Bacteria in Asthmatic Kuwaiti Patients

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Introduction:

Respiratory infections precipitate wheezing in many asthmatic patients and may be involved in the aetiopathogenesis of asthma. Most recently, studies are invoking atypical bacterial infections, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and *Legionella pneumoniae*, as factors in asthma symptom exacerbation. Objective: The aim of this work was to apply PCR for the fast detection of *M. pneumoniae*, *C. pneumoniae* and *L. pneumophila* in respiratory specimens from asthmatic patients .

Methods:

In our earlier studies, we have established and optimized PCR assays to detect the causative agents of atypical pneumonia in clinical specimens using a Uniplex-PCR. Throat swabs were collected from 43 and 70 chronic and mild asthma patients respectively and 35 controls (non-asthmatic), who have visited Al-Sabah Hospital emergency and medical ward for asthma treatment room asthma treatment. The statistical software SPSS was used for data analysis of significance.

Results:

The target sequence for *M. pneumoniae* was 462 bp DNA from 16s-rRNA gene. The target for *L. pneumophila* was 649 bp DNA segment from the coding region of the gene encoding 24 kDa macrophage infectivity potentiator (mip) protein. The target sequence for *M. pneumoniae* was 152 bp DNA from the cytoadhesin gene. The limit of detection by PCR was about, 1 pg, 2.4 fg and 12 pg DNA respectively. In our study *M. pneumoniae* PCR positivity was significantly higher in the asthmatic (15%) than in the non-asthmatic group (9%) ($p < 0.05$), this marked difference was observed in patients with acute asthma exacerbation (5/43 (12%) vs 6/70 (7%) in acute exacerbation and moderate (stable) asthma, respectively). There was a positive correlation between asthma severity and PCR positivity. The PCR results for *C. pneumoniae* and *L. pneumoniae* were statistically insignificant.

Conclusions:

In summary, the study suggests that infection with *M. pneumoniae* is related with exacerbation of asthma symptoms and could possibly have induced wheezing.

Key Words: Legionella; Mycoplasma; Chlamydia

Funding Agency: None

The Diagnosis of Latent Tuberculosis Infection in Contacts of Smear-Positive Pulmonary TB: The Role of Specific Interferon Gama -Release Assays

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Introduction:

Knowledge of the prevalence of latent Mycobacterium tuberculosis (MTB) infection is crucial for effective Tuberculosis (TB) control. In contacts of smear-positive pulmonary TB cases, tracing is usually done by tuberculin skin testing (TST), chest radiography and clinical signs and symptoms all of which are either nonspecific or difficult to interpret. Objectives: This prospective survey was done to compare the new interferon gamma-release assay, T. Spot TB, (Oxford Immunotech, UK) with the conventional tests and its value in the decision on administration of isoniazid (INH) chemoprophylaxis.

Methods:

All contacts of smear-positive pulmonary TB cases from September till December, 2008 were included in the survey. They were tested by TST T. Spot. TB and chest radiography. Their BCG status together with the administration of INH prophylaxis were recorded.

Results:

Out of 189 contacts, 107(57%) were Kuwaiti nationals and 169(89%) were BCG-vaccinated. TST was above the cut off value (10mm) in 173(92%) of the total. Only 33(17%) of those contacts had abnormal chest X-ray findings. In BCG-vaccinated contacts, 157(83%) showed TST above 10mm while only 75(40%) of them had reactive T. Spot. TB. Almost 50% of the contacts with TST above 10mm had non-reactive T. Spot. TB. Out of 17 contacts with TST readings above 20mm, 8 still had non-reactive T. Spot. TB. In contacts with reactive T. Spot. TB, 64 (34%) had normal chest X-ray while only 24(13%) had abnormal chest X-ray findings. Out of the 173 contacts with TST above 10mm, 65 contacts with reactive T. Spot. TB correctly received INH prophylaxis while 63 contacts with non-reactive T. Spot. TB correctly did not receive INH prophylaxis.

Conclusions:

T. Spot. TB, a type of interferon gamma release assays, shows promising results in the era of latent TB infection.

Key Words: Latent TB; Interferon gamma release assays; Contact tracing

Funding Agency: None

A Comparative Analysis of HLA-DR and -DQ Molecules Expressed in Healthy Subjects and Tuberculosis Patients Living in Kuwait

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Introduction:

Highly polymorphic molecules of Class II human leukocyte antigens (HLA)-DR and -DQ have been linked with susceptibility and resistance to many diseases of both infectious and non-infectious origin. The aim of this study was to identify and compare the expression of HLA-DR and -DQ molecules in healthy subjects and tuberculosis (TB) patients resident in Kuwait.

Methods:

Peripheral blood mononuclear cells (PBMCs) were obtained from healthy subjects (n=228) and TB patients (n=206) of both Arab and non-Arab origin. Genomic DNA was extracted from PBMCs by salting out technique. HLA-DR and -DQ genotypes were identified using polymerase chain reaction with sequence specific primers (PCR-SSP) obtained as a kit from Dynal AS (Oslo, Norway). The HLA-DR and -DQ phenotypes were determined from genotypic alleles using interpretation tables provided by the kit manufacturer. Relative risk (RR) was calculated using standard methods and Chi-square (χ^2) test was used for statistical analysis to determine significant differences ($p < 0.05$) in expression of HLA-DR and -DQ molecules in TB patients and healthy subjects.

Results:

The analysis of results showed that HLA DRB1*02 (RR= 2.11, $p < 0.001$), DRB1*14 (RR=2.43, $p < 0.05$), DRB5 (RR=2.54, $p < 0.001$), DQB1*05 (RR=2.80, $p < 0.001$), and DQB1*09 (RR=11.3, $p < 0.001$) were associated with disease susceptibility, and DRB1*11 (RR=0.35, $p < 0.001$), DRB1*13 (RR=0.47, $p = 0.0017$), DRB1*17 (RR=0.11, $p = 0.011$) and DRB3 (RR=0.60, $p < 0.05$) were associated with protection against TB. Moreover, DRB3 was positively associated with healthy Arabs ($p < 0.001$); and DRB1*02 and DRB5 were negatively associated with the same population ($p < 0.001$).

Conclusions:

Specific HLA-DR and -DQ molecules are associated with protection against and susceptibility to TB in people with Arab and non-Arab origin residing in Kuwait.

Key Words: HLA molecules; Tuberculosis; Susceptibility

Funding Agency: Kuwait University Research Administration Grant MI02/02

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Response of the Splenic Dendritic Cells in Plasmodium Vivax Infection

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Introduction:

Our aim was to control the spread of the infectious diseases in Kuwait and also to find how Plasmodium vivax is cleared from the peripheral blood without treatment.

Methods:

Thick and thin blood films were made from all the immigrants coming from malaria endemic countries and stained with Giemsa and checked for the presence of malaria. All the P. vivax infected individuals were followed for 4 weeks.

Results:

About 200, 000 immigrants were checked for malaria in 2008 and 103 (0.053%) were found positive. All the four species of malaria were detected and their distribution was found as; P. vivax 39.00%; P. falciparum 29.00%; P. ovale 4.00%; P. malariae 1.00% and mixed infection of P. falciparum and P. vivax 27.00%. The density of the parasites was found from 400 – 5, 600 parasites/μl of blood in 40 individuals and after four weeks, all the parasites were cleared from the peripheral blood except in one patient.

Conclusions:

All the infected individuals were free from P. vivax infection except in one patient without treatment after four weeks. All the infected RBCs with P. vivax are accumulated in the spleen which makes it palpable. These parasites are killed by splenic dendritic cells and presented to the immune system to produce the acquired immunity and also to remove the infected RBCs in P. vivax infected patients.

Key Words: Malaria; Acquired immunity; Splenic dendritic cells

Funding Agency: Ministry of Health, Kuwait

Prevalence of Extended-Spectrum B-Lactamase-Producing Enterobacteriaceae and Acinetobacter spp. at a Tertiary Care Hospital in Kuwait: An Update

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Introduction:

Extended-spectrum beta-lactamases (ESBLs) have become global invaders of virtually all hospitals where serious infections are treated. Because of the widespread distribution of these enzymes, the usage of broad-spectrum cephalosporins has become more restricted, and fewer options are available to treat infections caused by Gram-negative pathogens. OBJECTIVES: This retrospective study was done to evaluate the prevalence of ESBL producing Enterobacteriaceae in different samples sent to Ibn Sina Microbiology Laboratory from various centers and departments. The antimicrobial activity of tigecycline and comparator antimicrobial agents against ESBL producing isolates was also evaluated. The MIC50 and MIC90 for tigecycline against various organisms was also evaluated.

Methods:

All Gram-negative organisms isolated from different samples sent to Ibn Sina Microbiology Laboratory from January 2006 to June 2008 were included in the study. Identification and antimicrobial susceptibility testing were performed using Vitek 2. (bioMerieux, France). ESBL detection was done using E-test method (Ab Biodisk). The MIC50, MIC90 and percentage resistance of a proportion of ESBL-producing Enterobacteriaceae and Acinetobacter spp to tigecycline and other antibiotics were calculated.

Results:

Out of a total of 14, 991 clinical specimens (blood, urine, wounds, respiratory secretions and catheter tips) sent to Ibn Sina microbiology laboratory, 4976 were Enterobacteriaceae isolates. 1883 (38%) of Enterobacteriaceae isolates were ESBL producers. Forty and thirty nine percent of the total ESBLs were blood and urine isolates respectively. Out of 2807 E. coli isolates, 1154 (41%) were ESBL producers, while out of 1389 & 564 Klebsiella pneumoniae & Enterobacter species, 460 (33%) & 244 (43%) were ESBL producers respectively. The highest rates of ESBL production was seen in the Organ Transplant Center (44%), Kuwait Cancer Center (38%) and Pediatric Surgery Department (38%). The MIC50 and MIC90 for tigecycline against Escherichia coli was 0.25µg/ml, while for Klebsiella it was 1.5 & 3.0µg/ml respectively.

Conclusions:

Extended-spectrum B-lactamase- producing Enterobacteriaceae and Acinetobacter spp. are becoming endemic in Ibn Sina Hospital and surrounding centers

Key Words: ESBL; Enterobacteriaceae, Acinetobacter; Tertiary care

Funding Agency: None

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**The Association Between Consanguinity and Miscarriage and Other Adverse Pregnancy Outcomes Among Kuwaiti Women:
A Case Control Study**

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Introduction:

The practice of consanguineous marriage has been widely spread in Kuwait (54%) as indicated by previous studies. Several studies showed an association between consanguinity and reproductive morbidity and mortality. Therefore, we decided to study the association between consanguinity and miscarriage. The hypothesis of our study is: The proportion of consanguineous marriages is significantly higher among women who had a miscarriage or other adverse pregnancy outcomes compared with women who did not. The objectives of our study were: 1 to examine the association between consanguinity and miscarriage, and 2 other adverse pregnancy outcome.

Methods:

A case-control study, of 100 cases, defined to be Kuwaiti, less than 50 years old with a history of miscarriage. Each case was age-matched with 2 controls. Data were collected via a face-to-face interview.

Results:

Controls had a significantly higher educational level than cases ($p=0.004$). Similarly, the percentage of those who were ever employed was significantly higher among controls than cases ($p=0.009$). Women who got married at age ≥ 19 were significantly less likely to have had a miscarriage than women who got married at age ≤ 18 . The odds of miscarriage among women who had ≥ 5 pregnancies was 2.2 times higher than among women who had 0-1 pregnancy ($p=0.038$). Women who got married at ages 19-24 years were half as likely to have had a miscarriage compared to whom got married < 19 years ($p=0.014$). Furthermore, a larger percentage of consanguineous women reported a history of congenital abnormalities than non-consanguineous women ($p=0.013$).

Conclusions:

In contrast to the first part of our hypothesis, our study showed there was no association between consanguinity and miscarriage ($p=0.210$). A significantly larger percentage of consanguineous women reported a history of congenital anomalies among their children than non-consanguineous women ($p=0.013$). Thus, the second part of our hypothesis was confirmed.

Key Words: Consanguinity; Miscarriage; Adverse pregnancy outcomes

Funding Agency: None

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The Emerging Significance of the Molecular Mechanisms in the Role of the Epididymis in Male Infertility: Lesson from Rodents.

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Introduction:

Epididymis has an important role in the maturation of spermatozoa but the molecular mechanisms involved are poorly understood. Objective of study: To investigate the effects of Zinc deficiency in the sperm concentration and morphology, and antioxidant status of the rat epididymis.

Methods:

Twenty - four adult Sprague-Drew rats were randomized into three groups of 8 each with following diet plan; (a) Zinc only (b) 1mg of EDTA (Zn chelator) daily and (c) Control, and fed for 6 weeks. Thereafter the rats were sacrificed and serum level determined by Atomic Absorption flame spectrophotometer. After clapping the head and tail ends of the epididymis, it was dissected out and flushed with 5 ml of RPMI medium into a container. Sperm analysis was immediately carried out. The remaining portion was centrifuged at 850 g for 5 minutes and the supernatant was cryo-preserved at -80,°C until assayed for T helper cytokines, Bcl-2 proteins and C3 by ELISA and MDA and antioxidants by colorimetric methods. The residue was used for sperm chromatin structure assay with acridine orange and fluorescent microscopy and Electron microscopy for sperm apoptosis and diameter of the epididymis.

Results:

Serum zinc concentration was significantly reduced thus having zinc deficiency in EDTA treated rats compared to zinc supplemented and control groups ($p < 0.01$). Zinc deficiency was associated with reduced sperm concentration and sperm morphology, Bcl-2, total antioxidant capacity but increased Bax and C3 levels, sperm apoptosis and sperm DNA fragmentation. There were no significant differences in the end-point parameters between zinc-supplemented group and the control group.

Conclusions:

Zinc deficiency adversely affects the function of the epididymis and lead to infertility. Molecular mechanisms involved include oxidative stress, sperm apoptosis and sperm DNA fragmentation. The sperm abnormalities are reversed by antioxidants.

Key Words: Antioxidant; Oxidative stress; DNA fragmentation

Funding Agency: None

Vitamin C Level is not Altered in Women with Recurrent Spontaneous Miscarriage

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Introduction:

Recurrent spontaneous miscarriage (RSM) remains a very demanding and stressful condition for the patients and the treating physicians. RSM has a multifactorial aetiology although in 50-60% of the cases, the cause remains idiopathic and continues to call for intensive research. Oxidative stress induced endothelial damage and the subsequent abnormal placentation have been associated with recurrent spontaneous miscarriage. Whereas some studies have demonstrated elevated antioxidant levels in normal pregnancy others have reported decreased antioxidant activity in recurrent miscarriage. The objective of this study was to estimate the level of vitamin C, an anti-oxidant, in normal pregnancy and in RSM.

Methods:

The patients presenting with RSM and normal pregnancy at Maternity Hospital, Kuwait, from Feb 2008 – Jan 2009 were counseled and those who consented were recruited for the study. The standard investigations for RSM in our RSM clinic were performed on the patients with RSM. 5 ml of blood was extracted from the patients with normal pregnancy and RSM in the departmental lab, Department of Ob/Gyn, Faculty of Medicine, Kuwait University and the blood was processed. Vitamin C (Ascorbic Acid) level was estimated using M. V. Visible Spectrophotometer at a wavelength of 520nm.

Results:

This is a preliminary report of an on-going study. A total of 16 patients were studied: six patients with normal pregnancy and 10 patients with RSM. One patient with RSM had Antiphospholipid Syndrome and the others were unexplained RSM. There was no significant difference in the mean age and parity of the patients and the mean Vitamin C level in the normal pregnancy group was significantly higher than for the group with RSM, $3.193 \pm 0.974 \text{ mg/100ml}$ vs 2.215 ± 0.571 , $P=0.023$. The mean number of miscarriage in RSM patients was 4.0 ± 1.408 .

Conclusions:

The vitamin C level in the women with RSM was not altered and remained in the normal range.

Key Words: Pregnancy; Miscarriage; Vitamin C

Funding Agency: None

The Role of Natural Killer Cells in Recurrent Spontaneous Miscarriage

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Introduction:

Recurrent spontaneous miscarriage (RSM) remains a significant diagnostic problem for the treating clinician. In 50-60% of the patients, the cause of the miscarriage remains unexplained. It has been postulated that peripheral Natural Killer[NK] cells are dysregulated in unexplained RSM and this has formed the basis of a variety of modalities for therapy including the use of intravenous immunoglobulin[IVIG]. The objective of our study was to investigate the role of peripheral NK cells in unexplained RSM.

Methods:

The patients identified with unexplained RSM in our RSM clinic at Maternity Hospital, Kuwait, formed our study population. The patients were counseled and those who consented were recruited for the study. The study was carried out from Jan-Dec 2008. 5ml of blood was extracted from the patients in EDTA bottle at the departmental lab, Department of OB/GYN, Faculty of Medicine and taken to the special laboratory in the Faculty of Allied Health for appropriate processing and analyzed within 4-6 hours. Monoclonal antibodies specific for human T lymphocytes [CD3+] and subpopulations were used which included CD3+ CD16+ CD56+ (T cells with NK markers) within CD3+ compartment. Lymphocyte subpopulations were analyzed using Flow Cytometric Analysis.

Results:

This is a initial report of an on-going study. Fourteen patients were studied during the above period. The mean age of the patients was 34.07±3.689, mean parity 1.21±1.578 and mean abortions, 4.143±1.099. The mean CD3 population was 72.007±9.489, Mean NK 8.781±6.792 and CD3NK 4.338±4.333. Only 3 (33.3%) of the patients had elevated NK and CD3NK levels: one of the 3 patients was treated with IVIG and her pregnancy ended in a full term delivery while the other 2 patients had repeat first trimester miscarriages.

Conclusions:

There was no significant alteration in the level of NK cells in RSM and it did not play any role in the current pilot study.

Key Words: Natural Killer Cells; Recurrent; Miscarriage

Funding Agency: None

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Maternal-Fetal Transport of Arachidonic Acid in vitro in Insulin Dependent Diabetic Pregnancies

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Introduction:

Paucity of data relating to transport of essential fatty acids in human Type 1 diabetic pregnancies prompted us to undertake this study. Transport kinetics of a model essential fatty acid, arachidonic acid has been investigated in Type I diabetic pregnancies in vitro, using perfusion of isolated placental lobules.

Methods:

Human placentae were collected post-partum from control and diabetic women at term and suitable lobules perfused using National Culture and Tissue Collection medium diluted with Earle's buffered salt solution as the perfusate. ¹⁴C-labelled arachidonic along with tritiated water as reference were injected as a 100ul bolus into the maternal circulation and serial perfusate samples collected over 5-minute study period. Concentration of arachidonic acid and tritiated water in various samples was assessed using dual channel scintillation counting (LKW Wallac Scintillation Counter, Denmark)

Results:

In 8 successful perfusions, differential transport rate of arachidonic acid for 10, 25, 50, 75 and 90% of efflux in the fetal vein averaged 1.09, 1.12, 1.16, 1.20 and 1.17 times respectively that of reference marker in the diabetic group. In the control group (n=8), fatty acid transport indices for the corresponding efflux periods averaged 1.13, 1.15, 1.18, 1.17 and 1.16 times respectively that of the reference marker. Student's 't' test showed that the difference between the two groups was not statistically significant (p>0.05) for all the efflux fractions studied. In the diabetic series, arachidonic acid transport fraction (TF) averaged 36.2 ± 3.5% of corresponding water TF while in control group, the fatty acid TF averaged 42.6 ± 2.8% of water TF. Student's t-test showed the difference between the two series as statistically significant (p<0.05). Kinetic parameters such as area under the curve, clearance, elimination constant, time for maximum response, absorption rate, and elimination rate in the diabetic and control groups, showed varying differences.

Conclusions:

Our studies seem to indicate that transport kinetics of arachidonic acid, an essential fatty acid in vitro conditions, is altered significantly in placentae of Type 1 diabetic pregnancies

Key Words: Arachidonic Acid; Placental Transport; Diabetic Pregnancies
Funding Agency: Kuwait University Res Grant#MOO32

New Insight into the Pathogenesis of Uterine Fibroids and Management

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Introduction:

Uterine fibroid is a common growth affecting 25 to 30% women of the reproductive age group. It is a common indication for surgery especially total hysterectomy and consequent early menopause. Objective of study: To evaluate the pathogenesis of uterine fibroid through the role of Bcl-2 and factors that affect treatment options.

Methods:

One hundred and twenty-five women with uterine fibroids were evaluated over five year period (February, 2004 and January 2009). After surgery a cube 2x2x2 cm was obtained and divided into 2 portions. A portion was homogenized in 10 ml of RPMI and after centrifugation at 1200g, the supernatant was cryopreserved at -80, aC until assayed for Bcl-2, bax and C3 and T helper cytokines by ELISA. The remaining block was prepared and used for Immunohistochemical staining. Management options and outcome were documented in the outpatient clinic, ward post-operatively before discharge and follow-up clinic.

Results:

Increased expression of T helper 2 cytokine IL-4 and Bcl-2 in large fibroid and younger women compared to pre and peri-menopausal women and reduced expression of Bax, C3 and TNF- α by both ELISA and IHC staining ($p < 0.01$). About 20% were associated with pregnancy and in about 45 percent the women had completed their family size, showing that uterine fibroid may not directly affect fertility unless the fibroid growth caused tubal blockage or submucous with cyclical menorrhagia. Conservative management was successful in pre and perimenopausal women

Conclusions:

With better understanding of the pathogenesis of uterine fibroid, management of uterine fibroid should be individualized.

Key Words: Uterine fibroids; Bcl-2; Treatment options

Funding Agency: None

Immunological Basis of Leukocytospermia: Decreased Ability to Fight the Invader.

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Introduction:

Leukocytospermia is a common cause of male infertility in which there are more than 106 WBC/ml of semen, with an incidence of 20-40% in infertile men, through a significant decrease in sperm motility, increased sperm DNA damage and male infertility. The main objective: To investigate the role of regulatory T cells (Tregs), T helper cytokines, oxidative stress, antisperm antibodies and sperm DNA fragmentation in Leukocytospermia.

Methods:

Thirty - five men with Leukocytospermia and 20 men with normal sperm parameters were evaluated. Semen analysis was carried out according to WHO guidelines. Using 96 wells, seminal plasma was incubated with ConA overnight and expression of T helper cytokines estimated by sandwich ELISA. Surface antigen CD4 and CD25 were labelled with fluorescence-conjugated antibodies. CD4+CD25+ T reg cells were analysed by colour flow cytometry. Antisperm antibodies, Oxidant and antioxidant levels were assayed in the seminal supernatant and residue containing sperm for evaluation of Sperm Chromatin Structural Assay and Apoptosis with electron microscopy.

Results:

Leukocytospermia was associated with lower sperm concentration and motility ($p < 0.01$), but higher antisperm antibodies, MDA, TNF- α , IFN- γ and lower TAC ($p < 0.05$), compared to controls. Although CD3+ was higher with Leukocytospermia ($p < 0.05$), CD4+CD25+, IL-4 and IL-10 and TAC were higher in controls ($p < 0.05$) but DFI and Sperm apoptosis were lower ($p < 0.01$).

Conclusions:

Reduced immunological tolerance, low antioxidant capacity, T helper 2 cytokines and Treg lymphocytes may be involved in the pathogenesis of Leukocytospermia.

Key Words: Leukocytospermia; Sperm antibodies; Treg lymphocytes

Funding Agency: Research Administration, Kuwait University; MO 031

Impacts of Multiple Pregnancy in Non Indicated Induction of Ovulation

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Introduction:

The most common form of multiple pregnancies in humans is twins, however, cases of higher orders up to octuplets (8 babies) have been recorded with all siblings being born alive. Most of these pregnancies are the result of fertility medications and assisted reproductive technology (ART). The aim of this study is to evaluate costs of multiple pregnancies in non indicated induction of ovulation cases and risks associated with it.

Methods:

This was a retrospective analysis of medical records of 38 patients with multiple pregnancies who were admitted to Jahra hospital from October 2007 to March 2008.

Results:

Average age in this study was 28. 1 years, parity (p0-p8), marriage duration was 7 months -19 years, last pregnancy interval was 5 months-6 years. There was 1 quadriplete, 3 triplet & 34 twins, conception methods 4 unknown, 12 spontaneously & 22 were induced (all in private), 3 had valid indication while 19 did not. The total birth number was 82, 3 abortions, 79 alive 58 of them admitted to Neonate Intensive Care Unit (NICU). The average gestational age was 32. 25 weeks, complications included 1 case Pregnancy Induced Hypertension (PIH), 5 with Intra Uterine Growth Retardation (IUGR), 5 with Anti Partum Haemorrhage (APH), 3 with discordant growth, 3 with Premature Prelabour Rupture Of Membrane (PPROM), 2 with intrahepatic cholestas, 8 with Preterm labour (PTL). The average mother hospitalization period was 8.06 days, total cost of in-patient care 30880 KD (excluding surgery). Also the average NICU duration 2.9 days. With cost of 236790 KD, mean birth weight was 1.5 kg. Additionally, there were psychological, social, health, medicolegal, &developmental costs.

Conclusions:

Our data shows that there is an increase cost of mother& new born care due to unnecessary induction of ovulation. We recommend that concerned KUWAIT authority formulate law for assisted reproduction treatment, so best evidence based care can be provided to community.

Key Words: Multiple Pregnancy; Induction of Ovulation; Reproduction

Funding Agency: None

Hyperfractionated Irradiation with Concurrent Chemotherapy for Locally Advanced Head and Neck Cancer

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Introduction:

Radiotherapy is often the primary treatment for advanced head and neck cancer, but the rates of locoregional recurrence are high and survival is poor. The advantage of hyperfractionated radiation therapy has been reported. Furthermore, randomized trials and meta-analyses have confirmed the survival benefit of additional chemotherapy. We have investigated whether hyperfractionated irradiation plus concurrent chemotherapy is superior to results of conventional concomitant chemoradiotherapy reported in the literature

Methods:

From September 2003 to September 2008, 50 patients with advanced head and neck cancer were assigned to receive the protocol. All patients were treated with hyperfractionated irradiation 120 cGy twice daily, for a total of 6990 cGy, And continuous infusion fluorouracil 750mg/m² D1- D4 with cisplatin 75 mg/m² D1. Chemotherapy was repeated every 3 weeks for a total of three courses.

Results:

Forty patients(80%) received both radiation and chemotherapy according to the protocol. The median follow up was 2.5years. Two patients died of treatment complications, 30 patients (62%)had acute grade 2-3 mucositis, 3 patients(6%)suffered from grade 3 skin toxicity. Leucopenia was not a major problem (mean nadir 3.4 g/nl, no patient < 1.0 g/nl) and the mean hemoglobin value decreased from 13.2 to 10.5 g/dl. Confluent mucositis was the cause of treatment delay of more than 10 days in only 10% of patients. Grade 3 or 4 systemic toxicity occurred only in(12%)of patients and was the cause of drug dose reduction. The estimated 2 years overall survival rate was 84%. Complete responses were observed in 82% of patients. At a median follow-up of 24 months, 82.5% of patients were free of locoregional disease, 12% had distant failure and 12% died of their disease.

Conclusions:

The protocol was effective in patients with advanced head and neck cancer. Long-term disease control and survival was achieved with significant but acceptable toxicity

Key Words: Head and neck cancers; Hyperfractionated radiotherapy; Concurrent chemotherapy

Funding Agency: Kuwait Foundation For Advancement Of The Sciences (2002-1302-03)

The Role of Quantitative Analysis of Tissue Molecular Markers in Determining the Probability of Prostate Cancer on Repeat Prostate Biopsy in Arab Men

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Introduction:

Genomic and proteomic studies have shown that some molecular tumor markers, such as *N*-methylacyl-coenzyme A racemase (AMACR), enhance zeste homolog 2 (EZH2), HER2/neu and survivin, when overexpressed may assist in identifying patients with prostate cancer. The aim of this study was to determine whether the expression of these 4 molecular markers in prostate gland biopsy can aid in predicting the detection of prostate cancer at re-biopsy in men without prostate cancer at first prostate biopsy.

Methods:

We quantified the gene expression of AMACR, HER2/neu, EZH2 and survivin in prostate tissue biopsies of 98 Arab men with suspected prostate cancer using reverse transcriptase (RT) real-time PCR. Histological diagnosis was categorised into 4 groups: a) benign prostatic hyperplasia (BPH), b) BPH and prostatitis, c) BPH and prostatitis with High Grade Intra Epithelial Neoplasia (HG PIN) and d) prostate cancer. We compared levels of expression of the 4 markers in the 4 groups of patients.

Results:

Histological diagnosis was a) in 21 (21.4%), b) in 47 (48%), c) in 3 (3.1) and d) in 27 (27.6%) patients respectively. RT real-time PCR measurements of mRNA levels showed inconsistent levels of expression of survivin and Her2/neu in the 4 groups of patients respectively. The mean \pm SD of the relative expression of EZH2 was, in group a) 1.59 ± 0.85 , b) 3.30 ± 3.23 , c) 10.26 ± 13.58 and d) 12.91 ± 28.44 (p: a or b versus c or d < 0.001 , c versus d = NS). The mean \pm SD of the relative expression of AMACR was, in group a) 1.01 ± 1.30 , b) 1.57 ± 2.18 , c) 4.07 ± 3.37 and d) 6.87 ± 10.57 (p: a or b versus c or d < 0.001 , c versus d = NS).

Conclusions:

These data indicate that in patients with suspected prostate cancer, but a negative initial biopsy, those with higher levels of expression of EZH2 or AMACR are more likely to benefit from more rigorous prostate re-biopsy.

Key Words: Gene expression; Prostate cancer; Prostate biopsy

Funding Agency: This project was supported by Kuwait University Research Grant MS 01/05

Loss of Estrogen Receptor in Human Breast Cancer Cells is Associated with a Gradual Epithelial to Mesenchymal Transition

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Introduction:

Loss of functional estrogen receptor (ER) is central to development of endocrine resistant breast cancer. Subsequent therapeutic intervention would benefit from increased understanding of associated molecular events participating in continued proliferation. Global gene expression was analysed in breast cancer cell lines that either over-express ER (MCF7), are de novo ER negative (MDA231) or in which ER is constitutively (pII) or inducibly (E2) down-regulated by siRNA, to identify transcriptional response to ER blockade.

Methods:

Labeled cRNA transcribed from cDNA synthesised from extracted cellular RNA was hybridised to replicate low and high density gene microarrays to compare phenotypic profiles of these cell lines; chemiluminescence/fluorescence signals were quantified with appropriate software packages. Selected differentially expressed genes were analysed by realtime quantitative PCR.

Results:

Low density array scanning highlighted several genes that discriminated MCF7 from MDA231 and pII; confirmed and extended in the high density scans. pII cells exhibited elevated transcripts encoding proteins with motility functions, most crucially metastasis, such as urokinase plasminogen activator. Reduced ER expression was associated with loss of epithelial markers such as keratin 18/19 and increased appearance of transcripts of genes typically found in cells of mesenchymal origin; vimentin, fibronectin, cadherin 1, vascular endothelial growth factor and CD68. Differential expression of these genes was confirmed by PCR analysis. Tetracyclin-induced transient ER down-regulation in E2 cells failed to elicit the changes apparent in pII cells.

Conclusions:

Our observations suggest that a change from an epithelial to a more invasive fibroblastic phenotype may be concurrent with gradual adaptation to loss of the functional capacity of the ER transcriptional pathway, leading to a chemo-resistant estrogen independent cancer.

Key Words: Breast cancer; Gene expression; Gene microarrays

Funding Agency: Research Administration, Kuwait University; PC02/04, GM01/05, GM01/01

Radio-Immunotherapy for Lymphoma, Friend or Foe?

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Introduction:

Zevalin is a murine monoclonal antibody (Ibritumomab) conjugated to tiuxetan that chelates yttrium or indium and is directed against CD 20 molecules of B lymphocytes. Zevalin is FDA approved for treatment of low grade lymphomas that have failed prior therapy. Emerging trials show promising results in indolent as well as aggressive lymphomas, in both aggressive and relapsed settings.

Methods:

We treated 20 lymphoma patients from April 2005 until June 2008 with radio-immunotherapy (zevalin). 14 cases were indolent and 6 cases were aggressive lymphomas. 3 patients received zevalin as part of first line chemotherapy and the remaining 17, in relapsed setting. During administration the patients were closely monitored for infusion related complications. Serial complete blood counts were done on follow up. All patients were reevaluated after 3 months by CT scan and gallium scan. They were periodically reviewed in the clinic to look for long term complications.

Results:

Twelve patients achieved complete remission (60%) and 5 achieved partial remission(25%), constituting an ORR of 85%. 3 patients developed long standing myelosuppression (lasted more than 2 months) out of which 1 patient died due to related complications. 3 patients (15%) developed secondary myeloid leukemia and expired.

Conclusions:

Although zevalin produced high response rate in lymphomas, high incidence of fatal complications, especially secondary leukemias is worrisome and warrants long term follow up.

Key Words: Zevalin; Lymphoma; Response complications

Funding Agency: None

Adrenocortical Tumors in Childhood: a 10-year Analysis from Kuwait Cancer Control Centre

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Introduction:

Adrenocortical tumors in children are extremely rare, accounting only for 0.3-0.4% of all neoplasms in this age. In children, they commonly secrete hormones, resulting in virilization in females, and precocious puberty in males, with cushinoid features in both sexes. Because of rarity of this tumor, world-wide, very few cases have been reported from any single institute. Kuwait Cancer Control Centre in Kuwait is the only comprehensive cancer hospital in Kuwait. Between 40 – 50 new cases of pediatric solid tumors including lymphomas are seen every year. In last 10 years, we registered 5 cases of adrenal cortical carcinoma. We report the outcome of treatment of these 5 children.

Methods:

This is a retrospective analysis of all the cases registered with diagnosis of adrenocortical tumor.

Results:

There were 2 males and 3 females, with median age of 5.5 years (range 15 months – 12 years). Virilization was seen in all the patients. One child had hypertension at presentation. Two children had metastasis (liver / lung) at presentation. Three children underwent surgery and achieved complete remission, while 2 children were not fit for surgery. None of the child received adjuvant therapy after surgery. One child with metastatic disease at presentation was given only one cycle but died soon. Out of 3 children who underwent successful surgery, two relapsed with few months after surgery. One relapsed locally and underwent second surgery, while second child developed distant metastasis. The child who had second surgery also received chemotherapy including mitotane for 6 months. Only one child is surviving after 12 years of her initial surgery.

Conclusions:

ACTs are rare tumors of childhood with poor prognosis. They present with signs of virilization and/or cushinoid features. The long term survival depends upon extent of resection and presence or absence of metastasis. Chemotherapy and radiotherapy have very minimal role in its management.

Key Words: Adrenocortical carcinoma; Virilization; Mitotane

Funding Agency: None

Pathology

Category: Clinical

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Effectiveness of Vault Cytology in Detecting Recurrence of Malignancy after Hysterectomy : HMJCSS Experience.

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Introduction:

Vault cytology is accepted as a part of surveillance protocols for gynecological malignancies. Recent data suggest both widespread use and uncertain evidence of their effectiveness. The aim of this study was to determine the utility of vault smear examination in follow up of women who had undergone hysterectomy for gynecological malignancy.

Methods:

A total of 300 vault smears from 206 patients subjected to cytological evaluation over a period of 1 year (2008) at HMJCSS were reviewed. All the smears were obtained by a gynecologist or a radiation oncologist, fixed in ethanol and stained by Papanicolaou method.

Results:

In the study period 106 patients were Kuwaitis and 100 non Kuwaitis. The age ranged from 30- 80 years (mean 58.8). Carcinoma cervix(98) was the most common cause for hysterectomy followed by carcinoma endometrium (89), Leiomyosarcoma(7), Endometrial stromal sarcoma(7), Malignant mixed mullerian tumour² and ovarian carcinoma (3). Of the 300 vault smears, 31(10.3%) were unsatisfactory for evaluation, 214 (71.3%) benign, 40 (13.3%) showed radiation change, 6 (2%) foreign body reaction, 6 (2%) were atypical and 3 (1%) positive for malignancy. Among the atypical cytology most common cause was cervical carcinoma (50%), followed by carcinoma endometrium (33.3%) and Leiomyosarcoma (16.6%). All the cases reported as positive were of cervical carcinoma.

Conclusions:

Vault cytology though simple causes anxiety, consumes resources and its value is debatable. In our study only 1% of the smears were positive for malignancy . Routine vault cytology has limited role in detection of recurrence.

Key Words: Vault cytology; Recurrence; Gynecological malignancy

Funding Agency: None

Determination of Von Willebrand Factor Cleaving Protease (ADAMTS-13) Antigen and Activity Levels in Patients with Thrombotic Thrombocytopenic Purpura and other Thrombocytopenic Disorders in Kuwait

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Introduction:

Thrombotic thrombocytopenic purpura (TTP) is a life threatening disorder characterized by microangiopathic hemolytic anemia and thrombocytopenia as a result of microvascular platelet clumping. The pathogenesis of TTP is attributed to the presence of unusually large von Willebrand factor (vWF) multimers. While this protein is systematically removed in normal conditions, its continued presence is related to the deficiency of its proteolytic protease ADAMTS-13. Functional deficiency of this protease leads to the accumulation of unusually large vWF multimers in patient plasma. However, it was reported that the abnormalities of this protease are not specific for TTP, as low activity was also reported in other thrombocytopenic disorders. In this study we aim to characterize ADAMTS-13 protease and vWF activity and antigen levels in patients with thrombocytopenic disorders.

Methods:

Forty patients with thrombocytopenic disorders (e. g. TTP, idiopathic thrombocytopenic purpura, leukemia, disseminated intravascular coagulation and sepsis) were recruited for this study. An enzyme linked immunoassay-based test was used to measure ADAMTS-13 and vWF activity and antigen levels in patients and control groups.

Results:

Platelet counts and ADAMTS-13 activity and antigen levels were significantly lower in patients compared to controls ($p < 0.001$), while vWF antigen and collagen binding activity levels were higher in patients compared to controls ($p < 0.001$). TTP patients had the most severe deficiency in ADAMTS-13 activity and antigen levels (<3% and <8% respectively)

Conclusions:

This work is the first to report ADAMTS-13 levels in this part of the world. We present evidence that low levels of ADAMTS-13 are not specific to TTP and can also be found in other thrombocytopenic disorder although severe deficiency may be specific to TTP. Results of this work will improve diagnosis and overall management of patients with thrombocytopenic disorders in Kuwait.

Key Words: Thrombocytopenic Disorders; ADAMTS-13; Von Willebrand factor

Funding Agency: Research Administration, Kuwait University. Grant No (NM05/06)

Pathology

Category: Graduate MSc (Basic Science)

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Adipokines and Adiponectin Gene Single Nucleotide Polymorphisms as Potential Links between Obesity and Cancer

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Introduction:

Obesity is linked to excess risk for many cancers but mechanisms remain vague. We hypothesize that polymorphisms in adiponectin gene (ADIPOQ) in association with other obesity biomarkers cause insulin resistance (IR) which then leads to cancer development. This study on patients with cancer examines associations with obesity, adiponectin levels and single nucleotide polymorphisms (SNPs) in adiponectin gene and other adipokines.

Methods:

Indices of obesity body mass index (BMI), waist circumference (WC) and fasting adipokines (Adiponectin, Leptin, leptin receptor and free Leptin index (FLI)), insulin, IR(Homeostasis Model Assessment [HOMA]) and Sex steroids were measured in 250 breast, prostate and colon cancer patients and 136 age and sex matched controls. ADIPOQ SNPs (SNP276 G>T) were studied using Real Time Polymerase Chain Reaction.

Results:

BMI was associated with breast(OR=2.8, p=0.004), colon cancers(OR=1., p=0.03). diponectin concentration was associated with breast(OR=5.1, p<0.0001) and colon cancers(OR=5.0, p=0.009]. Factors such as Hyperleptinemia (OR=3.0, p<0.0001) and IR (OR=2.2, p=0.007)were significantly associated with cancer. Estradiol (OR=2.5, p=0.005)and testosterone (OR=1.3, p=0.03) were associated with breast cancer. GG genotype of SNP276 G>T was significantly associated with higher levels of adiponectin(OR=1.2, p=0.02), breast(OR=8.6, p=0.04) and colon cancers(OR=12, p=0.03).

Conclusions:

No associations were found between indices of obesity, adiponectin gene SNPs and prostate cancer. Our results demonstrate that SNPs in adiponectin gene may play a role in the pathogenesis obesity related cancers and confirm the association between obesity related factors, breast and colon cancers. We conclude that obesity-associated metabolic changes, dysregulation of adipokines (adiponectin and leptin), hyperinsulinemia and IR as well as altered levels of circulating sex hormones could explain in part the link between obesity and cancer.

Key Words: Adiponectin; Single Nucleotide Polymorphisms; Obesity Related Cancers

Funding Agency: Kuwait University Research Grant YM11/07, KFAS

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Role of Insulin-Like Growth Factor Family in Breast Cancer Development

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Introduction:

Insulin like growth factor 1 (IGF1) is a peptide hormone that stimulates proliferation of several types of cancer cells and inhibits apoptosis. Studies suggested that the majority of breast cancers harbor IGF1 receptors. It is presumed that free bio-available IGF-1 (BIGF1) in the circulation is the moiety responsible for tumor development. On the other hand, levels of Insulin-Like Growth factor Binding Protein-3 (IGFBP3), a major IGF1 binding protein in serum, are inversely associated with breast cancer risk. This study examined the association between IGF1, BIGF1, IGFBP3 and breast cancer.

Methods:

Fasting IGF1 was determined in 141 breast cancer patients and 77 sex and age matched control subjects using the IMMULITE 1000 automated immunoassay system. Body Mass Index (BMI) was used as index of obesity. Differences between mean values were evaluated for statistical significance using Student's t test. Spearman correlations were used to find correlations between variables. Univariate and multivariate regression analysis were performed to find associations between variables. The magnitude of association was measured by Odds ratio and their corresponding 95% confidence interval.

Results:

We found that levels of IGF1 in apparently healthy controls were significantly higher than in breast cancer patients [(211.4±73) ng/mL vs. (164.2±80) ng/mL, p<0.0001]. On the other hand BIGF1 were higher in breast cancer patients compared to healthy control subjects [(79.5±7) vs. (38.9±11.4)]. Levels of total IGF1 correlated negatively with BMI in this case control study (r= -0.2, p<0.0001). Higher levels of BIGF1 were associated significantly with breast cancer [OR=6.4, 95% CI (2.6-15.6), p<0.0001] whereas levels of IGFBP3 associated negatively with breast cancer [OR=0.8, 95%CI (0.8-0.9), p<0.01].

Conclusions:

Our study adds clarity and further support to the previous findings implicating serum BIGF1 and IGFBP3 in breast cancer carcinogenesis. We also conclude that markers of obesity are the most significant determinants of IGF1.

Key Words: IGF-1; IGFBP3; Obesity Related Cancers

Funding Agency: Kuwait University Research Grant YM11/07, KFAS, Grant No.2006-1302-05

HLA Gene Frequency in the Kuwaiti Arab Population and Establishment of a National Registry

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Introduction:

Stem cell transplantation (SCT) plays an important role in the treatment of hematopoietic disorders. The immunologic and genetic relationship between donor and recipient profoundly influences the outcome of SCT. This donor/recipient disparity is mainly coded by Human Leukocyte Antigen (HLA). This is a prospective study using DNA technology to assess the HLA allele frequency among Kuwaiti population.

Methods:

Two hundred healthy unrelated Kuwaiti blood donors were randomly selected. DNA based HLA typing was performed using microsphere based array genotype platform (Luminex 100) with sequence-specific oligonucleotide probes (SSOP) to distinguish HLA-A, -B, -C and HLA-DRB1, and – DQA1, DQB1 alleles. Assignment of HLA typing is based on the reaction pattern compared to patterns associated with published HLA gene sequence for HLA class I and class II.

Results:

A total of 93 HLA-A, 92 HLA-B, 92 HLA-C, 83 HLA DRB1, 99 HLA DQA1 and 96 HLA DQB1 alleles were identified. HLA-A*02, A*2402, A*6801, B*35, B*50, B*51, Cw*04, Cw*06, Cw*07, Cw*15, DRB1*03, DRB1*07, DRB1*11, DRB1*13, DQA1*01, DQA1*02, DQA1*03, DQA1*05, DQB1*02, DQB1*03, DQB1*05, DQB1*06 were found with frequencies higher than 10%. The most common haplotypes frequency are A*02: B*50: Cw*06: DRB1*07: DQA1*02: DQB1*02 (6.8%); A*33: B*14: Cw*08: DRB1*01: DQA1*01: DQB1*05 (25.4%); A*24: B*08: Cw*07: DRB1*03: DQA1*05: DQB1*02 (17%).

Conclusions:

Preliminary data show that allele distribution and haplotype analysis demonstrated that Kuwaiti population share HLA patterns with other Arab populations, while it also retains unique characteristics.

Key Words: Human Leukocyte Antigen; SSOP; Kuwaiti population
Funding Agency: KFAS

Pathology

Category: Clinical

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ABO discrepancy: causes and resolving methods

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Introduction:

A discrepancy exists when the results of red cell tests do not agree with serum tests in patient sample. Red cell and serum test results may be discrepant because of intrinsic problems with red cells or serum, or technical errors.

Methods:

Fifty - six cases with ABO discrepancy were collected from the routine work of the RBC patient immunohematology laboratory in the Kuwait central blood bank during the years 2007, and 2008. The results were analyzed for the causes and the methods used to resolve the discrepancy.

Results:

The most frequent cause of ABO discrepancy in our study was the presence of another antibody in the patient serum (62.5%), which was due to cold antibodies in 16 patients, alloantibody in 11 patients, and anti-A1 antibodies in 8 patients. The second cause was the presence of weak or missing antibody (30.4%), which was due to the age of the patient, the original disease or treatment of the patient. Four patients with discrepancy (7.1%) were due to weak antigen, 2 of them were due to A or B subgroups, and the other 2 were due to previous transfusion with packed RBC group O. A significant number of cases were resolved by incubation in 37oC, 4oC, or indirect antiglobulin test (57.1%). The second important method of resolving the discrepancy is by revising the request of the patient which may contain the cause of discrepancy (19.6%).

Conclusions:

The ABO discrepancy is a known problem in the immunehematology laboratories. When the blood is from a potential recipient, it may be necessary to administer group O red cells of the appropriate Rh type before the investigation has been completed.

Key Words: ABO discrepancy; Pretransfusion testing; RBC alloantibodies

Funding Agency: None

Fine Needle Aspiration (FNA) Cytologic Diagnosis of Kikuchi's Lymphadenitis: A Clinico-pathologic Study of 14 Cases.

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Introduction:

Kikuchi's lymphadenitis (KL) is a benign and self-limiting disease that commonly affects young Asian women and typically involves cervical lymph nodes. A polymorphous lymphoid cell population with abundant karyorrhectic debris and histiocytes, many with crescent nuclei, are characteristic cytologic features of KL. In absence of typical cytologic features, these cases may be confused with nonspecific reactive lymphadenitis (RL) and even, granulomatous lymphadenitis (GL). In this report we highlight the clinicopathologic features of 14 cytologically diagnosed KL cases.

Methods:

During a period of 5 years (2004-2008), 14 cases were diagnosed as Kikuchi's disease which constituted 0.6% of all lymph node FNAs. The clinicopathologic features of these 14 cases were compared with those of 125 cases of non-specific reactive hyperplasia and 165 cases of tuberculous/granulomatous lymphadenitis. The detailed cytologic features of KL cases, based on the count of 400 cells, were also analyzed.

Results:

Twelve (87.7%) of KL were in 3rd and 4th decades, which was higher than those in RL (40.8%, p= 0.0016) and GL (70.3%, p= 0.3554). Male to female ratio was 3:11 in KL as opposed to 61:64 in RL (p= 0.08702) and 64:101 in GL (p=0.2569). The KL patients were overwhelmingly expatriates (Kuwaity to expatriate ratio 1:13), which was significantly higher than the ratio observed in RL (84:41, p = 0.0001). There was predominance of cervical lymphadenopathy in all these three groups. In KL cases, the smears were moderate to highly cellular in 89.3%, and had capillaries in 96.4%. Histiocytes constituted 3 to 36% of all cells. Among histiocytes 62.1% had crescentic nuclei and 45.9% contained cell debris. Two cases subjected to histopathological examination were confirmed as KL.

Conclusions:

The KL cases have typical cytologic features and are distinct from nonspecific reactive hyperplasia in respect of age and sex distribution, and patients' country of origin.

Key Words: Kikuchi's lymphadenitis; Fine needle aspiration cytology; Reactive lymphadenitis

Funding Agency: None

Pathology

Category: Clinical

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Micropapillary Carcinoma of the Thyroid: Cytological Findings in 47 Histologically Documented Cases.

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Introduction:

Thyroid micropapillary carcinoma (MPC) is defined as tumor size equal to or less than 1.0 cm. It has a controversial risk of local or distant metastasis or recurrence. The purpose of this study is to assess the utility of fine needle aspirates (FNA) in detecting MPC and document any diagnostic cytological features.

Methods:

FNA from 47 histologically documented cases of MPC from three hospitals in Kuwait with a prior FNA were reviewed. Three cases were excluded because of insufficient material. Aspirates were categorized as benign cytology, suspicious/positive for papillary carcinoma (PC) and other neoplasms. Cytological findings were correlated with histological diagnosis.

Results:

Preoperative cytological diagnosis of PC was made in 35% of documented MPC cases. Tumor size ranged from 0.2 to 1 cm (mean 0.5 cm). Smears showed follicular cells in sheets and papillary configuration with pale cerebriform nuclei having open chromatin, nuclear grooves and intra nuclear inclusions. Associated rosy colloid, lymphocytic thyroiditis, microcalcification and fire flares was also seen. Site of aspiration was an important factor - in 12 of 15 cases of MPC the FNA was from the same side as that documented histologically. MPC was detected in right lobe (7 cases), left lobe (4 cases), and both lobes (1 case). MPC was multifocal in 4 cases. Of the 44 cases, the cytological diagnosis was benign (23 cases, 15.5%), hurthle cell neoplasm (4 cases, 9%), Hashimoto's thyroiditis (2 cases, 4.5%) and suspicious/positive for PC (15 cases, 35%). The sensitivity of cytological examination was 34.1%.

Conclusions:

Cytology is potentially useful but has limited sensitivity in the diagnosis of MPC. Finding tumor in aspirated material is purely accidental and when detected the thyroidectomy specimen had to be extensively sampled to find the tumor.

Key Words: Micropapillary carcinoma thyroid; Fine needle aspirates; Cytology

Funding Agency: None

Pathology

Category: Clinical

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Evaluation of ER alpha and ER beta with Progesterone Receptors and other Prognostic Markers in Fine Needle Aspirates from Breast Carcinoma

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Introduction:

Estrogen receptor (ER) alpha has been extensively studied as a prognostic and predictive marker in breast carcinoma. ER beta has a potential role to play in the progression of breast carcinoma and the development of antiestrogen resistance. The significance of progesterone (PGR) expression in breast cancers is less recognised. The aim of this study was to evaluate the expression of PGR in fine needle aspirates (FNA) from breast carcinoma and to analyse the impact of ER alpha and ER beta expression in FNA with other prognostic parameters namely cytologic grading, CerbB-2, Ki-67 and DNA ploidy.

Methods:

ER alpha, ER beta, PGR, CerbB-2, Ki-67 were studied by immunocytochemical methods in FNA from 38 cases of breast carcinoma. Their expressions were correlated along with cytologic grading and DNA ploidy.

Results:

ER alpha, ER beta, PGR, CerbB-2, Ki-67 were expressed in 47%, 45%, 68%, 64% and 11% of the cases respectively. Nine of 14 (64%) cases of breast carcinoma studied were diploid and 36% were aneuploid. Two-third of cytologic grade 3 tumors did not express ER alpha and ER beta. No statistical significant correlation was observed between the expression of Ki-67 and DNA ploidy with ER alpha and ER beta. However, 86 percent of ER beta positive tumors were positive for CerbB-2 in contrast to only 65 percent of ER alpha positive tumors ($p < 0.05$).

Conclusions:

Demonstration of PGR is feasible by immunocytochemistry but its role as a prognostic marker is debatable. Our data indicates that ER beta positive tumors are associated with more aggressive tumors. Further investigations are necessary to better assess this.

Key Words: Estrogen receptors alpha and beta; CerbB-2, Ki-67, PGR, FNA; Breast carcinoma

Funding Agency: Kuwait University Research Grant MG01/04.

Determinants of Microalbuminuria in Patients with Sickle Cell Disease

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Introduction:

Renal complications are common in patients with sickle cell disease (SCD). Microalbuminuria (MA) has been used as an early marker of nephropathy and prognostic indicator in several diseases. The aim of this study was to evaluate usefulness of screening for MA in patients with SCD.

Methods:

Forty - eight (21 male and 27 female) patients with SCD aged 13-63 years in steady status were studied. Medical records were reviewed for vasoocclusive crisis, blood transfusions, acute chest syndrome and hydroxyurea intake. Complete blood count and serum samples for glucose, lipids, urea, creatinine and albumin were performed. Early morning urine samples were collected for measurement of microalbumin (ratio of urinary albumin to urinary creatinine). Patients were categorized as normoalbuminuric (NA, ratio <30 mg/g); microalbuminuric (MIA, ratio 30-300 mg/g) and macroalbuminuric (MAA, ratio >300 mg/g). Demographic and clinical variables were compared between these categories by univariate and multivariate analyses.

Results:

In our cases 36/48 (75.0%) were NA, while 9/48 (18.8%) were MIA and 3/48 (6.2%) were MAA. Kruskal-Wallis ANOVA showed that age, weight, WBC, K+, calcium, albumin and bilirubin were significantly affected by the degree of MA. On binary logistic regression analyses, age (OR= 1.096, 95%CI= 1.019-1.179), and weight (OR=1.074, 95%CI= 1.006-1.146) were the main determinants of MA, while SCD severity parameters were not significantly associated with MA.

Conclusions:

MA is strongly and directly related to age and weight but not to disease severity. Identification of these risk factors for MA allows earlier intervention to prevent renal complications in patients with SCD.

Key Words: Sickle cell disease; Microalbuminuria; Renal impairment

Funding Agency: None

Drinking Green Tea after Fasting Induces Cellular Proliferation and the Expression of TGF-b in the Intestinal Mucosa of rat.

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Introduction:

Previous studies from our laboratory have shown that drinking green tea prior to fasting prevents the fasting induced intestinal mucosal damage in rats. This beneficial effect of green tea was linked to the expression of specific growth factors in the intestinal mucosa. Therefore, focus of this study is the effect of green tea on cellular proliferation and the expression of growth factors such as FGF, IGF, TGF-b in the intestinal mucosa of rats following 3 days of fasting as compared the animals that were given only water.

Methods:

Adult male Wister rats were used (n=12 per group) in this study. The animals were divided into four groups as follows:

- G1 : Normal controls.
- G2 : Animals on rat chow diet and water ad libitum were fasting for 3 days (only i. p. 10% glucose 40 ml/day).
- G3 : Same as G2 but on day 4 the animals were given water for another 7 days.
- G4 : Same as G3 but on day 4 the animals were given green tea solution for another 7 days.

At the end of the experiment, the animals were euthanized and 2 inches of jejunum was removed for immunohistochemical analysis of markers of cell proliferation (PCNA, Ki-67) and growth factors such as FGF, IGF, TGF-b

Results:

Compared to G3 group, the intestinal mucosa of G4 rats showed a significant increase ($p < 0.001$) in the expression PCNA and Ki-67. There was a significant increase in the expression of TGF-b ($p = 0.0001$) in G4 animals as compared to the G3 control. However, there was no increase in the expression of FGF or IGF.

Conclusions:

Green tea repairs the fasting induced damage in the intestinal mucosa of rats by inducing factors of cellular proliferation which in turn is regulated by the expression of the anti-mitotic factor TGF-b that restricts cell growth, differentiation and cell death.

Key Words: Green tea; Fasting; Intestinal mucosa

Funding Agency: Kuwait University Grant MS01/03.

Pathology

Category: Clinical

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**Unravelling the Diagnostic Challenges Of Polycystic Ovary Syndrome (PCOS):
Should We Do More And Can We Do Better?**

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Introduction:

Despite the recognition of a major role for metabolic disorders in the pathogenesis of PCOS, no metabolic feature is included in the definition. This study explores the hypothesis that PCOS is a predominantly metabolic disorder and evaluates use of metabolic indicators for diagnosis.

Methods:

We measured LH, FSH, estradiol, androstenedione, DHEA-S, testosterone, SHBG, free androgen index (FAI), lipid profile, adiponectin, leptin, leptin receptor, glucose, insulin and insulin resistance (HOMA-R and QUICKI) in subjects with PCOS (n= 92) and controls (n = 44). We used uni- and multi-variate regression analyses to find the associations between variables and PCOS; used ROC analysis to determine the diagnostic performance of biochemical parameters.

Results:

Insulin resistant (22.8%), overweight/obese (82.6%) and hyperandrogenic phenotypes (96.7%) are the predominant phenotypes of PCOS in our population. The best diagnostic tests with the highest area under the ROC curve (AUC) were: FAI (AUC = 0.868), SHBG (0.765), HDL-cholesterol (0.715), HOMA-R (0.670), QUICKI (0.658), adiponectin (0.644), leptin:adiponectin ratio (0.658). Oligomenorrhea (53.3%) and polycystic ovaries (68.2%) were not found in all PCOS and high androgens showed variable correlations with clinical indicators of hyperandrogenism. Logistic regression showed odds ratio (OR) of significant associations with PCOS were: testosterone (OR= 3.44), FAI (2.70), HDL-Cholesterol (0.10), SHBG (0.98), adiponectin (0.89), HOMA-IR (2.56) androstenedione (1.62) and DHEA-S (1.42).

Conclusions:

Whereas clinical presentation of Oligomenorrhea and hyperandrogenism are stressed as diagnostic criteria for PCOS, our data show that some metabolic parameters have comparable diagnostic performance and should be useful adjuncts for screening. As early diagnosis and treatment may improve the reproductive sequelae and reduce cardio-metabolic risks, should we do more and can we do better to screen for PCOS? Yes, we can.

*Key Words: Polycystic Ovarian Syndrome; Receiver Operating Characteristic Curve; Screening
Funding Agency: Kuwait University Grant MG01/05*

Pathology

Category: Graduate (Resident)

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Assessment of Adiposity in Routine Practice – Comparison of Bioelectrical Impedance Analysis of Body Fat Composition with Body Mass Index and other Anthropometric Measurements

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Introduction:

Body mass index (BMI) is widely used index of obesity but cut-offs for the definition and classification of obesity in different ethnic populations have been questioned. Bioelectrical impedance analysis (BIA) is a safe, accurate and inexpensive method that could be widely used to assess the degree of adiposity. This study evaluates and compares routine anthropometric measurements and the usefulness of BIA for the determination of the prevalence of overweight and obesity in young adults.

Methods:

One hundred and twenty - seven medical students (70F and 57M) aged 17-25 years were recruited in this cross sectional study. We measured: weight, height, BMI, waist and hip circumferences. Body fat percent (BF%) was measured using BIA. BMI>25 and >30 kg/m² were used as criteria for determining overweight and obese subjects, respectively.

Results:

The prevalence of obesity (BMI > 30) among males and females were 22.8% and 10% respectively; the prevalence of central obesity (WC > 102 M; >80 F) in males and females were 21% and 10% respectively. Cut-offs (upper 95% Confidence Intervals (CI)) for anthropometric indices for identification of obesity differed in males and females: In males with BMI > 30, upper 95% CI cut-offs were WC=115 cm, WHR=0.93, and BF%=34.5; in females, the upper 95% CI values were: WC=116, WHR=0.84, and BF%=48.5. Pearson correlation analysis showed that BMI (r=0.68) showed the best correlation with BF% compared to WC(r=0.41) and WHR (r=-0.027). WC (r=0.85) showed better correlation with BMI than WHR (r=0.37).

Conclusions:

Obesity is prevalent among medical students. Despite its limitations, BMI showed the best correlations with BIA and WHR showed the worst correlation. The cut-off values identified in this population is different from International guidelines. There is need to adjust the cut-off levels for definition of obesity in the Kuwaiti population. BIA is simple, easy to perform and it is recommended for the routine determination of adipose tissue burden.

Key Words: Body Fat Content; Bioelectrical Impedance Analysis; Body Mass Index

Funding Agency: None

Efficacy of Broncho-alveolar Lavage and Bronchial Brush Cytology in Diagnosing Lung Cancer: A Five-Year Review.

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Introduction:

Respiratory tract cytology is well established as a vital diagnostic procedure in the evaluation of patients with suspected lung malignancy. The aim of our study was to compare the efficacy of broncho-alveolar lavage (BAL) and bronchial brushings (BB) in the diagnosis of lung cancers and correlate them with bronchial biopsy findings.

Methods:

Over a period of 5 years (2003 – 2007), 352 cases of BAL samples and 66 cases of BB samples were evaluated in the cytology laboratory of Mubarak Al-Kabeer hospital. Of these cases, a cyto-histological correlation was available in 80 (22.73%) and 21 (31.81%) cases of BAL and BB specimens respectively. Of these, 41 were males and 39 were females. Diagnosis by bronchial biopsy was considered as the “Gold Standard”.

Results:

BAL cytology showed 8 true positive (TP), 61 true negative (TN), 10 false negative (FN) and 1 false positive (FP). BB cytology showed 9 TP cases, 8 TN cases and 4 cases as FN. There was no false positive case on BB cytology. Sensitivity of BB was 69.23%; while that of BAL was 44.44%. Specificity of BB was 100% and that of BAL was 98.38%. Similarly Positive Predictive Value and Negative Predictive Value, False Negative Index and False Positive Index were better for BB than for BAL. Accuracy of brush cytology was 80.95% while that of BAL was 86.25%.

Conclusions:

In our study, it was found that bronchial brushings is a more specific and sensitive technique in the diagnosis and morphological typing of lung cancer, in comparison to BAL.

Key Words: Broncho-alveolar lavage; Bronchial brush cytology; Lung cancer

Funding Agency: None

Effect of Single Nucleotide Polymorphisms in the Adiponectin Gene on Circulating Adiponectin and Cardio-Metabolic Risk Factors in Patients with Polycystic Ovary Syndrome.

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Introduction:

The genetic mechanisms underlying the hyperandrogenism and metabolic disorders in polycystic ovary syndrome (PCOS) are complex. We postulate that polymorphisms in the gene for adiponectin, an adipose tissue-derived hormone, determine the adiponectin level and play a significant role.

Methods:

In a study on 92 patients with PCOS and 108 controls, we used real time PCR to determine the 45T>G and 276G>T polymorphisms in the adiponectin gene and measured follicular phase LH, FSH, estradiol, testosterone, androstenedione, DHEA-S, SHBG, fasting lipid profile, adiponectin, glucose and estimated insulin resistance using the homeostasis model assessment (HOMA-IR). Body fat% was measured by Bioimpedance analysis. Univariate and multivariate regression analyses were used to find the associations of these variables with each other, adiponectin gene polymorphism and PCOS.

Results:

Adiponectin showed significant inverse correlations with waist circumference, fat%, HOMA-IR, free androgen index (FAI) and triglycerides but showed positive correlations with HDL-cholesterol and SHBG. Multivariate regression analysis showed that adiponectin is a significant determinant of insulin, HOMA-IR, SHBG and FAI. The distributions of the genotypes of both polymorphisms were not significantly different in PCOS patients and controls but TT and GT genotypes of 45T>G and TT and TG genotypes of 276G>T were associated with significantly lower adiponectin and HDL-cholesterol and significantly higher insulin, HOMA-IR, triglycerides and FAI despite similar obesity indices. Binary logistic regression analysis showed that the TT (OR = 0.89) and GT (OR = 0.83) genotypes of 45T>G and TT (OR = 0.90) and TG (OR = 0.87) genotypes of 276G>T were significant determinants of PCOS risk.

Conclusions:

We conclude that polymorphisms in the adiponectin gene are associated with lower adiponectin that may contribute to the pathogenesis of insulin resistance and hyperandrogenism in the patients.

Key Words: Adiponectin; Single nucleotide polymorphisms; Polycystic Ovarian Syndrome

Funding Agency: Kuwait University Grant No.s MGO1/05, CGS YM 21/07

Galactose-Induced Downregulation of IGF-1 Gene Expression in Neonatal Human Skin Fibroblasts is Nitric oxide Mediated.

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Introduction:

Galactosemia is an autosomal recessive disorder that often results in multiple organ dysfunction in affected children. IGF-1 is an important growth factor, now well known to mediate several cellular functions. We conducted this study to examine the effect of galactose on gene expression of IGF-1 in neonatal dermal fibroblasts.

Methods:

Cell cultures of skin fibroblasts from foreskin of neonates were established and treated with varying concentrations of galactose. Cell cultures treated with galactose were analyzed by RT-PCR for IGF-1 expression. Levels of nitric oxide were measured in culture supernatants as well as in cell homogenates.

Results:

Treatment of cell cultures with galactose resulted in a significant ($p < 0.01$) decrease in the mRNA levels of IGF-1 as determined by RT-PCR. Levels of nitrites were significantly increased ($p < 0.05$) following treatment with galactose. Treatment of fibroblasts with Nitric oxide donor (SNAP) also resulted in a significant decrease ($p < 0.01$) in gene expression of IGF-1, however NO synthase inhibitor markedly alleviated SNAP or galactose- induced decrease in IGF-1 gene expression.

Conclusions:

These results suggest for the first time that nitric oxide and IGF-1 might be important players in regulation of cellular functions during galactosemia.

Key Words: Galactosemia; Nitric oxide; IGF-1

Funding Agency: None

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Characterization of Angiotensin-(1-7)-Induced Relaxation in the Rat Corpus Cavernosum

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Introduction:

Relaxation of corporal smooth muscle is essential for normal erectile function. The objective of this study was to evaluate the ability of angiotensin-(1-7) [Ang-(1-7)] to produce relaxation of the corpus cavernosum.

Methods:

The reactivity of corpus cavernosal strips isolated from control rats was assessed in organ-bath chambers. Cumulative concentration response curves for Ang-(1-7) were established.

Results:

Ang-(1-7) (10^{-12} - 10^{-5} M) produced a concentration-dependent relaxation of the corpus cavernosal strips. In cavernosum strips from control animals, Ang-(1-7)-induced maximal relaxant response was significantly reduced in the presence of A-779 (10^{-6} M), a selective Ang-(1-7) receptor (AT_{1-7}) antagonist, saralasin (10^{-6} M) (a non selective angiotensin receptor antagonist) and losartan (10^{-6} M) (an AT_1 selective angiotensin receptor antagonist), respectively. Ang-(1-7)-induced relaxation was significantly attenuated after treatment of the cavernosum strips obtained from control animals with nitro-L-arginine methyl ester (L-NAME) (10^{-4} M), an inhibitor of nitric oxide synthase, indomethacin (10^{-6} M), an inhibitor of cyclooxygenase, glibenclamide (10^{-6} M) (an inhibitor of ATP-dependent potassium channels) or iberiotoxin (5×10^{-8} M), an inhibitor of calcium-activated potassium (BK) channels.

Conclusions:

These results demonstrate that Ang-(1-7) can produce nitric oxide/prostaglandin-dependent relaxation of the corpus cavernosum through activation of AT_{1-7} and ATP-dependent and calcium-activated potassium channels. Older and diabetic animals showed impaired Ang-(1-7)-mediated relaxation suggesting that aging and diabetes related erectile dysfunction (ED) may be partly due to decreased Ang-(1-7)-mediated relaxation of the corpus cavernosum.

Key Words: Erectile dysfunction; Nitric oxide; Diabetes

Funding Agency: Funded by Research Administration Project No. MR01/06

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Nerve Growth Factor Enhances Cough and Airway Obstruction via TrkA and TRPV1 Receptor - Dependent Mechanisms

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Introduction:

Nerve growth factor (NGF) is an important mediator of airway hyperresponsiveness and hyperalgesia but its role in cough is unknown. In this study, we investigated the effects of NGF on the cough reflex and airway caliber in guinea pigs. We also assessed the involvement of TrkA and TRPV1 receptors and p38 MAPK dependent pathway on any of the NGF-induced effects on cough and airway obstruction.

Methods:

Guinea pigs were placed in a transparent whole body plethysmograph box. Cough was assessed visually, acoustically and by analysis of the flow signal. Airway obstruction was measured using enhanced pause (Penh) as an index. Western blot analysis was used to detect the pp38 MAPK protein levels.

Results:

Exposure of guinea pigs to NGF immediately before 0.2 M citric acid inhalation resulted in a significant increase in the citric acid-induced cough (12.6±2.5 vs 1.9±1.2; P<0.05) and airway obstruction (5.2±0.9 vs 0.9±0.1; P<0.05) compared to vehicle treated animals. Pre-treatment with the TrkA antagonist, K252a, significantly inhibited the NGF enhanced cough (2.9±1.6 vs 8.6±2.0; P<0.05) and airway obstruction (0.9±0.3 vs 2.4±0.7; P<0.05) compared to the control group. The NGF enhanced cough and airway obstruction were both inhibited following pretreatment with the TRPV1 receptor antagonist, iodoresiniferatoxin, by (1.6±1.6 vs 17.2±5.8; P<0.05) and (1.3±0.3 vs 4.7±1.4; P<0.05) respectively compared to the control group. Exposure to NGF also significantly (P<0.05) increased p38 MAPK phosphorylation and pretreatment with the p38 MAPK inhibitor (SB203580) decreased this effect. Interestingly however, SB203580 pretreatment did not affect either the NGF enhanced cough or airway obstruction.

Conclusions:

The data show that NGF can enhance both cough and airway obstruction via a mechanism that involves the activation of TrkA and TRPV1 receptors but independent of the p38 MAPK pathway.

Key Words: Nerve growth factor; Cough; Airway obstruction

Funding Agency Kuwait University Research Administration, Grant No. PT 01/05

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Does TH9, a Theophylline Analog, Affect Long Term Potentiation in the Rat Hippocampus in Vitro?

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Introduction:

Dementias are a group of neuropsychiatric disorders characterized by cognitive deficit including memory impairment. Alzheimer's disease (AD) is the most prevalent form of dementia accounting for about 50% of dementia cases worldwide and afflicting 24-33% of people aged above 85 in the Western World. Impaired memory is associated with decrease in synaptic transmission and plasticity in memory related brain regions such as the hippocampus. This study tested if a novel theophylline derivative, TH9 enhances as long term potentiation (LTP) a cellular model of synaptic plasticity.

Methods:

Three hundred and fifty micrometer coronal slices of the forebrain containing the hippocampal formation were generated from male Sprague-Dawley rats (75-100gm). Evoked, field excitatory postsynaptic potentials (fEPSPs) were recorded from the dendritic layer of area CA1 of the hippocampus by stimulating appropriate afferents. LTP was triggered by applying high frequency stimulation (HFS; 100Hz) of the afferents.

Results:

Bath application of 10 micromolar TH9 increased the slope of the evoked fEPSP by $26.2 \pm 3.0\%$ (n=6). When LTP was induced in naïve slices, an increase of $33.7 \pm 2.6\%$ (n=8) in fEPSP slope was detected. In five of the six slices above, the peak of the TH-9-induced synaptic enhancement (8 minutes) application of the LTP protocol now resulted in a bigger enhancement of the synaptic response ($54.7 \pm 12.0\%$ (n=5, p<0.05). LTP was saturated by applying several 100Hz stimulations every 30 minutes, the synaptic response saturated after 3 repetitions (HFS1: $32.1 \pm 6.6\%$; HFS2: $52.9 \pm 17.6\%$ and HFS3: $63.4 \pm 28.3\%$. After saturation, TH9 no longer produced a significant increase ($73.1 \pm 40.8\%$ (n=3, p> 0.05 compared to HFS3 level).

Conclusions:

TH9 therefore enhances synaptic transmission and plasticity in the rat hippocampus.

Key Words: Dementia; Memory; Synaptic plasticity

Funding Agency: KU Grant # YM08/08.

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Substance P- and Cocaine-Induced Excitatory Synaptic Depression in the Nucleus Accumbens are Mutually Occlusive.

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Introduction:

Substance P (SP) is a neuropeptide that is present in the nucleus accumbens (NAc), a brain region involved in emotions and complex behavior including drug use and seeking behaviors. Cocaine works in this region to induce its biochemical and behavioral effects. These same behaviors occur in animals and humans without cocaine. The question then has been: what is the endogenous mediator of these cocaine-like effects in non drug users? Here we tested the hypothesis that SP may be the endogenous mediator.

Methods:

Using in vitro forebrain slice preparations containing the NAc, we recorded whole-cell excitatory postsynaptic currents (EPSCs) and tested the effects of SP on these currents in the presence of cocaine and vice versa.

Results:

Bath application of SP produced a concentration-dependent depression of the evoked non-NMDA receptor mediated EPSC. This effect had an EC₅₀ of 0.12 microM, with a maximal suppression of $33.4 \pm 4.8\%$ (n=7) at 1 microM. The effect was largely irreversible after 15-20 minutes washout. Cocaine on the other hand produced a reversible depression of the EPSC with an EC₅₀ of 8.3 uM and a maximal suppression of $65.7 \pm 5.0\%$ (n=7) at 100 microM. In addition to these effects on the fast non-NMDA responses, both SP (1 uM) and cocaine (30 microM) also suppressed the relative slow NMDA receptor EPSC by $31.7 \pm 4.5\%$ (n=7) and $47.8 \pm 4.5\%$ (n=4), respectively. At the peak of the cocaine (30 uM)-induced suppression of the fast EPSCs ($39.1 \pm 4.8\%$), application of SP (1 microM) did not produce an additional suppression of the EPSC ($5.7 \pm 2.8\%$, n=8). By contrast, when SP was first applied, it caused a suppression of $30.3 \pm 2.3\%$ (n=6). At the peak of this effect, subsequent addition of cocaine (30 microM) produced a further suppression of the EPSC ($15.5 \pm 3.6\%$).

Conclusions:

Our data indicate that cocaine and SP produce similar effects on excitatory synaptic transmission in the NAc and that their actions occlude one another.

Key Words: Glutamate receptors; Synaptic transmission; Substance abuse

Funding Agency: KU Research Administration grant # PT01/06

Development of a Simple and Rapid high Performance Liquid Chromatographic Method for the Quantitation of Ethosuximide in Human Plasma for Therapeutic Drug Monitoring

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Introduction:

Ethosuximide (ESM) is a succinimide-derivative antiepileptic drug. It is among the first line drugs, both as monotherapy or in combination with valproic acid or lamotrigine for the treatment of childhood and juvenile absence seizures and idiopathic generalized seizures with myoclonus. The objective of this study was to describe a simple, rapid and validated method for quantitation of ESM in human plasma by high performance liquid chromatography using solid phase extraction and ultraviolet detection for therapeutic drug monitoring.

Methods:

Plasma samples containing ESM and the internal standard (butobarbitone sodium) was extracted using Oasis MCX x 1cc(30mg)solid phase extraction cartridges. The chromatographic separation was achieved using Symmetry C18, 3.9 x 150 mm, 5 um column and a mobile phase consisting of phosphate buffer-Acetonitrile-Methanol. The quantitation was achieved using linear regression of peak area ratio.

Results:

Calibration curve was linear over a range of 5-125 mg/L ($r > 0.999$) with a limit of quantitation of 5 mg/L (RSD 19.1%, Bias -15.7%). The intra and inter-run precisions of ESM at three different concentrations (20, 50 and 100 mg/L) ranged from 2.2 to 5.0% with accuracy varying between 92.9 and 105.5%. Stability tests revealed that ESM is stable for at least 4 weeks when stored at -20 degree Celsius. The method proved to be specific, sensitive, accurate, linear, reproducible and free of interferences from other concomitant antiepileptic drugs.

Conclusions:

The method described is validated and standardized to measure ESM in plasma of patients receiving this drug. When assessed by a external quality control (EQC) TDM theme (Heathcontrol, Cardiff, UK) the described method was found to compare well with the consensus mean of different centers ($r = 0.978$, regression equation $y = 0.88x + 4.61$, $n = 44$). This method is suitable and is being used for routine Therapeutic Drug Monitoring of ESM in our laboratory.

Key Words: Ethosuximide; HPLC-UV; Therapeutic Drug Monitoring

Funding Agency: None

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Reactivity of the Pulmonary Artery to Vasoconstrictor Agents During Pulmonary Hypertension Induced by Hyperthyroidism.

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Introduction:

Pulmonary hypertension is a chronic disabling disease that affects the pulmonary artery. In this study, the effect of hyperthyroidism-induced pulmonary hypertension on reactivity of the pulmonary artery to vasoconstrictor agents was investigated.

Methods:

Adult guinea pigs were used in this investigation. They were treated with thyroxine for 10 days. The pulmonary artery was isolated and set up in 25.0 ml water-jacketed for tissue contraction.

Results:

Electrically-induced contractions were mediated mainly via adrenoreceptors but with some non-adrenergic components. In the presence of L-NAME to inhibit NO synthesis, T4 potentiated EFS- but not noradrenaline induced contractions suggesting that the effect of T4 on EFS-induced contractions was mediated prejunctionally. 5-HT and ET-1 also concentration-dependently contracted ring segments of the pulmonary artery. These contractions were not modulated by T4. The serum concentration of thyroxine in the control group was 10.1 ± 2.3 nmol/l. This increased to 54.4 ± 8.5 nmol/l and 242.4 ± 19.5 nmol/l following treatment with 0.5mg/kg and 1.0mg/kg thyroxine, respectively. Treatment with T4 for 10 days increased heart to body weight ratio as well as lung wet weight to body weight ration. Study of vascular reactivity of the pulmonary artery segments from T4-treated guinea pigs to noradrenaline showed an increase in sensitivity the but not the maximum response. There was also no change in reactivity to ET-1 in T4-treated groups. In contrast, 5-HT produced concentration-dependent contractions with no change in sensitivity. However, the maximum response was greater in T4-treated guinea pigs than the control groups suggesting increased reactivity to 5-HT could be due to a change in the signal transduction mechanism.

Conclusions:

It was therefore concluded that the increased pulmonary vascular resistance in pulmonary hypertension could be due to increased alpha1- adrenoreceptor and 5-HT receptor activity.

Key Words: Pulmonary Hypertension; Vasoconstrictor Agents; Hyperthyroidism

Funding Agency: College of Graduate Studies

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Angiotensin-(1-7) Produces Vasodilation of the Rat Renal Artery

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Introduction:

In the human, angiotensin-(1-7) [Ang-(1-7)] attenuates angiotensin II (Ang II)-induced vasoconstriction in resistant vessels and produces relaxation of several vascular beds. The objective of this study was to investigate the vasodilator effect of Ang-(1-7) in the renal artery of Wistar rats.

Methods:

The vasodilator effect of Ang-(1-7) was tested in the isolated renal artery using an organ-bath set-up.

Results:

Ang-(1-7) produced an endothelium-dependent vasodilator effect in isolated renal artery segments that were pre-contracted by a sub-maximal concentration of phenylephrine (10^{-7} M). Ang-(1-7) (10^{-12} - 10^{-6} M) induced vasodilation of the rat renal artery with a pD₂ value of 9.4 ± 0.3 and a maximal relaxation of $45 \pm 2\%$. Pre-incubation of the vessels with sarthran (10^{-5} M), losartan (10^{-6} M), PD123, 319 (10^{-6} M) or A-779 (10^{-5} M) resulted in 71%, 42%, 64% and 82% inhibition of Ang-(1-7)-induced maximal response, respectively. Pre-incubation of vessels with nitro-L-arginine methyl ester (L-NAME) (10^{-4} M), an inhibitor of nitric oxide synthase, indomethacin (10^{-6} M), a combination of L-NAME (10^{-4} M) and indomethacin (10^{-6} M), 1H-[1, 2, 4] oxadiazolo[4, 3-a]quinoxalin-1-one (10^{-5} M), an inhibitor of soluble guanylyl cyclase, glibenclamide (10^{-5} M), an inhibitor of ATP-sensitive K⁺ channels, or iberiotoxin (5×10^{-8} M), an inhibitor of calcium-activated potassium (BK) channels, resulted in 18%, 53%, 64%, 82%, 31% and 40% inhibition of Ang-(1-7)-induced maximum vasodilation, respectively.

Conclusions:

Data from this study showed that Ang-(1-7) produces vasodilation of the renal artery mainly through activation of AT₁₋₇ via activation of cGMP/nitric oxide pathway as well as activation of ATP-sensitive K⁺ channels and BK channels. These observations suggest that modulation of Ang-(1-7)-mediated signaling could be an important strategy to antagonize renal complications in cardiovascular diseases.

Key Words: Renal artery; Angiotensin; Endothelium

Funding Agency: Funded by Research Administration Project No. MR01/06

**Role of Cytochrome P-450 Metabolites of Arachidonic Acid
in the Enhanced Cardiac Dysfunction in Diabetic Rats
Following Ischemic Reperfusion Injury**

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Introduction:

We examined the contribution of cytochrome P-450(CYP450) metabolites of arachidonic acid in mediating ischemia/reperfusion (I/R)-induced cardiac dysfunction in normal and diabetic rats.

Methods:

We compared the metabolism of arachidonic acid in microsomes prepared from the hearts of control and STZ-induced diabetic rats. We then compared the change in left ventricular pressure (Pmax), left ventricular end-diastolic pressure(LVEDP), coronary flow (CF), and coronary vascular resistance(CVR)in isolated perfused hearts obtained from control and diabetic animals after 40 minutes of global ischemia(I)followed by 30 minutes of reperfusion(R).

Results:

The production of 20-hydroxyecosatetraenoic acid (20-HETE), a potent vasoconstrictor agent, was 2-fold higher in diabetic hearts than in control animals, while dihydroxyecosatrienoic acids (DiHETEs)and epoxyecosatrienoic acids (EETs), which are vasodilators, were similar in the two groups. The decline in cardiac function was 3 to 5-fold greater in the hearts obtained from diabetic versus control animals. Pretreatment of the hearts with N-hydroxy-N'-(4-butyl-2-methyl-phenyl)-formamidine(HET0016, 1μM), a selective inhibitor of the synthesis of 20-HETE, for 30 minutes before I/R resulted in significant improvement in the recovery of cardiac function in the hearts obtained from diabetic but not in control rats. Epoxide hydrolase inactivates EETs. Perfusion with an inhibitor of soluble epoxide hydrolase, 1-cyclohexyl-3-dodecyl urea(CDU), before I/R improved the recovery of cardiac function in hearts obtained from both control and diabetic animals. Pretreatment of the hearts with glibenclamide (1μM), an inhibitor of ATP-sensitive potassium channels, attenuated the cardioprotective effects of CDU and HET0016.

Conclusions:

This is the first study to suggest that acute blockade of the formation of 20-HETE and reduced inactivation of EETs could be an important strategy to reduce cardiac dysfunction following I/R events in diabetes.

Key Words: Diabetes; Ischemia; HET0016

Funding Agency: Funded by Research Administration Project No. MR03/06

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Determination of Ciprofloxacin in Rabbits Serum by LC-MS/MS: Preliminary Application for Evaluating the Pharmacokinetics of Ciprofloxacin

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Introduction:

Ciprofloxacin (CIP) is a fluoroquinolone with a broad-spectrum antibacterial activity. CIP is well-absorbed and distributed in tissues and fluids, therefore it is recommended for treating several infectious diseases. Monitoring of serum concentrations of CIP in body fluids is important for evaluating the bioavailability of CIP dosage forms. The objectives of this study are to develop a validated LC-MS/MS methodology for monitoring CIP in rabbits serum and to evaluate the pharmacokinetics profile of a brand of CIP tablets in rabbits.

Methods:

A validated LC-MS/MS assay for quantifying CIP in rabbits serum was developed using rifloxacin (RUF) as an internal standard. CIP and RUF were detected in SRM mode at m/z 332.3 and 364.4 respectively. The pharmacokinetics (PK) studies were performed in male NZW rabbits. The calculated dose of CIP tablet was surgically placed into the gastric cavity of the rabbit and the blood sera were collected from the ear veins. The PK parameters were computed using PK-software for non-compartmental pharmacokinetics data analysis.

Results:

The LC-MS/MS method showed a good linearity ($r: >0.99$) over the concentration range 2-10 $\mu\text{g/ml}$ of CIP with a LOQ of 2 $\mu\text{g/ml}$. The preliminary PK data for the absorption and elimination of CIP from tablets were 6 $\mu\text{g/ml}$, 1.0 hour, 56.1 $\mu\text{g. hr/ml}$, 170.2 $\mu\text{g. hr/ml}$, 0.019 hr^{-1} , and 35.9 hr for C_{max} , T_{max} , $\text{AUC } 0\text{-}t$, $\text{AUC } 0\text{-}\infty$, K_e and $t_{1/2}$ respectively. These values were in agreement with the reported values.

Conclusions:

The LC-MS/MS methodology is appropriate for monitoring serum concentrations of CIP. While the surgical administration of CIP in rabbits permits a complete placement of drug dose in the gastric cavity thus eliminating problems with oral dosing in rabbits. These methodologies will permit further comparative studies of the pharmacokinetics of several brands of CIP, which may shed some light on the varied therapeutic efficacies as reported during therapy.

Key Words: Ciprofloxacin; LC-MS/MS; Pharmacokinetics

Funding Agency: None

Pharmacy

Category: Undergraduate

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Prevalence and Awareness of Retinopathy among Diabetic Patients in Kuwait

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Introduction:

Retinopathy is a common microvascular complication of diabetes and is a leading cause of blindness in the world. This study was conducted to investigate the prevalence and awareness of retinopathy among diabetic patients in Kuwait.

Methods:

An anonymous, cross-sectional survey was conducted on a sample size of 218 diabetic patients. Data were collected using self-administered questionnaire to patients at diabetic clinics from two hospitals and six polyclinics representing Capital and Hawalli governorates of Kuwait. Multiple regression analysis and chi-square tests were used to analyze the data and evaluate any association.

Results:

The overall prevalence of retinopathy among diabetic patients was found to be 36.7%. Duration of diabetes, presence of hypertension, heart failure, and dyslipidemia were all significantly associated with increased retinopathy occurrence. Type of diabetes and obesity did not show any significant association with prevalence of retinopathy. 36% of patients were not aware of their type of diabetes and only 65% were aware of retinopathy as a complication of diabetes. In addition, 73% of patients were aware that retinopathy may lead to vision loss. Knowledge of risk factors by diabetic patients were as follows: 62% for hypertension, 35% for dyslipidemia, 38% for smoking, and 86% for glycemic control. Awareness of retinopathy and its risk factors was significantly associated with high educational level and advanced age of the patient.

Conclusions:

This study highlights the high prevalence of retinopathy among diabetic patients. Educational programs are needed to increase diabetic patient awareness about the ocular complications of diabetes and the importance of regular retinopathy screening.

Key Words: Prevalence; Diabetic Retinopathy; Awareness

Funding Agency: None

Comparison of Vancomycin Trough Concentration Prediction of Seven Population Methods at Al-Amiri Hospital in Kuwait.

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Introduction:

Seven published methods (Ambrose; Bauer; Birt; Burton; Burton revised; Matzke; Rodvold) were used to determine a vancomycin dosing regimen based on estimations of clearance (Cl_{vanco}) and volume of distribution (V_d). Many clinicians measure trough concentrations (C_{trough}) as a guide to dosing, but this does not allow the Cl_{vanco} and V_d for individual patients to be determined. Thus, prediction methods could be helpful if they reliably produced C_{trough} in the desired range. The objective of this study was to compare the predictability of the different methods for estimating the C_{trough}.

Methods:

One hundred and twenty - seven inpatients were identified for whom a confirmed steady-state vancomycin C_{trough} level was available (group 1). A sub-group (n = 76) of these patients (group 2) also had at least one steady-state C_{peak} together with a second C_{trough} level recorded in their notes. For each published method, the calculated Cl_{vanco} and V_d C_{trough} was used to estimate C_{trough} which was compared to the measured C_{trough}. For group 2, the measured first C_{trough} and C_{peak} were used to estimate the second C_{trough} which was compared to the second measured C_{trough} (individualized method).

Results:

The seven published methods gave r² (coefficient of determination) values in the range 0.111-0.279; bias, -2.91-6.56; precision, 6.54-10.38; predictions within 2.5 and 5 mg/L of the measured C_{trough} were in the range 11-30% and 27-55%, respectively; predictions within 25% and 50% of measured C_{trough} were 14-35% and 39-55%, respectively. In group 2 only using the individualized method, the corresponding values were 0.743, 0.03; 2.99, 67% and 83%, 65% and 87%, respectively. Of the published methods, the Birt and the Burton revised methods performed best in terms of the population methods,

Conclusions:

The Birt and the Burton revised methods performed best but, as expected, estimation of C_{trough} using therapeutic drug monitoring was superior.

Key Words: Vancomycin; Population pharmacokinetics; Trough concentration

Funding Agency: None

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Isolation and Identification of Bioactive Lead(s) with Potent Cytotoxicity against Human Cancers from Kuwait Flora Plants

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Introduction:

Fagonia bruguieri and *Oxalis corniculata* are part of Kuwait flora. *Oxalis corniculata* is widely used in traditional and herbal Chinese medicine to treat ailments such as hepatopathy. On the other hand, there is a little reports account for the biological activity of *Fagonia bruguieri*. This study aims at purifying, identifying and testing the cytotoxicity of the active lead(s) from both plants.

Methods:

Ninety – six percent ethanol extracts of *Fagonia bruguieri* (Fb) and *Oxalis corniculata* (Oc) were partitioned between four different solvents to afford four fractions; Fb, Oc-hexane, Fb, Oc-ethylacetate, Fb, Oc-butanol, and Fb and Oc-water. Fb, Oc-ethylacetate and Fb-butanol fractions yielded several subfractions after chromatography. Dose-dependent cytotoxic effects of the produced fractions and subfractions were evaluated against colon, lung, skin and breast cancer cells. Normal skin fibroblasts were used as a control. Cytotoxicity evaluation was done using MTT assay.

Results:

Fractions and subfractions that have promising cytotoxic activity with little effect (0-18%) on normal cells were Oc-water (81% growth inhibition of breast cancer at 3.125 mg/ml), Fb-water (60% growth inhibition of breast cancer at 6.250 mg/ml), Oc-butanol (98% growth inhibition of lung cancer at 1.562 mg/ml). In addition, one subfraction of Fb-ethylacetate showed selective activity against lung cancer with 80% growth inhibition at 0.125 mg/ml. Another Fb-ethylacetate subfraction showed about 100% growth inhibition against lung, breast, colorectal and skin cell lines at 0.500 mg/ml.

Conclusions:

Fagonia bruguieri and *Oxalis corniculata* afforded fractions with promising selective cytotoxic activity against human lung, breast, colorectal and skin cancer cell lines. Further, these fractions are currently underway to isolate the active lead(s) that will then be subjected to structure elucidation using spectral methods, and investigation of the underlying molecular mechanisms of action.

Key Words: *Fagonia bruguieri*; *Oxalis corniculata*; Cytotoxicity

Funding Agency: This work was supported by Kuwait University Grant # SL 05/04

Polypharmacy Among Psychiatric Outpatients in Kuwait

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Introduction:

Objective: To investigate the prevalence of polypharmacy with psychotropic medications among Kuwaiti patients attending outpatient department (OPD) of the Psychological Medicine Hospital (PMH).

Methods:

A prospective study was designed based on selection of the first 20 prescriptions for Kuwaiti patients treated in the OPD over four weeks period (n=484). Data including age, sex, diagnosis and list of psychiatric medications were recorded and analyzed.

Results:

Forty percent of patients were treated for an initial diagnosis of mood disorders, 37.5% for schizophrenia, and 10% for neurotic disorders. The mean number of psychotropic drugs used by the patients was 2.7 (SD± 1.3, range 1-7). 19.7% of the patients were under monotherapy treatments, while 30.1%, 26.1%, and 24.1% received two, three and four or more drugs, respectively. Polypharmacy was more prevalent in males, and in patients with schizophrenia, mood disorders and neurotic disorders. Prevalence was significantly more in the age group 45-65 years and among patients more than 65 years old (p=0.009). Frequency of prescribing was 64.9% for antipsychotics, 52.1% for antidepressants, and 45.6% for benzodiazepines. 20.7% of schizophrenics used combination of both atypical and conventional antipsychotics. 7% of mood disorders patients used two antidepressants at the same time.

Conclusions:

Polypharmacy is common among psychiatric OPD. Schizophrenia, mood, and neurotic disorders are associated with an increase risk of polypharmacy. Conventional antipsychotics and tricyclic antidepressants are also prescribed with an increase risk of polypharmacy. The introduction of educational programs and guidelines could be effective in decreasing the prevalence of polypharmacy in psychiatric practice.

Key Words: Polypharmacy; Psychotropics; Kuwait

Funding Agency: None

Pharmacy

Category: Undergraduate

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Self-Reported Adherence to Diabetes Medication Regimens among Kuwaitis

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Introduction:

In 2007, Kuwait was ranked fifth for the high prevalence of diabetes among 20 to 79 years old. Adherence to diabetes medication regimens is essential to improve glycemic control and prevent macrovascular and microvascular complications. The objective of this study was to estimate the level of adherence to diabetes medication regimens among Kuwaiti patients with diabetes mellitus.

Methods:

A questionnaire was administered to 258 Kuwaiti patients with diabetes. Adherence was measured using the four-item scale by Morisky. The questionnaire also included items eliciting demographic and other descriptive variables. Pearson's r correlation and chi square analyses were conducted to explore relations between adherence and other variables. Covariates were entered into a logistic regression equation to test their ability to predict adherence.

Results:

Adherence was judged to be adequate in 62% of the sample, who received a score of three to four in the four points scale used. Those who received score of zero, one, or two were judged to have inadequate adherence and comprised 38% of the sample. Three variables were positively related to adherence: age, duration of diabetes, and not having a family member with diabetes. In a logistic regression equation containing the three variables, age was not a significant predictor of adherence ($p = 0.254$, OR=1.02, CI: 0.99-1.05). However, longer duration of diabetes independently predicted adherence ($p < 0.015$, OR= 1.06, CI: 1.01-1.10) and having no family member with diabetes also independently predicted adherence ($p=0.05$, OR=2.87, CI: 1.37-5.99).

Conclusions:

This is the first known study in Kuwaiti patients measuring adherence to diabetes or any other medication regimens. As in studies elsewhere, non-adherence appeared to be a problem. To realize the benefits of treatment with medications, patients need to take them. Studying the barriers to adherence should become a priority for future research in Kuwait.

Key Words: Medication adherence; Diabetes Mellitus; Morisky's scale

Funding Agency: None

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Lyophilized Gliclazide: Poloxamer dispersions for enhanced solubility

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Introduction:

The present study aims to enhance the aqueous solubility and dissolution of a hydrophobic anti-diabetic drug i. e. Gliclazide (GLC) by freeze drying (lyophilisation), using Poloxamer 407 (PXM), a hydrophilic non-ionic surfactant.

Methods:

Phase solubility study with increasing PXM concentrations (0.5, 1, 2, 5 and 10%) was done to analyze its influence on solubility of GLC. SD's of GLC and PXM in three different w/w ratios (1:1, 1:3 and 1:5) were prepared by lyophilisation technique in order to improve drug dissolution. The lyophilized systems were compared with the original drug as well as the physical mixtures (PM) for in-vitro dissolution, saturation solubility and particle size. DSC and FTIR studies were performed to identify the physicochemical interaction between the drug and the carrier.

Results:

GLC solubility increased linearly with increasing PXM concentration depicting an AL type of phase solubility curve. Intrinsic solubility of GLC in water was found to be only 6.144 µg/ml. The dissolution properties of lyophilized system in 1:2 ratio (DP15min = 78.8%) were superior than those of GLC (DP15min = 2.91%) and Diamicon tablets (DP15min = 13.05%). Also, the lyophilized systems exhibited a uniform and narrow mean particle size distribution. Results of DSC and FTIR studies demonstrated that enhanced dissolution of GLC from SD might be due to the amorphous nature of dispersed GLC after lyophilisation.

Conclusions:

This study reveals the potential of formulating GLC:PXM lyophilized systems with improved aqueous solubility and dissolution rate as compared to the free drug.

Key Words: Gliclazide; Poloxamer 407; Solid Dispersions, Lyophilisation

Funding Agency: None

Synthesis and Evaluation of Newer Analogs of Anticonvulsant EnamiNones

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Introduction:

Epilepsy is a syndrome that affects about two percent of the world's population. The antiepileptic drugs (AEDs) used in the treatment of epilepsy cause adverse effects such as drowsiness, and ataxia. Hence, there is an urgent need to design newer and safer AEDs. The objectives of the research project are to design new AEDs, and evaluate their anticonvulsant effects.

Methods:

The newer analogs of enamiNones were synthesized from beta diketo intermediates and amino compounds. The anticonvulsant evaluation was performed using maximal electroshock (MES), seizures and subcutaneous metrazol (SCMET) seizures in mice. The UV spectroscopy in neutral, acidic, and alkaline media was determined; and the CLOGP values were determined for the enamiNones.

Results:

A series of 26 new enamiNones was synthesized, and evaluated for anticonvulsant activities. Four enamiNones displayed potent anticonvulsant activity at doses of 100 mg/kg, while four other enamiNones displayed moderate anticonvulsant activity at doses between 100 and 300 mg/kg. One of the eight active compounds had specific anticonvulsant activity against MES seizures in mice. Three enamiNones showed potent broad-spectrum anticonvulsant activity against MES and SCMET seizures. Phenyl analogs were particularly protective against SCMET seizures. The active enamiNones had peculiar UV absorption patterns. Generally, the tertiary enamiNones absorbed UV light at the higher end and secondary enamiNones towards the lower end of the UV wavelength range 259-336 nm in aqueous media. No direct correlation could be established between Clog P values and anticonvulsant activity of the enamiNones.

Conclusions:

A total of eight enamiNones had anticonvulsant activity. One enamiNone was specific against MES seizures, while three enamiNones displayed broad-spectrum activity against MES and SCMET seizures. Three other phenyl analogs were anticonvulsant against SCMET seizures.

Key Words: Anticonvulsant enamiNones; Synthesis and evaluation; UV and CLOGP

Funding Agency: KURA grant PR 02/02

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Evaluation of Ketorolac Sustained Release Pellets in Healthy Subjects Using A New HPLC Method

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Introduction:

Sustained-release Ketorolac tromethamine (KT) pellets were prepared using non-pareils; coated with Eudragit-RL® (RL) and Eudragit-RS® (RS). The aim of this study was to evaluate the in-vivo performance of the prepared KT pellets in human volunteers applying a newly developed HPLC method.

Methods:

The vivo study was carried out on six healthy male volunteers; ages 20-26 years and weights 60-69 kg. Each subject was given a tablet (10mg KT) or a capsule containing the prepared pellets (30mg KT) in a cross over design. The mobile phase consisting of acetonitrile-water (40:60) adjusted to pH 4 and flow rate was 1ml/min.

Results:

The retention times of ketorolac tromethamine and ketoprofen (internal standard) were 2.5 and 4.08 min. respectively. Higher plasma concentration values were observed with the sustained release pellets (C_{max} 0.55 to 0.83microg/ml) compared with the tablets (C_{max} 0.32 to 0.65microg/ml). T_{max} with tablets was relatively shorter, 0.5 h, compared with 3 h in case of the sustained release pellets. Absorption half-life for pellets was 0.378 h and for the conventional tablets 0.183 h. Based on the area under the plasma concentration-time curve to infinity (AUC_{0- inf}) the calculated % bioavailability (after dose correction of the pellets relative to tablets) was found to be 104%. The pellets exhibited plasma concentrations exceeding the reported minimum effective concentration of the drug (0.3 µg/ml) for about 8 hours; compared with about only 2 hours with tablets.

Conclusions:

The prepared pellets exhibited in vivo drug release which is extended over a longer period, which enable reduction of frequency of dosing and side effects; compared to the reference tablets. The developed HPLC method was simple and highly sensitive for determination of KT by direct injection of an aliquot of the clear plasma samples.

Key Words: Ketorolac; Bioavailability; HPLC

Funding Agency: None

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Preliminary Evaluation of Cosmetic Products Containing Vitamin-E Marketed in Kuwait

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Introduction:

Vitami E (alpha-tocopherol) is one of the better established ingredients in OTC products of skin ageing. The aim of this study was determine the content of vitamin E (E)/acetate (EAc) in cosmetic products marketed in Kuwait, designated as A, B, C and D.

Methods:

A gradient HPLC with variable wavelength programmable PDA 996 detector, a disposable guard column C-18 and RP Waters Symmetry C-18 column (3.9 x 150 mm; 5 microm) were used for determination of E/EAC. The mobile phase employed was a mixture of methanol and water (97:3 v/v). A 500 mg sample from each product was weighed and mixed with 5 ml methanol, followed by sonication for 15 min. The mixture was then transferred to 50 ml volumetric flask and made up to volume with methanol, centrifuged for 15 min and analyzed by HPLC as mentioned above.

Results:

The HPLC method applied in the present study was found to be specific for E and EAc, with retention times of 10 and 13 minutes respectively. The analytical procedure proved to be precise and accurate as indicated by low CV-values (Mean = 1.94, n = 12) and high accuracy (Mean = 98.74%, n = 12). The adopted method of extraction proved to be suitable for E and EAc, as indicated by high extraction efficiency (97.2 and 107.8% respectively). The found concentrations of EAc in the commercial products were 0.085, 0.487, 0.5, and 0.426% for product A, B, C, and D respectively.

Conclusions:

The commercial preparations revealed variable vitamin concentrations ranging between 0.085 and 0.426. The method of analysis proved to be suitable for evaluation of vitamin E/acetate ester activity in cosmetic products.

Key Words: Vitamin-E; Cosmetics; HPLC

Funding Agency: Kuwait University, Research Administration, Grant No. PP01/05

Retention Behavior of Ginsenosides on a Poly(vinyl alcohol)-Bonded Stationary Phase in Hydrophilic Interaction Chromatography (HILIC)

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Introduction:

Over 80 ginsenosides have been identified from *Panax* spp. but the most abundant are Rb1, Rb2, Rc, Rd, Rg1, Rf and Re. RPLC with UV detection is the most widely used technique for the routine analysis of ginsenosides owing to its simplicity and practicality. However HILIC provides an alternative approach for their separation and quantitative determination.

Methods:

Influences of the organic component of the mobile phase and the column temperature on the retention of ginsenosides on a PVA bonded stationary phase operated under HILIC mode were investigated.

Results:

Aqueous ACN (75-90%) gave the most satisfactory retention and separation of the ginsenosides Rf, Rg1, Rd, Re, Rc, Rb2 and Rb1 compared with aqueous methanol, isopropyl alcohol or tetrahydrofuran at the same composition levels. Effects of the different types of organic modifiers on the retention of the analytes were attributed to their solvent strength and hydrogen bond accepting/donating properties. Van't Hoff plots and enthalpy-entropy compensation plots both revealed that Rf, Rd, Rc, Rb2, and Rb1 were retained by the same mechanism, which was completely different from that of Rg1 and Re at subambient temperatures. Retention prediction models based on multiple linear regression showed that the number of hydrogen bond donors and the ovality of the molecules are important properties that govern the retention of the compounds on the chromatographic system.

Conclusions:

Using an organic modifier whose solvent strength and hydrogen bond accepting/donating properties are higher than those of ACN caused the ginsenosides to be eluted with no retention. Van't Hoff plots and EEC studies both revealed that Re and Rg1 are retained by different mechanism(s) as compared to the other ginsenosides. MLR models showed hydrogen-bonding interactions and shape of the molecules are important factors that govern retention on the PVA-bonded phase under HILIC mode.

Key Words: HILIC mode; Ginsenosides; PVA-bonded phase

Funding Agency: None

Assessment of the Stability of Novel Triazolyl-Oxazolidines Using a Stability-Indicating HPLC Method

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Introduction:

Oxazolidines, exemplified by linezolid are effective against Gram-positive bacteria. However, recent reports of linezolid-resistant strains emphasized pressing need for more potent derivatives. Selected novel triazolyl-oxazolidines from our laboratory with potent activity superior to linezolid showed higher MIC values in the presence of plasma. The purpose of this study was to assess the stability of selected oxazolidines in simulated gastric and intestinal fluids and human plasma using a stability-indicating HPLC procedure.

Methods:

Accelerated stability studies of oxazolidines in 0.1M HCl solution and in phosphate buffer solution (pH 7.4) at 37°C were conducted. Moreover, the stability of the compounds in human plasma was determined at 37°C. The pre-treated aqueous and plasma samples at the appropriate time-intervals were analyzed by HPLC using RP C8 column and mobile phase of acetonitrile-H₂O (50:50 v/v). The degradation kinetic parameters, namely, degradation rate constant (K_{deg}), half-life ($t_{1/2}$), and shelf-life (t_{90}) were determined from the stability profiles.

Results:

The data from stability studies revealed that the compounds PH-108 and PH-036 were more susceptible to degradation in 0.1 M HCl solution. The values of K_{deg} , $t_{1/2}$ and t_{90} of PH-036 and PH-108 were (0.180 hr⁻¹, 3.85, 0.58 hr) and (0.184 hr⁻¹, 3.76 hr and 0.58 hr) respectively. The results were confirmed by LC/MS analysis. However, in phosphate buffer solution (pH 7.4) and human plasma, all the compounds were found to be stable as indicated from the kinetic parameters ranges: K_{deg} 0.0012-0.011hr⁻¹, $t_{1/2}$ 63-602 hr, and t_{90} 10-91 hr.

Conclusions:

All investigated oxazolidines were stable in simulated biological fluids at 37°C except PH-108 and PH-036. The triazolyl-oxazolidines PH-108 and PH-036 were completely degraded in simulated gastric fluid within 24 hr, and this could result in subsequent loss of antibacterial activity when administered orally. All the compounds were stable in human plasma, at 37°C.

Key Words: Triazolyl-oxazolidines; Stability; HPLC

Funding Agency: Kuwait University Research Grant PC01/05 (OAP)

The Influence of Squaramide and Tetraethyleneglycol Triazolyl Substituents on the Antibacterial Activity of Novel Oxazolidinones

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Introduction:

Oxazolidinones, exemplified by linezolid are inhibitors of bacterial protein biosynthesis with strong antibacterial activity. Recent mechanism studies showed that linezolid binds to the A-site of the 50S subunit. On the basis of accumulated data on mechanism of action and structure-activity relationships, we proposed the synthesis of tetraethyleneglycol (TEG; 6a-j) and squaramide (7a-e) oxazolidinone derivatives to potentially improve water solubility and ribosomal binding at the site of action, probably by effective hydrogen bonded base pair formation.

Methods:

The novel oxazolidinones were synthesized by a variety of synthetic methods. The tetraethyleneglycol (TEG) spacer containing compounds were prepared from propargyl bromide and excess glycol to give the propargylated TEGs, followed by bromination. Displacement of the bromo group with nucleobases cytosine and thymine gave the alkylated nucleobases. The covalent bonding of TEG-nucleobases with oxazolidinones was performed using copper ion catalyzed 1, 3-dipolar cycloaddition reactions of azides with terminal alkynes known as click reaction gave the TEG-oxazolidinones (6a-j). While reaction of the amino oxazolidinones with squaric acid diester gave the squaramide derivatives (7a-e). The compounds were evaluated against Gram-positive and Gram-negative clinical isolates, and standard reference strains, in comparison to linezolid, PH027 and vancomycin. Minimum inhibitory concentrations (MIC's, µg/ml) were determined by agar dilution method on Mueller-Hinton agar with the medium containing dilutions of antibacterial agents ranging from 0.12-64 µg/ml.

Results:

The novel oxazolidinone derivatives were characterized by spectroscopic analytical (IR, ¹H and ¹³C NMR and MALDI-TOF MS) methods. All the 15 compounds were devoid of activity against both Gram-positive and Gram-negative bacterial strains with MIC values >64 µg/ml compared to the reference agents linezolid, PH027 and vancomycin with MIC ranges of 0.25-4 µg/ml.

Conclusions:

The introduction of the tetraethyleneglycol spacer and squaramide moieties did not favor antibacterial activity. This study highlighted structural requirements for this class of oxazolidinones.

Key Words: Antibacterial agents; Squaramide-oxazolidinones; Tetraethyleneglycol
Funding Agency: Supported by Kuwait University Research Grant PC01/05 (OAP)

Bioactivity Evaluation of *Centaurea alexandrina* Alcoholic Extract

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Introduction:

Centaurea alexandrina (Asteraceae) is a wild biennial plant distributed around the Mediterranean area. Various species of *Centaurea* are used as herbal remedies for their digestive, expectorant, antipyretic, and antidiarrheal effects. Some species of *Centaurea* were reported to have analgesic, anti-inflammatory, antipyretic, cytotoxic, immunological, cardiotoxic activities and are useful for skin, and liver diseases. However, the biological activity of *Centaurea alexandrina* has not been explored. The aim of the study is to investigate the possible biological activity of *Centaurea alexandrina*.

Methods:

The shade-dried aerial parts of *Centaurea alexandrina* were coarsely powdered and extracted with ethanol (96%). The cytotoxic activity of the dried alcoholic extract was evaluated against liver, breast, cervix, colon, and larynx carcinoma cell lines beside the normal fibroblast cell line according to reported method [Skehan et al, 1990]. IC₅₀ (µgram/150 µliter) of the extract was determined using doxorubicin as a standard cytotoxic agent. Moreover, the anti-inflammatory, antipyretic, analgesic, antioxidant, and hepatoprotective activities of the same extract were investigated.

Results:

The alcoholic extract of *Centaurea alexandrina* aerial parts exhibited selective cytotoxic activities against liver, breast, cervix, colon, and larynx carcinoma cell lines. IC₅₀ values were 0.50, 2.05, 4.32, 2.75, and 0.50 respectively. Also, the extract proved to be active as anti-inflammatory, antipyretic, analgesic, antioxidant, and hepatoprotective agent.

Conclusions:

This study illustrated the potential and selective cytotoxic activity of *Centaurea alexandrina* alcoholic extract against breast, cervix, and colon carcinoma cell lines. However, the most potent cytotoxic effect was against liver and larynx carcinoma cell lines. Moreover, the extract showed an anti-inflammatory, antipyretic, analgesic, antioxidant, and hepatoprotective activities.

Key Words: Centaurea alexandrina; Cytotoxicity; Hepatoprotective

Funding Agency: None

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Novel Self-Emulsifying Drug Delivery System of Ibuprofen: Formulation, Optimization and Characterization Studies

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Introduction:

Ibuprofen (IB) has poor dissolution and many gastrointestinal side effects. Self-Emulsifying drug delivery system (SEDDS) has proved its efficacy to improve the solubility and dissolution of poorly soluble drugs. The objectives of this study were to formulate, optimize and characterize a IBSEDDS applying experimental design.

Methods:

The solubility of IB in different oils, surfactants and co-surfactants was investigated. Ingredient showing high drug solubility were used to formulate several IBSEDDS after being tested for physical and chemical compatibility with the drug. A three factor, three level Face Centered Experimental Design was used for the optimization process. The prepared formulations were evaluated for dissolution, turbidity and droplet size and referred to as the responses Y1, Y2 and Y3 respectively.

Results:

The results showed high solubility and compatibility of IB with soybean oil, Cremophore EL and Capmul MCM-C8 which are referred to as the variables X1, X2 and X3 respectively. The amounts of X1- X3 showed significant effects on the responses Y1-Y3. The polynomial equation relating the response Y1 and variables X1-X3 was obtained. The optimized and predicted values of Y1 were found to be in close agreement. According to the design, 50% oil, 40% surfactant and 10% co-surfactant were shown to maximize Y1 up to 100% after 60 min.

Conclusions:

The findings indicated that IBSEDDS with high drug release and reasonable physical properties could be prepared and the experimental design applied helped in understanding the effects and the interaction effects between the three variables applied. The optimized formulation is expected to show high absorption with minimal side effects.

Key Words: Self-Emulsifying Drug Delivery System; Ibuprofen; Experimental Design

Funding Agency: Kuwait University, PP02/06

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Rat Placental Beta-Catenin and Cyclin D1 mRNA and Protein Expression: Possible Regulation by Estrogens and their Receptors during Pregnancy

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Introduction:

Although estrogenic hormones are essential for the initiation and maintenance of pregnancy in the rat, high levels of estrogens have been shown to retard placental growth. During pregnancy, high levels of estrogens down regulate the estrogen receptor (ER) thus limiting their harmful effects on the placenta. Studies showed a link between estrogens, their receptors and the expression levels of beta-catenin and cyclin D1 which are involved in cell cycle progression. Thus, we hypothesized a possible mechanism by which this effect is achieved in which down-regulation of ER up-regulates the expression of beta-catenin and cyclin D1 or affects their localization (nuclear vs cytosolic expression) and thus their function.

Methods:

Placentae were collected from Sprague-Dawley rats at 16, 19, and, 21 days gestation (dg). Beta-catenin and cyclin D1 mRNA and protein expression were studied using real time polymerase chain reaction (ReT-PCR) and Western blotting methodologies, respectively. Protein expression was further studied in homogenates and in both the cytosolic and nuclear fractions.

Results:

There was an increase in placental weight between 16 and 19 dg, but no change was noticed between 19 and 21 dg. Beta-catenin protein expression appeared to decrease significantly only in the cytosolic fraction at 21 dg in comparison to 19 dg. ReT-PCR data also indicated a decrease in beta-catenin and cyclin D1 mRNA expression at 21dg.

Conclusions:

We were expecting, considering our hypothesis, to see an increase in beta-catenin and cyclin D1 expression along with progression of pregnancy, however, a decrease of mRNA and protein expression for both beta-catenin and cyclin D1 was found between 19 and 21 dg, which may explain the stable weight of placenta during this period. The molecular mechanisms responsible for placental growth during pregnancy are complex and may involve more than one pathway to counteract the harmful effects of high estrogen levels.

Key Words: Placenta; Beta-catenin; Cyclin D1

Funding Agency: College of Graduate Studies and Graduate Research Grant #YM05/08

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The Effect of Clothing and Cultural Practice on Bone Mineral Density (BMD) in Kuwaiti Pre-Menopausal Women

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Introduction:

Vitamin D deficiency is one of the most important risk factors in the development of osteoporosis. It is more frequently encountered than expected in the Mediterranean and Gulf countries, which are sunny most of the time. As Kuwait is one of these sunny countries we aimed to investigate the effect of outfitting style on bone mineral density (BMD) in middle-aged pre-menopausal women.

Methods:

Two groups of pre-menopausal single Kuwaiti females (25-35 yrs of age; 20 per study) were recruited in this study. Written informed consent was obtained from each subject. A questionnaire was filled in by all subjects to obtain data including age, sex, mean duration of exposure to sunlight indoors and outdoors/day, past medical history and family history of vitamin D deficiency, and daily dietary intake. The 2 groups were: Group I included females wearing the black veil since puberty and not exposed to the sun. Group II included females wearing the hijab with face and hands exposed to the sun. BMD was measured by dual energy x-ray absorptiometry (DEXA) at the lumbar spine, femoral neck and total body.

Results:

The two subjects were matched for age mean±SD (24.57 ± 3.13 vs 22.9 ± 2.16) and BMI (25.39 ± 7.46 vs 27.11 ± 5.92 g/cm²). The mean total BMD of the two groups were (-0.04 vs 0.41). The T-scores of BMD of total body (-0.04 vs 0.41), L1-L4 spine (-1.4 vs. -1.29), and left femur neck (-0.53 vs -0.48), and they were not statistically different.

Conclusions:

Despite various clothing styles, bone mineral density was not significantly different in pre-menopausal women. This study indeed indicates the need for a larger cohort to be studied and followed up to note if these observation remain at a later age.

Key Words: Bone Mineral Density; Clothing habits; BMI

Funding Agency: College of Graduate Studies and Graduate Research Grant #YM04/08

Expression of Phosphate Transporters mRNA in Intestine, Kidney and Mammary Gland Before and During Lactation.

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Introduction:

Lactation alters phosphate transport in several tissues. This study assesses expression of class II (NaPi2) and Class III (PiT) phosphate (Pi) transporters in control (n=5) and lactating (n=5) female mice.

Methods:

Total RNA from kidney cortex, jejunal and ileal mucosae and mammary gland were extracted (Trizol). Expression of NaPi2 a, b and c, that mediate trans-epithelial transport, and of PiT1 and PiT2 that regulate cell Pi were measured using Real Time PCR (Applied Biosystems), specific primers and Syber Green. . The Cycle threshold (Ct) method (earliest cycle for exponential amplification), using beta-actin as reference, was used to quantify their abundance.

Results:

Beta-actin mRNA abundance was highest in ileum and jejunum(DeltaCt=18), intermediate in kidney cortex and lower in breast(Delta Ct=15). Lactation did not alter ($P>0.1$) beta-actin expression. In kidney cortex, abundances of NaPi2a and PiT1 were 10% relative to beta-actin($\% = 2^{-\text{expDelta DeltaCt}} \times 100$). NaPi2c and PiT2 abundances were 1.5 and 1% respectively, while NaPi2b was absent. With lactation, their decrease were insignificant($P>0.1$). In jejunum, only PiT1 (0.7%) was expressed, consistent with no trans-epithelial Pi absorption in mice jejunum. During lactation, expression of NaPi2a (0.15%) became significant while that of PiT1 decreased($P<0.05$). Ileum expressed PiT1(0.23%), NaPi2b(0.13%) and NaPi2a(0.05%). With lactation, PiT1 and NaPi2b decreased ($P<0.01$)but expression of NaPi2c (0.02%) was higher($P<0.05$). In mammary gland NaPi2a (0.6%), PiT1(0.4%) and PiT2(0.3%) had the highest abundance but NaPi2c(0.04%) and NaPi2b (0.03%) were also detected. With lactation expression of all transcripts except NaPi2b (0.06%), decreased($P<0.01$).

Conclusions:

With lactation, most transcripts had reduced abundance as in response to parathormone or high Pi diet. Exceptions were NaPi2a in jejunum and NaPi2c in ileum where they may mediate Pi absorption and NaPi2b in lactating breasts where it may mediate Pi secretion into milk.

Key Words: Phosphate transporters mRNA NaPi PiT; Lactation; Intestine
Funding Agency: Department. Physiology, General Facility

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Possible Link Between Estrogen Levels, Estrogen Receptors and the Tumor Suppressor Gene P53 during Gestation in Rat Placenta

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Introduction:

Estrogen is essential for initiation and maintenance of pregnancy in the rat. However, high levels of estrogens during pregnancy may have a specific growth-retarding effect on the placenta. Consequently, there has to be a control mechanism that enables the placenta to proliferate regardless of the otherwise high inhibitory levels of circulating estradiol. This may partially be mediated through a decrease in estrogen receptor (ER), which has been reported before, and a parallel decrease in p53 expression as a link between the expression of these two genes has been reported. Therefore, we hypothesize that a decrease in placental ER protein expression correlates with a decrease in placental p53 expression during pregnancy. This study was designed to investigate whether the placental expression of p53 changes during pregnancy in rat placenta.

Methods:

Placentae were collected from Sprague-Dawley rats at 16, 19, and, 21 days gestation (dg). P53 gene expression was studied using reverse transcription real-time PCR (ReT-PCR). Taqman probes specific for our target gene p53 and for two housekeeping genes, 18S and beta-glucuronidase (BGLUC) were used.

Results:

Placentae weight increased significantly between 16 dg and 19 dg and 16 dg and 21 dg, while there was no significant increase between 19 and 21 dg. Both 18S and BGLU were found to be suitable housekeeping genes as their expression was not changed with gestation. The expression of p53 decreased significantly by 19 dg and increased by 21 dg.

Conclusions:

According to our results, we found that the expression of p53 decreased at 19 dg allowing the placenta to increase in weight while at 21 dg the p53 expression increased suppressing placental growth. This was reflected in the weights that we obtained. This is in agreement with our hypothesis when studying the changes at 19 dg.

Key Words: Placenta; p53; House keeping genes

Funding Agency: College of Graduate Studies and Graduate Research Grant #YM019/07

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Evaluation Of Antioxidant And Anti Lipidimic Potential Of Pimpinella Tipatiensis Ethyl Alcohol Extract In Stz Induced Rats

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Introduction:

Diabetes is known to involve oxidative stress and change in lipid metabolism. Many secondary plant metabolites have been shown to possess antioxidant activities, improving the effect of oxidative stress due to diabetes. The present investigation was aimed to evaluate the effect of ethyl alcohol extract of Pimpinella tirupatiensis tubers on antioxidant enzymes and lipid profiles of STZ induced rats.

Methods:

The plant material was extract with 100% ethyl alcohol for 2 days. Albino wistar rats (n=24) were divided into four groups. Diabetes was induced by Streptozotocin injection (ip) at a dose of 60mg/kg. Animal of treated groups were given the dose of 750mg/kg of the extract. The excised rat tissues were immersed in ice cold liquid nitrogen at stored -80c

Results:

The results clearly suggest that the ethyl alcohol extract of pimpinella tirupatiensis tubers possessed antioxidant activity as shown by augmented activities of scavenging enzymes catalase (CAT), superoxide dismutase, (SOD) reduced glutathione (GSH)and glutathione reductase (GR) and decreased in malondialdehyde levels .

Conclusions:

Administration of extract also improved the lipid profile of treated groups indicating there by that the high levels of triglyceride and total cholesteaol associated with diabetes can be also be significantly with the extract.

Key Words: Antioxidant enzymes; STZ; Plant extract

Funding Agency: None

Expression of Nucleoside Transporters in the Rat Heart: Effects of Streptozotocin-Induced Diabetes

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Introduction:

It has been shown in the rat that insulin affects expression of the rat equilibrative nucleoside transporter (rENT)2 and rat concentrative nucleoside transporter (rCNT)1 and 2 in cardiac fibroblasts 1 and adenosine uptake by cardiac myocytes 2. The aim of this study was to explore the effects of streptozotocin(STZ)-induced diabetes in rat on the expression of rENT1 and 2 and rCNT1, 2 and 3 in the heart.

Methods:

Diabetes was induced in Sprague-Dawley rats by an i. p. injection of STZ (60 mg/kg); controls were treated with vehicle. Diabetes was confirmed by plasma glucose >17 mM. Rats were sacrificed after 4 weeks, cardiac muscle samples were frozen in liquid N₂. Real time polymerase chain reaction was used to estimate the threshold cycles for target amplification (Ct) values. The difference between the Ct values for ENTs and CNTs and the Ct values for the housekeeping gene beta actin was calculated (Δ Ct) and the difference between diabetic and control rats tested for significance as explained(3). Data are presented as mean \pm SD from 3 samples.

Results:

The Ct value of beta actin did not differ significantly between the groups ($p>0.05$), so, this gene was used as the endogenous control. In the control group, the mRNA for rCNT2, rENT2, rENT1 and rCNT1 were detected with the Δ Ct 2.4 \pm 0.4, 4.3 \pm 0.3, 7.4 \pm 0.6 and 8.1 \pm 0.1, respectively. The mRNA for rCNT3 was apparently absent. Four-week diabetes has caused significant decrease in the amount of mRNA for rCNT1 ($p<0.05$ vs control) while the amount of mRNA for other transporters did not change significantly.

Conclusions:

The observed changes in rCNT1 mRNA amount may indicate a decrease in the amount of this pyrimidine-preferable transporter in the membrane, which in turn could reduce cellular uptake of pyrimidines in diabetes.

Key Words: Nucleoside transporters; Heart; Diabetes

Funding Agency: None

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Effects of Omeprazole Treatment on Nucleoside Transporters Expression and Adenosine Uptake in the Rat Gastric Mucosa

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Introduction:

An increase in adenosine concentration has been shown to inhibit gastric acid secretion in rat via adenosine receptors. This study aimed to examine the effects of omeprazole-induced achlorhydria on the expression and functional activity of nucleoside transporters in rat gastric mucosa.

Methods:

Wistar rats were treated either for 1 or for 3 days with 0.4mmol/kg omeprazole via gavage; controls were treated with vehicle. The expression of nucleoside transporters at the transcript level and at the protein level were explored by quantitative real time PCR assays and by immunoblotting, respectively. The functional activity of nucleoside transporters was explored by observing [3H]adenosine uptake in vitro.

Results:

Corporeal mucosa expressed rat equilibrative nucleoside transporters (rENT)1 and 2, and rat concentrative nucleoside transporter (rCNT) 1, 2 and 3 at the transcript level. Immunoblots revealed the presence of rENT1, rENT2, rCNT1 and rCNT3 at the protein level. In vitro uptake of [3H] adenosine by gastric mucosa consisted of Na⁺-dependent and Na⁺-independent components. One-day omeprazole treatment caused no changes in nucleoside transporter mRNA levels or in [3H] adenosine uptake. Three-day omeprazole treatments led to a 12-fold and 17-fold increase in rENT2 and rCNT1 mRNA levels, respectively; samples taken after 3-days treatment also took up significantly more [3H]adenosine than samples from the corresponding control.

Conclusions:

The observed changes in rENT2 and rCNT1 mRNA amounts as well as an increase in [3H]adenosine in vitro uptake in rat gastric mucosa after omeprazole treatment could cause reduction in extracellular concentrations of that nucleoside. Modification of nucleoside transport by changes in intraluminal acidity may represent a novel regulatory feedback mechanism to control gastric acid secretion.

Key Words: Gastric mucosa; Nucleoside transporters; Omeprazole

Funding Agency: Kuwait University Grant No MM 06 / 05

Expression of nucleoside transporters in rat cortical astrocytes in primary culture: effects of hypoxia and glucose deprivation

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Introduction:

The aim of the study was to explore the amount of mRNA for rat equilibrative nucleoside transporter (rENT)1 and 2 and rat concentrative nucleoside transporter (rCNT)1, 2 and 3 in the rat cortical astrocytes in primary culture under normal conditions, after 1h exposure to hypoxia (2%O₂, 5%CO₂ in N₂) and glucose deprivation (10mM 2-deoxy-D-glucose (2-DG)) (ischemia group) and after 1 hour exposure to ischemic like conditions, followed by 1 hour exposure to normal conditions (5% CO₂ in the air, 5 mM glucose)(reperfusion group).

Methods:

Primary cultures of rat cortical astrocytes were produced as explained¹. Real time polymerase chain reaction (PCR) was used to estimate the threshold cycles for target amplification (Ct) values. The difference between the Ct values for ENTs and CNTs and the Ct values for the housekeeping gene glyceraldehyde 3-phosphate dehydrogenase (GAPDH) was calculated (Δ Ct) and tested for significance as explained².

Results:

The Ct value of GAPDH did not differ significantly between the control, ischemia and reperfusion groups, so, this gene was used as the endogenous control. In the control group, the mRNA for rENT1, rENT2 and rCNT2 were abundant with the Δ Ct (mean \pm SD, n=5) 4.44 \pm 1.57, 5.04 \pm 0.69 and 1.72 \pm 0.57, respectively. The abundance of mRNA for rCNT1 was less (15.49 \pm 0.32), while the mRNA for rCNT3 was apparently absent. There was a significant increase (p<0.05) in the amount of mRNA for rCNT1 in the ischemia group, with a significant increase in the mRNA for rCNT1 (p<0.01) and for rENT2 (p<0.05) in the reperfusion group.

Conclusions:

Rat astrocytes contain mRNA for all nucleoside transporters, except for rCNT3. The major effect of exposure to ischemic-like conditions and to reperfusion-like conditions was an increase in mRNA for the pyrimidine-preferable rCNT1, which may indicate the importance of pyrimidine uptake under those conditions.

Key Words: Astrocytes; Nucleoside transporters; Ischemia
Funding Agency: Kuwait University Grant No MY 01 / 05

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The Effects of the Streptozocin Induced Diabetes in Rat on the Expression of Tight Junction Proteins in the Choroid Plexus

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Introduction:

The cognitive decline in diabetes may be partially caused by an altered microenvironment in the brain. The paracellular permeability of the blood brain barrier increases in streptozotocin (STZ) induced diabetes 1, as a consequence of altered expression of tight junction (TJ) proteins 2. This study investigated the effects of STZ-induced diabetes in rat on the expression of TJ proteins in the choroid plexus epithelium (CPE), which forms the blood-cerebrospinal fluid barrier (BCSFB) in vivo.

Methods:

Diabetes was induced in Sprague-Dawley rats by i. p. injection of STZ (55mg/kg) and was confirmed by an increased plasma glucose (>17 mM); corresponding controls received a vehicle. After 7 or 28 days animals were sacrificed and choroid plexuses collected. Immunoblotting was performed using the primary antibodies against rat occludin, claudin 1 and claudin 2. The band densities were expressed relative to that of rat beta actin.

Results:

The molecular weights (MW) of rat beta actin, occludin, claudin 1 and claudin 2 are 42kDa, 65kDa, 22kDa and 23kDa, respectively; they migrated in the preparations with an apparent MW ~43kDa, ~64kDa, ~27kDa and ~20kDa, respectively. The relative density of bands are presented in Table 1; there was no significant difference in band densities between 7 and 28 days diabetic rats and the corresponding controls ($p>0.05$).

Conclusions:

Our results indicated that STZ-induced diabetes lasting for 7 or 28 days did not alter the expression of TJ proteins in the CPE at the protein level significantly.

Table 1.

Relative expression of TJ proteins (band density/beta actin band density), presented as mean \pm SEM, n=3.

	7 d control	7 d diabetic	28 d control	28 d diabetic
Occludin	0.36 \pm 0.20	0.21 \pm 0.11	0.24 \pm 0.02	0.21 \pm 0.05
Claudin 1	0.63 \pm 0.20	0.16 \pm 0.08	0.29 \pm 0.06	0.24 \pm 0.01
Claudin 2	1.38 \pm 0.24	0.90 \pm 0.35	0.57 \pm 0.08	0.53 \pm 0.04

Key Words: Choroid plexus; Diabetes; Tight junction proteins

Funding Agency: College of Graduate Studies and Kuwait University

Central Sympatholysis Shifts Heart Rate Oscillations toward Uncorrelated White Noise

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Introduction:

Moxonidine, an imidazoline I1 receptor agonist, effectively reduces blood pressure, particularly in patients with metabolic syndrome X. However, its administration to heart failure patients was associated with increased mortality despite significant reduction of sympathetic overactivity. Changes in non-linear properties of cardiovascular oscillation are strong predictors of all-cause mortality in heart failure patients. Hypothesis was tested that central sympatholysis causes break down of fractal properties as well as decline in complexity of cardiovascular fluctuations.

Methods:

Wistar male rats were implanted with telemetric transmitters to monitor blood pressure and ECG. Moxonidine alone or in the combination with yohimbine or efaroxan was applied s. c. Self-similarity and complexity of interbeat interval (IBI) and systolic blood pressure (SP) time-series were estimated by short and long-range scaling exponents, approximate entropy, Lempel-Ziv entropy, symbol dynamic entropy and percentage of forbidden words.

Results:

All doses of moxonidine (0.04, 0.12, 0.36, 1.08, 3.24 mg/kg) were sympatholytic and made short-range IBI fluctuations less correlated. The largest moxonidine dose that is also parasympathomimetic caused long-range IBI fluctuations to be more similar to the 1/f noise. This dose increased the complexity of IBI fluctuation but reduced the entropy of SP oscillations. Moxonidine has no effect on symbol dynamic with the exception of the largest dose that increased the symbol dynamic entropy and reduced the number of forbidden words. All changes were blocked by pretreatment either with yohimbine, an alpha-2 adrenoceptor antagonist, or with efaroxan, an imidazoline I1 receptor blocker.

Conclusions:

Moxonidine breaks down the short-range fractal (correlated) organization of IBI. Fluctuations of IBI became more random, more similar to the uncorrelated white noise. This change was mediated by both, imidazoline I1 and alpha-2 adrenergic receptors.

Key Words: Moxonidine; Fractals; Heart failure

Funding Agency: This work was supported by Kuwait University Research Grant No. MY02/04.

Annual Treated Psychopathological Morbidity. Demographic and Diagnostic Features Findings from Kuwait Psychological Medicine Hospital 2002

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Introduction:

Despite extensive information obtained from studies on the epidemiology of mental disorders, these have limited capacity to assess in depth the nature and patterns of care provided to patients. In this observational study we have used the records of the Kuwait Psychological Medicine Hospital case register, to report data on the characteristics of psychiatric patients treated in routine clinical settings and to describe psychiatric patterns.

Methods:

All newly opened case notes during the period from 1st of January – 31st of December 2002 were reviewed. A special form was completed for each case note reviewed, which included patient age, sex, nationality, diagnosis, number and type of treatments prescribed, and whether treatment was carried out on an in or out patient basis. The researcher had made sure to read the psychiatrists' notes to make sure that the symptoms listed comply with the diagnosis made.

Results:

Nine hundred and sixty (62.7%) were men. Nine hundred and eighteen (59.9%) were Kuwaitis. The most common diagnostic category (36.6%) was mood disorder, followed by anxiety disorder (12%), schizophrenia (10.1%), acute psychotic episode (7.9%). Non-Kuwaitis were more often given the diagnosis of schizophrenia/acute-psychotic episode (26.1%), compared to Kuwaitis (12.4%). Patients received a mean of 2.83 psychotropic medications. Three hundred and ninety seven required admission (25.9%), where as (74.1%) were treated as out patient.

Conclusions:

Given the rapid evolution of managed care and the changing health care system, it will be critical continue to examine variations in practice associated with system factors (e. g, setting, health plan) and their relationship to patient outcomes. Psychiatric services in Kuwait are rapidly developing and a continuous survey of the services assures providing the best level of care.

Key Words: Psychiatric epidemiology; Psychiatric services; Psychiatric care

Funding Agency: None

Physical, Psychological and Sexual Abuse among a Nationwide Sample of Kuwaiti High School Students: Correlation with Family Characteristics, Anxiety, Depression, Self-esteem and Quality of Life.

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Introduction:

We estimated the lifetime and 12 - month prevalence of physical, psychological and sexual abuse among a stratified random sample of Kuwaiti government high school students, and explored the association of child abuse with parental characteristics, subjective quality of life (QOL), self-esteem and anxiety/depression.

Methods:

They were assessed for experience of abuse by their parents and others, using: a 7-item scale on psychological abuse; 4-item scales on physical and sexual abuse; the 26-item WHOQOL-Bref; and a 13-item scale for anxiety/depression.

Results:

We obtained responses from 4467 students (49% boys), mean age 16.9(SD 1.2) years. About 18%, 15%, and 18%, respectively, indicated that for at least six times in the past 12 months, they experienced psychological abuse by their mothers, fathers and others. The corresponding figures for lifetime experience were similar. The respective figures for experience of physical abuse in the past 12 months were: 4.3%, 5.8%, and 6.4%. The girls had significantly higher physical/psychological abuse scores. There were no significant gender differences in the prevalence of sexual attacks (8.6%) and being threatened with sex (5.9%). The prevalence of someone sexually exposing themselves to the students (15.3%) was significantly higher among the boys. One-third of those abused had experienced multiple abuses. Experience of abuse was significantly associated with parental divorce, diminished QOL and self-esteem, high scores on anxiety/depression, and difficulty with studies and social relationships. Psychological abuse by mothers was the most predictive of QOL, self-esteem, and psychopathology. Good quality of parental relationship seemed protective.

Conclusions:

Child abuse is being experienced by a significant number. Preventive education should include limits on disciplinary measures, the vulnerable groups, the impact on psychosocial functioning, and the protective effect of parental harmony.

Key Words: Physical -psychological; Sexual -abuse; Parents -others

Funding Agency: Kuwait Society for the Advancement of Arab Children (KSAAC): 2006

Psychopathological Status, Behavior Problems, and Family Adjustment of Kuwaiti Children whose Fathers were Involved in the First Gulf War

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Introduction:

Following the end of the First Gulf War, there are no reports on the impact of veterans' traumatic exposure and posttraumatic stress disorder (PTSD) on their children. We compared the severity of anxiety, depression, deviant behavior and poor family adjustment among the children of a stratified random sample of four groups of Kuwaiti military men, viz: the retired; an active –in-the-army group (AIA) (involved in duties at the rear); an in-battle group (IB) (involved in combat); and a prisoners – of- war (POWs) group.

Methods:

Subjects were interviewed at home, 6 years after the war, using: the Child Behavior Index to assess anxiety, depression, and adaptive behavior; Rutter Scale A2 for deviant behavior; and Family Adjustment Device for adjustment at home. Parental PTSD was assessed.

Results:

The 489 offspring (250 m, mean age 13.8 yrs) belonged to 166 families. Children of POWs tended to have higher psychopathological and abnormal behavior scores. Those whose fathers had PTSD had significantly higher depression scores. However, children of fathers with both PTSD and POW status (N =43) did not have significantly different outcome scores. Mother's PTSD, anxiety, depression and social status were significantly associated with all child outcomes. Parental age, child's age and child's level of education were significant covariates. Although children with both parents having PTSD had significantly higher anxiety/depression scores, the mother's anxiety was the most important predictor of child outcome variables. The frequency of abnormal test scores was: 14% for anxiety/depression, and 17% for deviant behavior.

Conclusions:

Child emotional experiences in vulnerable family situations are associated with the particular behavior of significant adults in the child's life. The primacy of the mother's influence has implications for interventions to improve the psychological functioning of children in such families.

Key Words: Anxiety- depression; PTSD -children; Gulf War -Kuwait

Funding Agency: None

Subjective Quality of Life in a Nationwide Sample of Kuwaiti Subjects Using the Short Version of the WHO Quality of Life Instrument.

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Introduction:

The usefulness of quality of life (QOL) as an outcome measure has inspired efforts to establish normative values. The objectives of the study were to: (i) highlight the pattern of satisfaction with aspects of life circumstances among a nationwide sample of Kuwaiti subjects, using the 26-item WHOQOL Instrument (WHOQOL-Bref); (ii) establish QOL domain normative values; (iii) highlight the relationship of QOL with socio-demographic variables, anxiety and depression; and (iv) assess the relationship between domains of QOL.

Methods:

A one-in-three systematic random proportionate sample of consenting Kuwaiti nationals attending the large cooperative stores and municipal government offices in the six governorates completed the questionnaires.

Results:

There were 3303 participants (44.8% m, aged 35.4, SD 11.9). As a group, they were only moderately satisfied with their life circumstances. The domain scores for physical health (14.6 or 66.2%) and psychological health (14.2 or 63.9%) were significantly lower than the mean scores for the WHO 23 - country report ($P < 0.01$). The scores for social relations (15.0 or 68.8%) and environment (14.5 or 65.4%) domains were significantly higher than the corresponding WHO means ($P < 0.01$). The general facet (GF) score (71.6%) was significantly higher than other domains ($P < 0.01$). Lower QOL was significantly associated with female gender, older age, divorce, unemployment, and high scores on anxiety/depression ($P < 0.01$). In regression analysis, depression was the most important predictor of QOL.

Conclusions:

QOL was sensitive to distressing and unfulfilled life circumstances. Hence, a cost effective way of tracking societal distress is by including a brief measure of QOL during national census. Clinicians need to be aware of QOL issues because QOL is associated with clinical and social variables. The difference between GF and the domains has implications for QOL theory.

Key Words: Quality of life; Kuwait; WHOQOL-Bref

Funding Agency: Kuwait Foundation For The Advancement Of Science: 2006

Quality of Life in Schizophrenia: Association with Unmet Needs for Care, Family Burden, Service Satisfaction and Psychopathology

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Introduction:

Schizophrenia is a devastating disease that affects several domains of living. Since quality of life(QOL) is sensitive to distress, it can be used to assess the association of several domains of living with psychosocial outcome. We highlight the subjective QOL profile of a sample of Kuwaiti schizophrenia subjects, in comparison with European data, and examine the contribution of socio-demographic characteristics, unmet needs for care, family burden, service satisfaction and psychopathological symptoms in predicting QOL. The results could inform interventions to enhance quality of care.

Methods:

Consecutive schizophrenia subjects (DSM-IV criteria) in stable condition, and their family caregivers, attending Kuwait's psychiatric hospital, were interviewed with the Lancashire QOL Profile, as well as measures of needs for care, service satisfaction, caregiver burden and psychopathology.

Results:

There were 130 patients(66.1% male, mean age 36.8). 56% felt satisfied with nine domains of life investigated (range 39.5% living situation – 84.1% religion). Majority felt “averagely” happy(44.6%) or “pretty happy” (30%). Staff and patients' rating of subjective wellbeing (58.2, 58.7, respectively) were similar. In stepwise regression analysis, the predictors of total QOL score were: number of children (6%), family income (4.9%), duration of illness (4.3%), social unmet need (8.7%), staff perception of unmet need(12.8%), general satisfaction with services(16.7%), burden of caregiver supervision (5.7%), and negative symptoms(4.8%)(total variance, 52.5%).

Conclusions:

The profile of QOL scores was similar to European data, indicating a comparable standard of care. The relative strength of staff perceptions and patients' service satisfaction indicate the usefulness of staff professional development and service improvement in outcome. Coupled with these, the ideal of a broad based intervention to improve outcome can be narrowed down to the predictors noted above.

Key Words: Schizophrenia -quality of life; Predictors -unmet needs -caregiver; Service

Funding Agency: Kuwait University: MQ01/05

Evaluation of a Studer's Ileal Neobladder After One Year Follow Up

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Introduction:

Objective: The purpose of this study was to evaluate early and late complications; reservoir functional outcome, continence status and upper tract status after one year follow up of Studer ileal neobladder.

Methods:

Thirty - two patients were included in this study and followed at regular interval of three months for one year postoperatively. Early and late complications, urinary continence and upper tract configuration and function were evaluated.

Results:

There was no postoperative mortality. Early and late postoperative complications rates were 28.1% and 12.5% respectively. Out of 32 patients prolonged urinary leakage occurred in 2 patients, unilateral hydronephrosis in 3 patients, urethra-ileal stricture in 3 patients, and metabolic acidosis in one patient. The mean functional pouch capacity increased over time from 298+65 ml at 3 months postoperatively to 423+93 at 9 months of follow up and became fixed thereafter. The mean post voiding residual urine was 46+18 at 6 month of follow up. All patients underwent urodynamic evaluation at 6 and 12 month postoperative. The maximal pouch capacity was 395+75 ml with the pouch pressure at maximal capacity was 30+6 cm water at 6 month postoperative with similar value at 12 month and thereafter. Continence status improved over time. The night time continence rate was lower than daytime. Unsatisfactory night continence that needed more than one pad per night was recorded in 12.5% then reduced to 3.1% at 6 month and 12 months postoperative respectively. IVU at 6 months showed no upper tract ectasia or dilatation in all patients through out the follow up period.

Conclusions:

Studer ileal neobladder is a satisfactory surgical technique of orthotropic urinary diversion. It provides an acceptable rate of postoperative complications with good functional reservoir outcome and continence status while preserving upper tract function.

Keywords: ileal neobladder, diversion, Studer.

Key Words: Ileal neobladder; Diversion; Studer

Funding Agency: None

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Steinstrasse After Extracorporeal Shockwave Lithotripsy: Adan Hospital Experience Using the Siemens Multiline Lithotripter

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Introduction:

Objective: To present the experience in the management of steinstrasse that developed after extracorporeal shockwave lithotripsy (ESWL) using the Multiline lithotripter in Adan Hospital.

Methods:

Between March 2005 and January 2007, 237 patients with renal stones were treated using a Multiline lithotripter. Patients were evaluated four weeks after lithotripsy by plain X-ray film and ultrasonography if required. Twenty-eight patients with steinstrasse were identified and treated. All patients were initially treated conservatively but when there was obstruction, infection or no progression of the stone fragments, further treatment was used. These treatment modalities were repeated ESWL, percutaneous nephrostomy (PCN), endoscopic manipulations and finally open surgery. All patient data, stone and renal characteristics and data of SWL were reviewed.

Results:

The overall incidence of steinstrasse was 11.8%. It was in the lower ureter in 57.1% of the cases, in lower and middle ureter in 25%, in the upper ureter in 14.3% of the patients and the whole ureter was the seat of steinstrasse in one patient. Conservative management was successful in 4 patients (14.3%), repeated ESWL in 9 (32.1%), PCN in one (3.5%), ureteroscopy in 12 (42.8%) and open surgery in one (3.5%).

Conclusions:

Steinstrasse is a well-recognized complication of ESWL. Early diagnosis and meticulous follow-up of patients with steinstrasse should prevent renal function deterioration. When there is obstruction and/or infection or renal impairment, active intervention is indicated. Also, prophylactic pre-SWL ureteral stenting is recommended in certain conditions.

Key Words: Steinstrasse; Shockwave; Calculi

Funding Agency: None

Retrograde Ureteropyeloscopic Holmium Laser Lithotripsy for Shockwave Refractory Renal Calculi

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Introduction:

Shock wave lithotripsy (SWL) has become the standard treatment for renal stones 20 mm or less, while primary percutaneous nephrolithotripsy (PCNL) remains the preferred approach for larger stones. Stone-free rates after SWL are about 70% for all renal calculi but they can be as low as 41% to 55% for lower pole. When stone fragments persist after multiple SWL sessions, they may be too small to justify treatment with PCNL. Although it has a high success rate, the procedure is invasive and harbors potential morbidity. We present our experience with the ureteroscopic laser lithotripsy for treating upper tract stones that were refractory to previous SWL in 23 patients.

Methods:

A total of 23 patients underwent flexible ureteroscopy and laser lithotripsy. They had been treated with a mean of 2.87 previous SW sessions. Mean stone size was 1.23±0.4 cm (range 0.5 to 2.3 cm). Nineteen patients had intrarenal stones, 3 had combined ureteral and renal stones and one had ureteral stone. A 7.5 Fr flexible ureteroscope and a 200-365 μ laser fiber were used via a 3.6F working channel. Holmium-YAG laser was used at an energy setting of 0.8 J and a rate of 5-10 Hz. Success was defined as stone-free status or residual fragments less than 3 mm and it was assessed by postoperative abdominal radiography, CT or ultrasonography.

Results:

The overall success rate of stone fragmentation was 78.2%. Eighteen patients had no stone fragments or residual fragments less than 3 mm that were expected to pass spontaneously. Of the 23 patients 4 had lower pole residual stones > 5 mm in size, 3 of them underwent second ureteroscopic procedure and one underwent PCNL as the stones were not accessible because of lower pole infundibular stricture. After the second treatment, the success rate reached 91.3%. No major complications were encountered in our series.

Conclusions:

Ureteroscopic laser lithotripsy can be used effectively and safely to treat upper tract stones unresponsive to SWL.

Key Words: Ureteroscopy; Shockwave; Calculi

Funding Agency: None

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**New Therapeutic Approaches using Anti-vascular Endothelial Growth Factor (VEGF) in Ophthalmology:
The European Vitreoretina Society Members Survey**

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Introduction:

Human vascular endothelial growth factor (VEGF) is a powerful mediator of vascular permeability as a potent endothelial cell mitogen and angiogenic factor. Targeting VEGF therefore allows a double hit strategy: antiangiogenesis and anti permeability. These two pathogenic mechanisms are in part responsible for severe vision loss in two leading causes of visual disability and blindness world wide; namely age-related macular degeneration and diabetic macular edema. The objective of this study was to identify the pattern of practice using anti-VGEF in different retinal pathologies among vitreoretina specialists focusing on the sight threatening conditions.

Methods:

A web-based self-administered questionnaire was designed for data collection. The questionnaire was used to collect information about the clinical practices of the members of the European Vitreo Retina Society. A total of 115 members responded and the description of their use of Anti-VGEF was evaluated. Coded data from the questionnaire were analyzed using SPSS, version 16, Inc, Chicago, IL, USA.

Results:

The use of anti-VGEF was described by 52% of retina specialists treating diabetic retinopathy and 13.9% indicated using anti-VGEF in combination with focal laser to treat diabetic macular edema. Specifically, 70% used Bevacizumab (Avastin), 10% used Ranibizumab (Lucentis) and 6% used pegaptanib (Macugen). Age related macular degeneration with classic choroidal neovascular membrane was treated with Avastin by 47%, 26% by Lucentis, and a combination of Photodynamic therapy (PDT) and anti-VGEF by 15% of respondents. The retina specialists described their preferred practices in terms of preparation of the ocular injection site, the preoperative anesthesia used and the use of antibiotics before and after injecting the new anti-VGEF agents in different etiologies.

Conclusions:

We are in a very interesting era of anti-VEGF therapy for ocular pathologies as indicated by this practice survey among the members of a specialist professional ophthalmology society.

Key Words: Anti-vascular endothelial growth factor; Age related macular degeneration
Funding Agency: None

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Per-operative End-to-end Anastomosis of the Recurrent Laryngeal Nerve: the Kuwait Experience

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Introduction:

Injury to the recurrent laryngeal nerve (RLN) is disabling and may carry a significant rate of morbidity. There has been a considerable controversy surrounding suturing of the RLN due to the fact that it contains irregularly located and functionally antagonistic nerve fibres. However, a review of the literature and this retrospective study provide meagre evidence of laryngeal synkinesis. Objective: to evaluate the outcome of neuroorrhaphy of the RLN.

Methods:

Six patients who underwent neuroorrhaphy of the RLN at the Al-Jahra hospital between 1996 and 2008 were recruited. The severed nerve was repaired by an immediate end-to-end anastomosis of the RLN. The patients were all subjected to a regular follow-up. The follow-up included the quality of voice, phonation time and the size of the glottic space. Three patients were subjected to stroboscopy. All patients underwent fibroptic laryngoscopy before and after surgery.

Results:

Total patients=6(4=females, 2=males). Age range(24-52 years) with a mean age of 39 years. In all cases there was traumatic RLN section; four surgical (3 thyroidectomies and 1 oesophageal surgery) and two stab wounds. The anastomosis was performed by interrupted, symmetrical epineural sutures using nonabsorbable-8/0-prolene. Operating microscope was utilized in four cases. The glottic gap, quality of voice and phonation time was satisfactory. Near-total recovery of laryngeal function was noted in one patient. Mean follow-up after treatment averaged 9 months.

Conclusions:

Patient satisfaction was high. End-to-end anastomosis of the sectioned RLN preserved muscle tone and minimized muscle atrophy. The result of the procedure was optimized by speech therapy. Operating microscope is an invaluable adjunct. Signs of improved laryngeal function reinforce our belief that neuroorrhaphy of the RLN is a reasonable option. However, the result of this procedure should be approached with vigilant, analytical enthusiasm.

Key Words: Recurrent Laryngeal Nerve; Section; Neuroorrhaphy

Funding Agency: None

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The Value of Second TUR for Superficial Bladder Cancer

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Introduction:

Objectives: We evaluated the necessity of a second transurethral resection of bladder tumor (TURB) in patients with newly diagnosed superficial bladder cancer and its value on subsequent treatment strategy.

Methods:

We performed a prospective study of 72 patients with newly diagnosed superficial bladder cancer in whom 2nd TURB was done 2-6 weeks after initial resection, in the period of September 2006 to December 2007, to evaluate the incidence of residual tumors and adequacy of clinical and pathological staging.

Results:

Of the 54 patients who underwent second resection, 34 (63%) had no tumors, 12 (22%) had visible residual tumors, and 8 (15%) had microscopic residual tumors. Overall residual tumors were found in 20 (37%) patients. Of the 20 patients, 5 had pTa, 8 had pT1, and 7 had pT2 disease. Of residual tumors detected, 80% were high grade tumors (16 cases), and only 20% were low grade tumors. Upstaging and change of treatment strategy due to the result of the second resection occurred in 13 (24%) cases, in which 7 cases (13%) underwent radical cystectomy for muscle invasive tumors.

Conclusions:

Residual tumors could be identified in more than one third of patients with superficial bladder cancer. A second cystoscopy ± TURB is recommended 2-6 weeks after initial resection of stage Ta and T1 bladder cancer.

Key Words: Bladder cancer; Transurethral resection; Second look

Funding Agency: None

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A Comparative Study of Post Operative Outcome Between Ureteral Catheter Insertion, DJ Stenting and Non Stenting after Ureteroscopy for Lower Ureteric Stones.

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Introduction:

Ureteroscopy with or without the use of a lithotripsy is the preferred endourological treatment of distal ureteral calculi. It is common practice in these patients to place a ureteral stent postoperatively. The main advantage of stenting is the prevention of ureteral obstruction and renal colic that may develop as a result of ureteral edema from balloon dilation or stone manipulation during ureteroscopy. However, the incidence of stent related symptoms and/or morbidity have been reported from 10% to 85%. These problems plus the additional cost of a stent have brought into question the necessity for stent placement after ureteroscopy.

Methods:

A total of 160 patients who underwent ureteroscopy were divided into three groups namely ureteral catheter group I (n=52), non-stented group II (n=53), and DJ-stented group III (n=55). Standard ureteroscopic stone extraction with or without intracorporeal lithotripsy was performed through an ureteroscope (Storz, 9.5 Fr) with ureteric dilatation. Tested variables were patients' sex, age, stone characteristics and previous surgery. The operative and postoperative variables were also tested.

Results:

There was no significant difference between the groups with regard to age, sex, or stone burden. Operative time was less in group II & group I than in group III (37.79± 8.93 minutes, 33.77±6.50 minutes and 46.73±9.92 minutes respectively with P<0.05). Dysuria and urgency were similar in group I and group III, but significantly less in group II. Also, average length of hospital stay was lower in group II (28.30±10.81 hours vs. 47.54±15.39 hours in group I and 41.45±15.63 hours in group III with P<0.05). There was no significant difference in postoperative flank discomfort among the study groups (P=0.689).

Conclusions:

In patients undergoing ureteroscopy for distal ureteral stones, stents can be safely omitted, thereby reducing operative time, surgical costs, and patient morbidity.

Key Words: Stents; Ureteroscopy; Calculi

Funding Agency: None

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Active Management of Post-renal Transplantation BK Virus Nephropathy a Preliminary Report

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Introduction:

There is no active treatment for post-renal transplantation BK virus nephropathy (BKVN) that has proved to be effective so far. Leflunomide, intravenous immunoglobulin, ciprofloxacin and cidofovir are still under investigation as active measures for BKVN treatment and our aim was to assess their efficacy on graft outcome after one year.

Methods:

Renal transplant recipients with positive BKV-PCR in urine and blood twice underwent graft biopsy to confirm BKVN. Once BKVN was diagnosed, anti-metabolites (mycophenolate mofetil or azathioprine) were changed to leflunomide and a course of immunoglobulin and oral ciprofloxacin were given.

Results:

Eighteen patients were reviewed, 72% were males, deceased donors were 50%, mean HLA mismatches was 3.6, all patients received induction therapy (61% thymoglobulin) and 61% received antirejection treatment before diagnosing BKVN. Maintenance immunosuppression was mainly prednisolone (93%), MMF as 2gm daily (93%) and Tacrolimus (61%). Baseline mean creatinine clearance (CCI) was 35.6 ± 11.5 which was reduced to 29.3 ± 17.3 ml/min/1.73m² at one year (p 0.012). According to baseline CCI value above and below 40, patients were divided into two equal groups; with mean CCI 44.5 and 25.3 ml/min/1.73m² for group 1 and 2 respectively. At one year, mean CCI was reduced to 42.6 (p 0.229) for group 1 and 16.7 ml/min/1.73m² (p 0.009) for group 2. Three grafts were lost by the end of the study (16.7%), all were in group 2 (p 0.031).

Conclusions:

Late diagnosis and heavy immunosuppression are predisposing factors for development of BKVN. Early active treatment for BKVN may improve graft outcome at one year.

Key Words: Immunosuppression; Viral infection; Graft outcome

Funding Agency: None

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Serial Soluble CD30 Measurement as a Predictor of Kidney Graft Outcome

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Introduction:

Pre and post-renal transplantation high soluble CD30 (sCD30), a marker for T helper 2-type cytokine-producing T cells, is a relevant predictor for development of rejection episodes and may contribute further to the selection of appropriate immunosuppressive regimens in high risk recipients. Objective: To evaluate accuracy of serial sCD30 post-transplantation as a predictor for acute rejection versus other pathology which affect graft outcome over one year.

Methods:

Fifty renal transplant recipients were randomly selected to check sCD 30 at day 0, 3, 5, 7, 14, 21, 1 month, 3 months, 6 months and 12 months post-transplantation. Results were analyzed for development of acute rejection, ATN or other pathology and graft outcome at one year.

Results:

Compared with pre-transplantation sCD30, there was significant reduction of the average sCD30 immediately post-transplantation from day 3 onwards ($p < 0.0001$). One graft was lost due to renal vein thrombosis immediately post transplantation. Patients were divided into four groups: 1- Uncomplicated course (56%), 2- Acute rejection (18%), 3- ATN (16%) and 4- Other diagnoses (10%). There was significant reduction of sCD30 immediately post-transplantation for group 1, 2 and 3 ($p < 0.0001$, 0.004 and 0.002 respectively) but not group 4 (p 0.387). Patients who developed acute rejection after one month had higher pre-transplantation sCD30 value than others who had rejection before one month (p 0.019) with odds ratio 1.649 for the graft loss. All groups had significant improvement of graft function over one year of follow up without significant difference between them.

Conclusions:

Though significant drop of sCD30 post-transplantation is recorded, measuring sCD30 serially post-transplantation didn't help to differentiate between acute rejection, ATN and other diagnoses. In this study, higher sCD30 levels pre-transplantation were reported in patients who developed rejection episodes later than one month of transplantation.

Key Words: Graft rejection; Immunosuppression; Graft outcome

Funding Agency: None

Calciphylaxis Resulting in Penile Gangrene: Presentation and Outcome of Management in Mubarak Hospital, Kuwait

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Introduction:

Calciphylaxis is a rare syndrome characterized by deposition of calcium in soft tissue and blood vessels leading to ischemic tissue loss in patients with end-stage renal failure (ESRF). The purpose of this study is to analyse the mode of presentation of patients with calciphylaxis induced penile gangrene and the outcome of management of this debilitating illness.

Methods:

Patients presenting with penile gangrene secondary to calciphylaxis from 1998 to 2007 were analysed with respect to aetiological factors, mode of presentation, patient characteristics and the outcome of management.

Results:

Ten patients were managed in our Urology Unit in the ten years period. Nine patients had ESRF and were on dialysis at presentation. The disease occurred in one patient within three months of a successful renal transplantation. Poorly controlled diabetes mellitus was a co-morbidity in eight patients. Areas of gangrene were limited to the glans penis in nine patients and extended to the scrotum in one patient. All patients had generalized calcified blood vessels on plain X ray of the abdomen and pelvis. Nine of ten patients had partial amputation of the penis. One patient was too ill for surgical intervention. Six of ten patients were dead within three months of the diagnosis of penile gangrene.

Conclusions:

Penile gangrene due to calciphylaxis is a rare disease seen mostly in patients with ESRF on chronic dialysis. Poorly controlled diabetes is a risk factor for the onset of penile gangrene. The disease has a high mortality and immediate partial or total penile amputation may result in a satisfactory outcome in less than fifty percent of patients.

Key Words: Calciphylaxis; Penile amputation; Penile gangrene

Funding Agency: None

Revision of Failed Bariatric Procedures to Roux-en-Y Gastric Bypass

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Introduction:

Bariatric surgery for morbid obesity has been established as an effective treatment method and has been shown to be associated with resolution of co-morbidities. Despite its success, some patients may require revision because of weight regain or mechanical complications.

Methods:

From September 2005 to August 2008, 19 patients underwent revisional Rou-en-Y gastric bypass (RYGBP). All procedures were performed by one surgeon. Demographics, indications for revision, complications and weight loss were reviewed.

Results:

Sixteen patients were treated with laparoscopic (n=15) or open (n=1) RYGBP after failed LAGB. Two patient were treated with laparoscopic (n=1) or open (n=1) RYGBP after failed VBG and 1 patient underwent open redo RYGBP. Conversion rate from laparoscopy to open surgery was 6.2%. Mean operative time was 182.10+ 31.41 and hospital stay 3.63+1.34. There was no mortality. Early complications occurred in 15.8%. There were no late complications. The mean follow up was 13.10 + 9.55 months. Mean preoperative BMI was 46.07 + 7.48 and decreased to 34.11 + 6.13 and mean %EWL was 34.11 + 6.13 after RYGBP within our follow up period.

Conclusions:

RYGBP as a revisional bariatric procedure is effective to treat complications of restrictive procedures and to further reduce weight in morbidly obese patients.

Key Words: Revisional surgery; Bariatric surgery; Morbid obesity

Funding Agency: None

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Incidence of Lower Limb Deep Venous Thrombosis after Laparoscopic Gastric Bypass: Efficiency of Venous Thromboembolism Prophylaxis

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Introduction:

Bariatric surgical procedures are associated with higher risk of lower limbs deep venous thrombosis (DVT) and pulmonary embolism (PE). Limited data is available regarding the dose of low-molecular-weight heparin for morbidly obese patients. The aim of our study is to determine the therapeutic effect of this dose by measuring anti-Xa and correlate the findings with the incidence of DVT clinically and by color Doppler ultrasound after laparoscopic Roux-en-Y gastric bypass (RYGPB).

Methods:

Prospectively collected data from 8 consecutive patients who underwent laparoscopic gastric bypass patients were reviewed. All patients were given 30 mg enoxaparin subcutaneously once daily preoperatively and continued for 5 days and all patients had sequential compression devices perioperatively. Individuals with previous DVT and heparin allergy were excluded. Anti-Xa level was obtained at second and fifth postoperative day. Anti-Xa level between 0.4-0.8 units/ml was considered appropriate. Diagnosis was based on clinical and color Doppler ultrasound of the lower limb extremity preoperatively and at 5 days and 6 weeks postoperatively.

Results:

There were 6 (75%) females. Mean age was 41 years, mean weight was 142.6 Kilograms and mean body mass index (BMI) was 48.3. The mean operative time and hospital stay was 164.6 minutes and 57 hours respectively. The mean anti-Xa level preoperatively at 2 days and 5 days was 0.12 u/ml and 0.02 u/ml respectively. None of our patients developed evidence of DVT or PE on clinical as well as objective evaluation.

Conclusions:

Prophylactic dose of enoxaparin of 30 mg once daily in Bariatric surgery for 5 days appears to be not adequate to reach therapeutic anti-Xa level. This dose however, was not associated with increased bleeding tendency or increased incidence of DVT both clinically and by color Doppler ultrasound and suggests that obesity might not be a major risk factor for DVT after laparoscopic RYGPB. Further studies are required.

Key Words: Gastric bypass; Deep venous thrombosis; Morbid obesity

Funding Agency: None

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Cause of Burn in Relation to Demographic and Clinical Features among Burn Patients in Kuwait

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Introduction:

The cause of burn and the related characteristics are extremely important to understand its epidemiology and management of burn patients, an attempt therefore, has been made to study all the burn patients, admitted at Al-Babtain Burn Center, Kuwait, during the period 1993 to 2007. The objective was to find the associated demographic and clinical features with cause of burn among burn patients in Kuwait.

Methods:

This prospective study was based on a total number of 3210 burn patients. The data on cause of burn and related available variables; such as, age, gender, nationality, total body surface area (TBSA), duration of hospital stay and patient's outcome, was recorded from inpatients files. The statistical software, SPSS (16.0), was used for analysis and presentation of significant findings.

Results:

The main cause of burn was found to be flame (52.4%), followed by Scald (36.6%) in a total of 3210 burn patients. The median burn % (TBSA) was significantly high ($p < 0.001$) in case of flame as compared to other causes of burns. Burns due to Flame, Electric and Chemical were significantly high ($p < 0.001$) among Males as well as non-Kuwaitis. The median duration of hospital stay, too was maximum (15 days) as compared to other causes (9 days), being significantly higher ($p < 0.01$). There were 94.3% fatal cases due to flame burns alone, among over all deaths.

Conclusions:

Our study showed that flame and scald burns need to be given a high importance, and special public health programs should be conducted to avoid these injuries and fatalities in Kuwait. There is also a need to find new, effective and more efficient treatment modalities to minimise the duration of stay

Key Words: Burns; Causes; Outcome

Funding Agency: None

Oncology

Category: Clinical

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Outcome of Children with Brain Tumors: A 10 Years Analysis from Kuwait Cancer Control Centre (KCCC)

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Introduction:

Central nervous system, or CNS tumors constitute nearly 20 of all childhood tumors. CNS tumors refer to neoplasms that originate in the brain and spinal cord, with over 90% located in the brain. Primary treatment of brain tumors is surgery followed by radiotherapy and or chemotherapy.

Methods:

This is a 10 years retrospective study (1998 -2007). During this period, 74 new cases of primary brain tumors were registered.

Results:

Out of 74 patients, 47 were males (63.5%) and 27 were females (36.4%). Median age was 6 years (range-10 months to 14 years). Fifty two children(70.2%)had infratentorial tumor, while 19 (25.6%) had supratentorial tumor. Medulloblastoma was most common histology(31%) astrocytoma (23%), high grad gliomas(8.1%) and ependymoma (6.7%). Majority of children had only partial excision (67.5), complete excision was achieved in only (14.8%), while no surgery was performed in 17.5%. A total of 47 (63.5%) patients received radiotherapy (RT), no RT was given in 21 (28.4%), while no data was available for 6 patients (8.1%). Chemotherapy was given to 40 patients (54%). The survival analysis was difficult to perform as many of the children were lost to follow-up. However from limited available data, the overall survival (OS) was 92% at 6 months time, which dropped down to 54% in two years time. The median overall survival time was 25 months. There was no statistical significance in survival between male and female patients. For the children who achieved complete remission (CR) after treatment, the disease free survival (DFS) was 50% at 1.5 years time. The median survival time was 14.2 months.

Conclusions:

The treatment of children with CNS tumors is a big challenge for neurosurgeons as well as pediatric oncologists. Achieving a CR status with primary surgery is very important. Late recurrences are common. Radiotherapy and chemotherapy are also important treatment modalities for CNS tumors.

Key Words: Childhood Malignancy; CNS tumors; Radiotherapy

Funding Agency: None

CASE REPORT

Ethical Approach in Introducing Innovative Surgical Techniques: A Case

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CASE REPORT

Background:

Surgery cannot progress without the continuous and creative efforts of its best surgeons constantly exploring how to improve patients' care. Surgeons however need to ethically monitor and guide that progress before exposing their patients to the risks that inevitably accompany the potential benefits of a new procedure or a new use of an existing device.

Case summary:

A 78-year old Kuwaiti lady known to have rheumatic heart disease with mitral stenosis and a fixed thrombus in the left atrium with no clinical manifestation was managed medically. She presented with dense left sided hemiplegia and unconsciousness. CT brain showed infarction of the right temporal parietal and occipital regions with no midline shift. Echocardiographic examination showed a freely floating thrombus clearly resulting in embolization and brain infarction. The patient was referred to the chest diseases hospital and following extensive discussions, surgery with cardiopulmonary bypass was declined due to her poor general condition. She was referred to the interventional cardiologists who suggested a minimal interventional approach with establishing access to the left atrium by a small thoracotomy and inserting catheter directly into the heart. This proposed technique was new and not reported in the literature. The proposed technique was based on utilizing devices that are already being used in routine interventional cardiologic procedures. Several ethical issues were raised by this proposal:

- 1- The loss of decision making capacity as the patient was unconscious.
- 2- The inability of her next of kin to make a unanimous decision.
- 3- The "experimental" nature of the interventional procedure.

Conclusion:

The clinical situation was extensively discussed with the ethicist and other involved staff. In addition, family members agreed to the new technique and they signed a specially designed informed consent for this procedure. The procedure was performed uneventfully with the purpose of the intervention being satisfied.

Key Words: Surgical Innovation; Catheterization; Ethical considerations

Dentistry

Category: Clinical

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RME in Adults

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CASE REPORT

Back ground:

Jackscrew have been used to open the mid palatine suture since 1860 but only since 1950's, the procedure has found wide spread acceptance. Transverse maxillary hypoplasia correction is one of the most complex discrepancies seen and is seen not only in syndromal but also in non-syndromal adolescent and adult patients. Surgically Assisted Rapid Maxillary Expansion (SARME) is generally done in adults after the mid palatal suture have closed with a remarkable amount of discrepancy.

Case summary:

Adult Female Patient 20 years with bilateral complete anterior and posterior crossbite with constricted maxillary arch and labially placed high canine was done non surgically with a hyrax jack screw. Attempting non-surgical RME in the above said situation would normally end up in tipping of the posteriors buccally but in this particular case as the posteriors were tipped palatally added as an advantage to treating this case non-surgically which inevitably led to a favourable and stable occlusion.

Conclusions:

In adult patients attempting expansion by non surgical means could be considered in cases where there is dental arch constrictions due to palatal tipping of the posterior teeth which will lead to a stable occlusion after the expansion. These type of cases should be clinically evaluated before considering SARME.

Key Words: RME; Maxillary Expansion; Cross Bite

Genomic Instability and Rapid Progression in Adult T-cell Leukemia Patient

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CASE REPORT

Background:

Adult T-cell leukemia/lymphoma (ATLL) is a distinct clinical entity characterized by a clonal proliferation of malignant T-lymphocytes. The Human T-cell lymphotropic virus type I (HTLV-I) is believed to be the etiologic agent of the disease. The disease occurs almost exclusively in areas where HTLV-I is endemic, however fewer than 5% of infected individuals develop ATLL. Karyotyping findings and their clinical significance are still limited in ATL, complicated by clinical heterogeneity and a plethora of secondary abnormalities. This study describes detailed cytogenetic and fluorescence in situ hybridization (FISH) findings observed in a patient with ATLL and correlates them with clinical characteristics.

Case summary:

The patient was a 32-year-old woman with two weeks history of pulmonary symptoms and bilateral ankle pain. Laboratory findings revealed elevated white cell count, elevated serum lactate dehydrogenase and abnormal T-lymphocytes in blood smears characterized by the presence of a polymorphous population of lymphocytes with typical flower-like or clover leaf cells (ATLL cells). Karyotyping and FISH from leukemic cells displayed extensive and varied forms of genomic anomalies involving chromosomes 3, 7, 11, 12, 13, 14, 17, 18, 19, 20 and 22. Of these abnormalities, involvement of chromosomes 3p, 17q, 13q, partial trisomy of 7q, del(14) and i(18) has been indicated to be specific for T-cell ATLL. Based on clinical and laboratory findings the diagnosis of ATLL was made, confirmed by a positive HTLV-I serology. She was started on interferon, anti-retroviral therapy and antibiotics but died shortly after the diagnosis.

Conclusions:

This study showed that genomic instability, which is thought to be a major contributor to the HTLV-1 associated ATL, clearly correlated with karyotypic complexity and poor prognosis. To our knowledge the present case is the first reported of ATLL from Kuwait in which these features are associated with HTLV-1 infection.

Key Words: Genomic instability; Adult T-cell leukemia/lymphoma; Flower-like cells

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Renal Cell Carcinoma (RCC): U/S and MDCT SCAN: Can Color and Pulsed Doppler Study Differentiate Between Benign And Malignant Renal

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CASE REPORT

Back Ground:

Renal cell carcinoma is the commonest renal malignancy, comprising 85 % of all malignant renal tumors. It occurs bilaterally in 3-5% of cases, and is the eighth most common malignancy, accounting for 3% of newly diagnosed neoplasms. Most cases arise spontaneously in the fifth to seventh decade. Renal cell carcinoma is seen in about 36% of patients with Von Hippel-Lindau disease. There is also an increased incidence of renal cell carcinoma in patients on long-term haemodialysis.

Case summary:

A 56 years old male patient complained of left renal pain and lower urinary tract symptoms. PRE AND POST CONTRAST SPIRAL MD-CT SCAN: revealed a huge left renal, anterior, lower polar, exophytic, solid mass lesion, just below the level of its hilum, measuring 7 X 8 cm in its dimensions, with claw sign of the rest of the renal parenchyma, showing no calcifications (On Plain CT). After contrast administration, this mass shows immediate 'definite' marked contrast enhancement, on arterial phase with contrast washout on delayed scan, as well as internal breakdown area of degeneration. No evidence of perinephric fat stranding (fogging) detected. No evidence of para-aortic lymphadenopathy detected. Staging of this mass lesion: Stage-I (tumor within the capsule). DOPPLER STUDY, Color Doppler mapping and Pulsed Doppler interrogation: revealed central vascularity with low impedance blood flow, the neovascularity. On U/S: this mass lesion shows a hypoechoic pattern, compared with the rest of renal parenchyma. Radical nephrectomy was done. Diagnosis: RCC.

Conclusion:

All RCCs are, by definition, Adenocarcinomas, derived from renal tubular epithelial cells. RCCs are typically yellow when they are bivalved and are highly vascular, containing a network of delicate vascular sinusoids interspersed between sheets or acini of tumor cells. Angiogenesis occurs as part of the disordered growth of renal tumors. As a consequence it was felt both color Doppler and spectral Doppler might provide a means of assessment of angiogenesis. However, reports are varied in terms of the success of color Doppler in distinguishing between benign and malignant pathology of the kidney. Characteristic color flow patterns are of large irregular marginal vessels extending into the center of the tumor with an abnormal irregular branching pattern. Spectral Doppler may show scattered high-frequency signals both at the margin and within the body of the tumor, presumably representing flow through the vessels supplying arteriovenous communications. Color Doppler flow may refine the ability of real time scanning to evaluate invasion/thrombosis of the renal vein.

Key Words: Renal cell carcinoma; Hypernephroma; Renal Mass

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Can MRI Diagnose Ovarian Dermoid Cysts With Confidence?

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CASE REPORT

Background:

Germ cell tumors are among the commonest ovarian tumors seen in women less than 30 years of age. Overall, only 2-3% of germ cell tumors are malignant. Dermoid cysts (mature cystic teratoma) are the only benign germ cell tumors and are quite common. They are most common in young women with a median age at presentation of 30 years.

Case summary:

A female patient aged 23 years old presented by right loin pain, and lower abdominal “suprapubic” swelling. U/S revealed a complex central pelviabdominal mass, measuring 15 X 13 X 11 cm in its length, transverse and AP dimensions respectively, presenting well-defined regular contour echogenic internal echoes (2/3 of the mass), that showing calcifications as well as floating echogenic internal bodies at its superior aspect with fluid-fluid level appearance. On MRI, these echogenic internal echoes represent fatty component with fat intensity in all pulse sequences giving multilevel fat-fluid level with floating Rokitansky nodules (seen as hyperintense rounded bodies within the mass, giving mosaic appearance at the anterosuperior aspect of the lesion). Associated calcifications are seen as signal void foci on MRI yet clearly seen on plain CT-scan that suggestive to be teeth. This mass lesion was likely to be ovarian origin, from right ovary. Another fatty mass lesion is seen involving the left ovary = 6 X 7cm with multiple Rokitansky nodules. **DIAGNOSIS:** Bilateral Dermoid Cysts.

Conclusion:

Dermoid cysts stem from cells that differentiate into embryonic tissues and account for around 40% of all ovarian neoplasms. MRI can diagnose dermoid cysts with confidence as the fat or sebum within the cyst parallels the signal intensity of fat on all pulse sequences, notably when a Rokitansky nodule/protuberance is depicted within the lesion. Rokitansky nodule/protuberance= oval/round solid tissue mass “sebaceous material around 10 mm (reaching 65 mm) dermoid plug attached to cyst wall. Specifically, by exploiting the precessional frequency differences between and water protons, fat saturation techniques cause the fatty elements to lose signal and are 100 % specific and 96 % accurate in identifying dermoid cysts.

Key Words: Germ Cell Tumor; Dermoid Cyst; Mature Cystic Teratoma

Medicine

Category: Clinical

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**Isolated Sarcoid Renal Granulomatous Tubulointerstitial Disease:
A Case Report**

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CASE REPORT

Background:

Granulomatous interstitial nephritis (GIN) is a rare histologic diagnosis that is present in between 0.5-0.9% of renal biopsies. GIN may be the first manifestation of systemic diseases such as sarcoidosis.

Case summary:

Thirty - seven years old lady presented with lethargy, body aches, arthralgia, and weight loss for three months for which she was using non steroidal anti-inflammatory drugs. There was no arthritis or deformities. Her renal function (RFT) on presentation showed BUN of 15.7 mmol/l, serum creatinine 480 μmol/l, serum corrected calcium 3.17, serum phosphorus 1.7, and serum alkaline phosphatase 68 IU/L. Urine analysis showed no active sediments. Further investigations showed sonographically normal kidneys, negative skeletal survey, normal high resolution CT of the chest and abdomen, negative PPD test. Protein electrophoresis, tumor markers, and immunology screening were negative. Serum angiotensin converting enzyme was high. No Bence Jones proteinuria. Renal biopsy showed normal glomeruli with extensive lymphocytes and multinucleated giant cells infiltration forming interstitial non necrotizing granulomata. Immune staining as well as staining for acid fast bacilli was negative. The possibility of sarcoid granuloma was raised and the patient was started on oral prednisolone 40 mg/d. After one week RFT showed BUN of 11mmol/l, serum creatinine 243μmol/l, serum corrected Calcium 2.79 mmol/l. After one month of treatment RFT as well as serum calcium normalized. Treatment was continued for 6 months then tapered off slowly with stable RFT.

Conclusions:

Sarcoidosis is a multi system disease in which the kidney may be involved. Only 100 cases of isolated renal sarcoidosis have been described. Steroids for 6 months to 1 year usually give an excellent response. So, isolated renal sarcoidosis should be suspected in any case of acute renal failure with hypercalcemia and GIN even in the absence of any systemic manifestation of sarcoidosis.

Key Words: Acute renal failure; Hypercalcemia; Interstitial granuloma

Medicine

Category: Clinical

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Diabetes Mellitus and Retinitis Pigmentosa

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CASE REPORT

Background:

Although the occurrence of diabetes mellitus and retinitis pigmentosa are independently common, four rare syndromes have been reported describing this combination. These include Bardet-Biedl syndrome, Alström syndrome, Kearns-Sayre syndrome, and Wolfram syndrome. Diagnosis can be done clinically based on other manifestations. Molecular genetic testing may be needed for accurate diagnosis and genetic counselling. We describe two cases that presented with diabetes mellitus and retinitis pigmentosa along with other manifestations.

Case 1 summary:

A 34-year-old gentleman presented with insulin resistant diabetes, hypertension, blindness, deafness, and primary infertility. Clinical examination revealed retinitis pigmentosa and normal cognitive functions. Investigations revealed C-peptide level of 2247 pmol/L and macroalbuminuria. His diabetes was gradually improved with increasing doses of insulin along with metformin and subsequently rosiglitazone. Both drugs were discontinued because of liver and renal impairment. Further investigations revealed non alcoholic steatohepatitis. He was diagnosed clinically as Alström syndrome.

Case 2 summary:

A 35-year-old gentleman presented with insulin treated diabetes, hypertension, dyslipidemia, impaired renal function, proteinuria, and blindness. Clinical examination revealed obesity, polydactyly, retinitis pigmentosa, normal cognitive functions, and ataxic gait. C-peptide level was 137 pmol/L. Abdominal ultrasound showed multiple renal cysts. He was diagnosed clinically as Bardet-Biedl syndrome.

Conclusion:

We report two rare cases of diabetes mellitus combined with retinitis pigmentosa. The cases were diagnosed clinically as Alström syndrome and Bardet-Biedl syndrome based on the coexistent clinical manifestations. The use of insulin sensitizers for the management of insulin resistant diabetes in Alström syndrome was restricted by the presence of renal and hepatic dysfunction.

Key Words: Diabetes; Retinitis pigmentosa; Kuwait

Medicine

Category: Clinical

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Eating Epilepsy Refractory to Antiepileptic Drugs

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CASE REPORT

Case History 1:

24 years old Kuwaiti male with H/O epilepsy since age 11. Has generalized tonic-clonic(GTC)seizures initially treated with Valproic acid and Levetiracetam.His seziures were better controlled but at age 21 he started to have new type of seizures : at onset of lunch meal only. Topirimate was added but seizures continued and occur only at lunch meals despite use of 3 antiepileptic drugs. attacks were not related to type or quantity of food ingested.MRI Brain and EEG was normal.

Case History 2:

Thirty-two years old Kuwaiti male with epilepsy since age 10. His seizures were GTC that became controlled on carbamezapine.He had long period of remission. At age 25 developed new type of seizures:daily stereotypic seizures occurring exclusively during lunch meals.He is treated with Levetiracetam and Oxcarbezaoine but attacks are refractory to drugs.MRI Brain normal.Regular and ambulatory EEG WERE normal.SPECT scan :brain perfusion defect in right temporal and left posterior parietal region.

Conclusion:

Seizures induced by eating do not comprise a specific epilepsy syndrome. Rather, eating-induced seizures occur in individuals with symptomatic localization-related epilepsy and considered as reflex epilepsy. seizures may occur at the sight or smell of food, at the beginning of eating a meal,or postprandially.These type of disorders are rare and few case reports in literature was sescribed. Large case series were described and familial in certain parts of Indian subcontinent.In our 2 patients, unlike what described in literature, the seizures are refractory despite absence of structural lesion or localization related pathology on MRI or EEG. Also the occurrence of seizures during lunch only represents a puzzle. We suggest that reflex epilepsy of this type should be considered refractory and search for an underlying pathology should be intense. A consideration for epilepsy surgery is wise step at this stage of the disease.

Key Words: Eating epilepsy; Reflex ; Refractory

Medicine

Category: Clinical

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**A Case of King Cobra Bite in Kuwait: Ethical, Public Health,
and Legal Issues**

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CASE REPORT

Background:

The king cobra is the longest venomous snake in the world. The venom of this snake is neurotoxic, composed mostly of proteins and polypeptides and can kill humans in a single bite. The mortality rate can be as high as 75%. The growing trend toward the collection of exotic snakes by private collectors increases the likelihood that emergency doctors will face the challenge of treating such cases.

Case summary:

A 26 years old Kuwaiti gentleman presented to a hospital medical causality upon being bitten by a "snake". The patient went into complete respiratory arrest and was intubated and shifted to the intensive care unit. He received multiple doses of polyvalent antivenom that antidotes the indigenous snakes in Kuwait with no effect. After initially giving misleading information, detailed questioning of the family members revealed that a smuggled highly toxic King Cobra was the culprit in question and that the patient own more than 180 snakes at his home in a residential area in Kuwait. Tedious actions to locate and bring the specific antivenom from Thailand were taken. Within 30 minutes of administering the antivenom, the patient total paralytic status was reversed. The Patient was successfully extubated and discharged to the general floor the next day. This case raises numerous issues that need careful evaluation and analysis:

- 1- The consequences of hiding information or misleading the medical team.
- 2- The patient did not have the necessary permits to possess these snakes in Kuwait.
- 3- One of the patient's employees was admitted with a snake bite to the same hospital two months earlier without exposing his 'work environment'.
- 4- The conflict between protecting confidentiality and the duty to report any identified public health hazards.

Conclusion:

This is the first reported King Cobra bite case in Kuwait which presents challenging medical, ethical, legal and public health/safety issues.

Key Words: King Cobra; Ethical considerations; Public health and safety

BKV Hemorrhagic Cystitis in Post-renal Transplant Recipient

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CASE REPORT

Background:

BK virus (BKV) is widely spread human polyomavirus that remains latent in the kidney and, possibly, also in the blood. Although virus-induced hemorrhagic cystitis is a frequent complication after allogeneic hematopoietic cell transplantation it is rare after renal transplantation. We diagnosed 2 cases of BKV hemorrhagic cystitis in our center.

Case 1 summary:

A 54 year old man with renal failure secondary to FSGS underwent renal transplantation. His post-transplant course was uneventful with normal graft function. 15 months post-transplant he presented with macroscopic hematuria. Detailed evaluation included urine culture, AFB and cytology, ESR, tumor markers, coagulation profile, immunology screen, ultrasound and cystoscopy, all revealed normal results. Urinary bladder histology showed intranuclear inclusions. Qualitative BKV-PCR was positive in blood and urine. Quantitative BKV-PCR in blood was more than 1000000 copies/ml. A diagnosis of BKV-induced hemorrhagic cystitis was made. Hematuria had disappeared completely after reduction of his immunosuppressive medications.

Case 2 summary:

A 20 years old young man with renal failure secondary to congenital hypoplastic kidneys underwent his third renal transplant 9 years ago with normal graft function. 4 months ago he presented with macroscopic hematuria. Detailed investigations including urine culture, AFB, TB culture and cytology, ESR, coagulation profile, immunology, US, adenovirus PCR, and cystoscopy, all revealed normal results. Urinary bladder histology showed just inflamed urothelium but no viral inclusions were identified. BKV-PCR was positive in blood and urine. By exclusion a diagnosis of BKV hemorrhagic cystitis was made depending on viremia and viruria.

Conclusion:

Although BKV hemorrhagic cystitis is rare in renal transplant patients, it should be considered in the deferential diagnosis of macroscopic hematuria.

Key Words: BKV; Hemorrhagic cystitis; Renal transplant

Medicine

Category: Clinical

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Tuberculosis Presenting as an Erythema-nodosum in a Renal Transplant Recipient: A Case Report

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CASE REPORT

Background:

Erythema nodosum is a cutaneous reaction consisting of inflammatory, tender, nodular lesions, located on the lower extremities. It may be associated with infections, sarcoidosis, rheumatologic or inflammatory bowel diseases, medications, autoimmune disorders, pregnancy, and malignancies. It is rare among transplant recipients. We present a renal transplant case with such lesion.

Case summary:

A 60-year-old lady was suffering end stage kidney disease secondary to chronic pyelonephritis. Hemodialysis was started on Jan 1st, 2003. In June 2003 she received an allograft from an emotionally related living donor, 34-year-old guy with the same blood group and zero mismatches. The primary immunosuppression was fashioned without induction and maintained by triple agents. The transplant procedure was successful and she enjoyed normal graft function. On Nov 2nd, 2008 she developed painful erythematous lesions on the anterior aspects of both lower limbs which clinically were classic of erythema nodosum. The autoimmune disorders were ruled out by the negative results of anti-ds-DNA, rheumatoid factor, ASO, (c&p) ANCA, ANA, C3 and C4, anti-cardiolipin, and B-glycoprotein. However, ESR was moderately elevated. We investigated for infections especially: HBV, HCV, CMV, HIV and EBV and all results came negative. Antibodies against legionella and mycoplasma were also negative. CT chest revealed pleural and pericardial effusion and calcified mediastinal LN. Both tuberculin and TB spot tests were positive, however we failed to isolate acid fast bacilli. So, the patient was managed with empirical anti-TB therapy for 6 months followed by INH prophylaxis for 12 months with complete recovery of skin and chest lesions. She is now enjoying normal graft function.

Conclusion:

TB infection should be considered in the differential diagnosis of lesions suggestive of erythema nodosum in immunocompromised patient.

Key Words: Renal transplant; Erythema nodosum; TB

Medicine

Category: Clinical

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Ulcerative Colitis Presenting with Erythema Nodosum in Renal Transplant

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CASE REPORT

Introduction:

Erythema nodosum is a cutaneous reaction consisting of inflammatory, tender, nodular lesions, usually located on the anterior aspects of the lower extremities. The process may be associated with infections, sarcoidosis, rheumatologic or inflammatory bowel diseases, medications, autoimmune disorders, pregnancy, and malignancies. It is rare among transplant population. We present a case of ulcerative colitis presenting with erythema nodosum.

Case summary:

A 26-year-old gentleman was suffering from end stage renal failure secondary to Ig-A nephropathy. At Aug 13th, 2003, he received an allograft from an emotionally motivated aunt, 44- year-old with the same blood group and zero mismatches. Primary immunosuppression was tailored without induction and maintained by triple drugs. He underwent smooth post-operative course with normal graft function till the middle of March 2008 when he was suffering chronic diarrhea. One month later he developed painful erythematous lesions on the anterior aspect of both lower limbs which clinically were classic of erythema nodosum. Rheumatologic disorders were ruled out by the negative results of anti-dsDNA, rheumatoid factor, (c&p) ANCA, ANA, C3 and C4, and anticardiolipin. HBsAg, anti HCV, anti-CMV, anti-HIV and anti-EBV antibodies all were negative. In spite of high ESR and moderate leucocytosis we failed to isolate AFB and TB spot test was negative. Stool analysis for cryptosporidium was also negative. However, anti- mycoplasma antibodies were positive. Colonoscopy and biopsy revealed left side ulcerative colitis and resolving infective colitis and had no evidence of CMV. Hence, the patient was managed by salazopyrin with marked improvement of both skin lesion and diarrhea and he is doing well till now and maintained on steroid, CsA and MMF.

Conclusion:

IBD should be considered in the differential diagnosis of lesions suggestive of erythema nodosum in renal transplant patients.

Key Words: Renal transplant; Erythema nodosum; Ulcerative colitis

Medicine

Category: Clinical

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Retroperitoneal Fibrosis with Obstructive Uropathy

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CASE REPORT

Background:

Retroperitoneal fibrosis (RPF) encompasses a range of diseases characterized by the presence of a fibro-inflammatory tissue, which usually surrounds the abdominal aorta and the iliac arteries and extends into the retroperitoneum to envelop neighboring structures-eg, ureters. Retroperitoneal fibrosis is generally idiopathic, but can also be secondary to the use of certain drugs, malignant diseases, infections, and surgery.

Case summary:

A 51 year old male patient presented with low back pain with left loin pain for 6 months before admission. Pain started to progress gradually and started to involve right loin also for the last 14 days before admission. He also complained of anorexia and generalized weakness. PMH: Type II DM on OHG. Medications: NSAID for the last 3 months. No abnormality was detected on examination of chest, heart and abdomen. CBC showed leukocytosis with neutrophils predominance, normochromic normocytic anemia and ESR:105. RFT showed renal impairment with Cr: 732, BUN: 30.0 and K: 6.0. CT angio and ultrasound of abdomen and pelvis showed retroperitoneal para-aortic mass encasing and compressing the abdominal aorta, IVC and ureters (likely retroperitoneal fibrosis) with consequent bilateral hydronephrosis. FNAC under CT guidance was done and supported the diagnosis of idiopathic RPF. Patient was treated by corticosteroid, bilateral percutaneous nephrostomy (due to double J stent insertion failure) and he was referred to the urologist for ureterolysis and surgical excision of the mass.

Conclusions:

Prompt diagnosis of idiopathic retroperitoneal fibrosis improves chances of preserving renal function, preventing involvement of other organs, and relieving symptoms. Computed tomography or magnetic resonance imaging helps to exclude secondary causes, but open biopsy remains the gold standard for diagnosis. Management typically includes surgery (ureterolysis, stent placement), and drug treatment (corticosteroids), or a combination of both.

Key Words: Retroperitoneal Fibrosis; Obstructive Uropathy; Corticosteroids

Medicine

Category: Graduate (Resident)

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Tuberculous Meningitis Presenting with Unusual Clinical Features

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CASE REPORT

Background:

Tuberculous meningitis, a serious form of tuberculosis that affects the meninges covering the brain and spinal cord, is associated with high mortality and disability among survivors. The incidence of CNS TB is related to the prevalence of TB in the community, and it is still the most common type of chronic CNS infection in developing countries.

Case summary:

A 40-year-old woman who presented with a 3-week history of weakness of the right upper and lower limbs, a 6-hour history of inability to speak and irrational behavior. She had no remarkable past medical history. Physical examination revealed pyrexia (temperature of 38.2°C) and altered level of consciousness (Glasgow coma score = 7/15). The signs of meningeal irritation were present and she had anisocoria and right spastic hemiparesis. Other aspects of physical examination were normal. Laboratory investigations showed an elevated erythrocyte sedimentation rate, normal cerebrospinal fluid protein and reduced glucose. The brain computed tomography scan showed features in keeping with obstructive hydrocephalus and she was immediately commenced on antituberculous drugs, intravenous steroids and mannitol. She made a remarkable clinical recovery and was discharged home 6 weeks after admission.

Conclusion:

Early diagnosis, antituberculous drugs, adjunctive therapy with corticosteroids and proper management of hydrocephalus should be considered while managing patients with Tuberculous meningitis.

Key Words: Tuberculous meningitis; Corticosteroids; Antituberculous drugs

Medicine

Category: Clinical

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Infliximab-Induced Demyelination

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CASE REPORT

Background:

Tumour necrosis factor alpha is a proinflammatory cytokine involved in lymphocyte signaling and plays an essential role in cell-mediated immunity. It is raised in inflammatory auto-immune diseases such as rheumatoid arthritis and Crohn's disease. Tumour necrosis factor alpha is thought to be an important mediator in these disorders. Anti-tumour necrosis factor agents include infliximab or remicade which is a monoclonal antibody against this cytokine.

Case summary:

We report a 21-years lady, known case of rheumatoid arthritis on methotrexate and hydroxychloroquine for the last 2 years who started to complain of fever, generalised progressive weakness and inability to swallow few days after she received the first dose of infliximab. Neurological examination showed generalised hypotonia with bilateral extensor plantar responses. Initial CT & MRI brain were normal. Lumbar puncture showed elevated protein and lymphocytes. Oligoclonal bands were present in the cerebrospinal fluid and absent in the serum. Culture for fungus and for acid-fast bacilli were negative. Cold agglutination test and brucella agglutination test were negative. PCR for herpes simplex virus in the blood and CSF was negative. ANA & anti DNA were negative. Transthoracic and transoesophageal echo done and showed mild mitral regurgitation and no evidence of vegetations. The patient received third generation cephalosporin, ampicillin, acyclovir and anti-tuberculosis without improvement of the fever. The fever subsided after starting amphotericin. MRI brain was repeated and showed diffuse periventricular signal alteration noted as T2 hyperintensities, scattered hyperintense foci in the left subcortical area of the occipital region, midbrain & both thalami.

Conclusions:

Infliximab is a novel drug for the treatment of rheumatoid arthritis, but it can induce neurological complications in the form of demyelination and although it is a rare complication, it should be used with caution.

Key Words: Side effect of Infliximab; Rheumatoid Arthritis; Meningoencephalitis

Cryptococcus Case

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CASE REPORT

Background:

Cryptococcus neoformans is a ubiquitous yeast that causes disease ranging from subclinical infection of the lungs to severe meningitis. Although infections with *C. neoformans* predominantly occur in immunocompromised hosts, severe cryptococcal infections are rarely encountered in apparently healthy individuals. Here, we report a case of cryptococcal meningitis in an apparently healthy person.

Case summary:

A 69-year-old Afghani male presented with a history of progressive headache, confusion, dizziness, and dysarthria of one month duration. About a month ago, he fell down from stairs with no injury to head. He has been diabetic, hypertensive & smoker for many years, and was diagnosed with benign prostatic hypertrophy. On presentation, he was febrile & conscious, but dysarthric & restless. Kernig's sign was absent & ECG showed left axial deviation & 1st degree AV block. CAT scan of the head showed lacunar infarctions & small vessel ischemic changes. In the absence of any diagnostic clue, the patient was provisionally classified as a case of meningoencephalitis & empirically treated with antibacterial and antiviral drugs for 10 days. Since he continued to remain unwell, anti-TB drugs were started. On day 12, CSF culture yielded a yeast growth which was identified as *C. neoformans*. The patient was started on fluconazole 400 mg OD orally, to which he responded. Although, repeat culture of CSF was negative for the yeast, the patient continued to demonstrate cryptococcal antigen in the CSF and serum. Despite patient's treatment with fluconazole, his urine culture yielded *C. neoformans* suggesting a possible nidus in the prostate. The patient has been started on liposomal Amphotericin B & is doing fine during a two weeks follow-up.

Conclusion:

This case is noteworthy in two respects: firstly the infection occurred in an apparently healthy individual and secondly, the causative species is *C. neoformans*, which predominantly infects immunocompromised individuals.

Key Words: Cryptococcus neoformans; Meningoencephalitis; Fluconazole

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Pneumocystis Jiroveci Pneumonia in Immunocompetent Patient

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CASE REPORT

Background:

Pneumocystis jiroveci pneumonia (PCP) is a potentially life-threatening infection that occurs primarily in immunocompromised individuals. The most significant risk factors for PCP in patients without HIV infection are glucocorticoid use and defects in cell-mediated immunity in addition to cancer, hematopoietic stem cell or solid organ transplantation, primary immunodeficiencies and severe malnutrition.

Case summary:

We report a 3-year-old girl, who is known to have Hereditary Sensory and Autonomic Neuropathy type 2 (HSAN II) with non-resolving pneumonia. She was placed on inhaled steroid and bronchodilator for reactive airway disease but never on systemic corticosteroid. Despite systemic antibacterial therapy she developed progressive hypoxic respiratory failure for which she required intubation and ventilation. Plain chest radiography showed diffuse, bilateral infiltrate. Deep endotracheal aspirate was negative for both bacterial and viral organisms but positive for Pneumocystis jiroveci. She was treated with intravenous Co-trimoxazole for three weeks. She was extubated after few days of initiating the above therapy. Her immunological investigation revealed leukocytosis with no lymphopenia and microcytic hypochromic anemia and mild thrombocytosis. The serum immunoglobulin G, M, A and E were normal for age with normal antibody production for both protein (Tetanus toxoid and Diphtheria) and polysaccharide (H. influenza and pneumococci) antigens. Lymphocyte phenotype was normal in percentage and number for CD3+, CD3+/CD4+, CD3+/CD8+, CD19+, CD15,56+ markers as well as normal lymphocyte proliferative response to mitogen (PHA). She had normal MHC class I and II expression and normal in vitro phagocytic function. HIV antigen / antibody were negative. In addition, autoimmune markers were negative.

Conclusion:

This is a case of Pneumocystis jiroveci pneumonia in otherwise immunocompetent host with no specific risk factors.

Key Words: Pneumocystis Jiroveci; Immunocompetent; Pneumonia

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Generalized Vesicular Rash Caused by an Enterovirus in an Immunocompetent Healthy Individual

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CASE REPORT

Background:

Enterovirus is a group of single stranded, positive sense RNA. They belong to the picornaviridae family. Enteroviruses cause a wide range of infections. They are transmitted mainly via the fecal-oral route. The virus replicates in submucosal tissue of the alimentary tract. Intact humoral immunity is required for control and eradication of enteroviral disease. Most enteroviral infections are mild and resolve spontaneously; however, I.V., intrathecal or intraventricular immunoglobulin have been used with apparent success for the treatment of chronic enteroviral meningoencephalitis.

Case summary:

M.N. is a 35 year old Indian lady. She is working as an educational instructor at the Ministry of Health. She is previously healthy. She presented to Sabah Dermatology Centre with a generalized maculopapular rash, mainly on both lower limbs. Rash was painful and itching. One week later, vesicles, of different stages, started to develop all over the body. There was no fever, no history of contact with individuals with similar presentation, no history of insect bite and no history of recent travel. At the dermatology centre, a biopsy was taken on 23 November, 2008. A diagnosis of leukocytoclastic vasculitis has been reported. A previous clinical diagnosis of varicella-zoster was suggested. Yet, the distribution and the nature of rash fit neither with varicella or zoster. She was referred to Clinical Virology Unit at Mubarak Al-kabeer Hospital and possible enterovirus infection could not be ruled out. A sample of blood, vesicle swab and vesicular fluid were investigated for varicella-zoster, enterovirus, HSV and HHV-6. Enterovirus was detected by PCR in all above samples. There was no other virus detected by PCR.

Conclusion:

We believe that this may be the first generalized vesicular rash reported due to an enterovirus in healthy immunocompetent individual.

Key Words: Vesicular rash; Enterovirus; Immunocompetent

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Peritonitis due to *Neisseria gonorrhoeae* secondary to Tuboovarian Abscess

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CASE REPORT

Background:

Pelvic inflammatory disease (PID) affects approximately 1-2% of young, sexually active women of which, 10% are complicated by the development of tuboovarian abscess (TOA). Cultures taken from abdomens of patients with TOA almost never grow *N.gonorrhoeae* or *Chlamydia trachomatis* although these organisms are often considered to cause the initial insult to the genital tract resulting in PID. The etiology of TOA is polymicrobial with preponderance of anaerobes.

Case summary:

A 43-year-old woman was admitted with a 24 h history of abdominal pain starting in the umbilical region & radiating to right iliac fossa. The pain was associated with nausea, vomiting, constipation, fever & dysuria. The patient had been diagnosed with diabetes mellitus five years back and was receiving hypoglycemic agents ever since. On examination she presented with acute abdomen with sepsis. Empiric therapy with triple antibiotics was initiated & an emergency diagnostic laparoscopy was performed for suspected appendicitis. Although appendix appeared normal there was evidence of pyogenic pelvic inflammation. A sample of pus & a swab of vaginal vault, collected at the time of surgery, were cultured but failed to grow any organisms. However, culture of a sample of fluid drained from the abdominal cavity post-operatively yielded a pure growth of *N.gonorrhoeae*. Even before the culture report was available patient showed signs of improvement & was discharged after 9 days of hospital stay.

Conclusion:

This case is unusual in that no identifiable initiating events for the source of the infection were present. Since a broad-spectrum antimicrobial agent is usually chosen to treat TOA treatment of *N.gonorrhoeae* per se does not pose a problem. However, early recognition of a TOA is important to prevent associated morbidity & mortality.

Key Words: Peritonitis; Tuboovarian abscess; Neisseria gonorrhoeae

**Mass Lesions in the Large Intestine and the Liver:
Tumor Metastases or Infectious Agent**

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CASE REPORT

Background:

Protean clinical manifestations of infectious agents in patients presenting in a non-endemic desert such as Kuwait pose a diagnostic problem. We report a patient with a mass in the cecum and ascending colon interpreted as a tumor with metastases to the liver. The final diagnosis was of an easily treatable infectious agent.

Case summary:

A 67-year old Lebanese male presented with anorexia, poor appetite and weight loss for two weeks. A physical exam showed an upper abdominal mass, possibly a (?) tumor. A search for the primary site led to imaging studies which confirmed a thickened wall on the ascending colon. Endoscopy and colonoscopy showed diffuse ulceration involving the cecum and ascending colon. Provisional diagnoses were (?) lymphoma and (?) tuberculosis. The biopsy at colonoscopy identified “trophozoites of ameba” and he was treated with oral Metronidazole. The serology was in the significant range too. The patient was discharged but readmitted later with no change in the size of the amebic liver abscess (ALA). The lesion was drained and a follow-up CT showed the abscess had decreased markedly in size. Significant laboratory results that suggested ALA were the high WBC count on initial presentation, elevated alkaline phosphatase and liver enzymes. The pathology findings and serology were compatible with invasive amebiasis. The clinical impression of a tumor arose initially after the colonoscopy. However, the travel history to Saudi Arabia during the Haj pilgrimage, the initial presentation, the presence of trophozoites in the colon, the serology and the ALA were all compatible with the symptoms.

Conclusions:

This case illustrates that amebiasis is easily spread in large gatherings. It is incumbent to rule out a treatable infective agent such as *Entamoeba histolytica* thereby sparing the patient the agony of a presumed tumor that had metastasized

Key Words: Tumor; Metastases; Amebiasis

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Neoscytalidium Dimidiatum as a Cause of Cutaneous Pheohyphomycosis Identified by Molecular Methods: First Case Report from Kuwait

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CASE REPORT

Background:

Neoscytalidium dimidiatum (*Scytalidium dimidiatum*) is a dematiaceous ascomycete belonging to the family Botryosphaeriaceae. The production of both arthroconidial and pycnidial (*Nattrassia*) synanamorphs had led to the taxonomic and nomenclatural controversy in the correct identification of the species. To overcome this identification enigma, a new genus *Neoscytalidium dimidiatum* for isolates of *S. dimidiatum* has been proposed with type species *Neoscytalidium dimidiatum*. Here, we describe a case of cutaneous pheohyphomycosis in a 30-year-old Bangladeshi male caused by *N. dimidiatum*.

Case summary:

The fungus was isolated from the skin biopsy of the lesions present on the planter surface. The identity of the isolate was established by typical colonial and microscopic morphology and by DNA sequencing of the internal transcribed spacer (ITS) region of rDNA. The genomic DNA from the isolate was prepared and the ITS region (ITS-1, 5.8 S rRNA and ITS-2) of rDNA was amplified by using ITS1 and ITS4 primers. The amplicon was purified and both strands were sequenced. Results: The culture of the skin scrapings yielded a dark grey mold, which grew slowly attaining a diameter of 14 mm in one week on Sabouraud dextrose agar. The isolate was provisionally identified as *Scytalidium* species as it formed pigmented arthroconidia in chains. A BLAST search of ITS region DNA sequence showed nearly 100% identity (only one and two nucleotide differences) with the corresponding sequence from *N. hyalinum* (GenBank accession no. AY213688) and *N. dimidiatum* (GenBank accession No. EU597630), respectively. Thus, molecular identification based on DNA sequencing confirmed the identity as *N. dimidiatum*. The patient was successfully treated with topical application of clotrimazole cream.

Conclusion:

To the best of our knowledge, this is the first report of cutaneous *N. dimidiatum* infection diagnosed by phenotypic and molecular method in Kuwait.

Key Words: *Neoscytalidium dimidiatum*; *Cutaneous pheohyphomycosis*; *Molecular identification*

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**Posaconazole-Resistant *Mucor Circinelloides*, a Dimorphic Pathogen,
as a Cause of Invasive Maxillofacial Zygomycosis**

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CASE REPORT

Background:

Zygomycosis is a life-threatening infection in immunocompromised patients associated with high mortality. Since, the drug of choice, amphotericin B, is associated with significant nephrotoxicity, posaconazole has been suggested as a first-line therapy for zygomycosis. Here, we report a case of maxillofacial zygomycosis caused by posaconazole-resistant *Mucor circinelloides* isolate.

Case summary:

The infection had developed following the teeth extraction and the fungus was isolated from the debrided maxillary tissue. On the basis of characteristic morphological features, it was provisionally identified as a *Mucor* species. Molecular identification was achieved by direct DNA sequencing of internally transcribed spacer (ITS) region of rDNA and of D1/D2 region of 28S rRNA gene. Drug susceptibility testing was performed by E-test. Results: Lactophenol-cotton blue examination of the isolate showed circinate lateral branches of sporangiophores and chains of thick-walled chlamydospore. The conversion of the isolate into yeast forms showed bipolar and multipolar budding structures. The ITS region amplicon of ~600 bp, amplified with panfungal ITS1 and ITS4 primers, was sequenced and BLAST search of DNA sequence data revealed complete identity (100%) in ITS-1 and ITS-2 regions with corresponding sequences for several strains of *M. circinelloides*. Similarly, ~700 bp amplicon of D1/D2 region of 28S rRNA obtained with NL-1 and NL-4 primers was sequenced and BLAST search revealed nearly complete identity (1 or 2 nucleotide differences) with the corresponding sequences from two strains of *M. circinelloides*. The isolate was found to be resistant to posaconazole but susceptible to amphotericin B, and treated successfully with liposomal amphotericin B and surgical debridement.

Conclusions:

The report highlights the emerging role of *M. circinelloides* in invasive zygomycosis and cautions about using posaconazole as primary therapy without prior susceptibility testing.

Key Words: Mucorcircinelloides; Maxillofacial zygomycosis; Posaconazole resistance

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**Prolonged Progression Free Survival with Recurrent Cancer Colon Patient
Receiving Bevacizumab (Avastin) Maintenance: A Case Report**

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CASE REPORT

Introduction:

Bevacizumab is a humanized monoclonal antibody targeting VEGF. VEGF is a critical determinant of tumor angiogenesis, a process that is a necessary component of tumor invasion, growth, and metastasis. In 2004, FDA approved it in first line metastatic colorectal cancer with chemotherapy. (1-2)

Case summary:

We report a case of a forty-four year old Kuwaiti woman who had no known co morbidities. On October 2004, she experienced 4 months duration of constipation with exacerbations of abdominal colic responded partially to medical symptomatic treatment. On November 2004, colon mass adherent to urinary bladder (UB) dome on left side were detected. She had left hemicolectomy with partial cystectomy. Pathological examination revealed PT4PN2M0 moderately differentiated adenocarcinoma. On December 2004, she was impacted on postoperative adjuvant FOLFOX-4 for six months between late December 2004 and early June 2005. She was regular and her tolerance was acceptable. She had experienced peripheral neuropathy (PN) G II, nausea and vomiting G I-II and neutropenia G II-III. All were manageable. On December 05; about one year disease free survival; she had relapsed locally as documented by CT scan and PET scan showing right common iliac LN enlargement. It was not resectable as noted by KCCC onco-surgeons. Between early March 2006 and September 2006, she received six courses of FOLFIRI + Avastin. She tolerated the treatment in acceptable way. She got neutropenia GII and G IV, diarrhea GI-III and mucositis GI-II. Response achieved as partial response (PR). Thereafter; she had stable disease (SD). Because of poor compliance and tolerance shifted to Xeloda + Avastin. For 4 courses and she had G III hand and foot syndrome affecting her QOL. She received Avastin alone from January 2007 to November 2008); around two years of maintenance. She achieved three years of PFS (Dec. 05 - Nov 08). There were a series of CT scans to evaluate the response to maintenance Avastin (Jan. 07 to Nov 08) all showing maintaining the response. On September 2008, she developed elevation of blood pressure to 160/100 (GII). It was uncontrolled even by two antihypertensive drugs combination. So, we were obligated to stop Avastin.

Conclusion:

The antiangiogenesis effect of Avastin may produce a prolonged stabilization of cancer. This might support the idea of maintenance in one arm and on the other hand support the need for further investigation for a better ways to have antitumor effect synergistic with that static effect of Avastin. In this case, the use of Avastin alone after stoppage of chemotherapeutic agents succeeded to maintain the achieved partial response up to two years.

Key Words: Avastin; Colorectal; Cancer

Oncology

Category: Clinical

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Complete Remission in Renal Cell Carcinoma using Half the Standard Dose of Sorafenib: A Case Report.

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CASE REPORT

Background:

Clear subtype represents nearly 85% of RCC. Until recently, systemic treatment options for metastatic RCC were limited to cytokine therapy and clinical trials of novel agents with poor outcome. Although cytokines (IL-2 and IFN) have been standard of care for about 15 years, recently targeted therapy utilizing tyrosine kinase inhibitors have shown excellent results. It is now used as first and second line treatments for metastatic, recurrent, or unresectable clear cell RCC. To date, three such agents have been approved for the treatment of advanced RCC: Sunitinib, Sorafenib, and Temsirolimus. Sorafenib is a small molecule that inhibits multiple isoforms of the intracellular serine/threonine kinase Raf (including c-raf and b-raf) and also other receptor tyrosine kinases, including VEGFR-1, VEGFR-2, VEGFR-3, PDGFR-#946, Flt3, and c-kit. We report as case of renal cell treated with Sorafenib and achieved complete response.

Case summary:

Sixty - seven old lady with multiple co-morbid illnesses was diagnosed with renal cell carcinoma in May 2007. She had left radical nephrectomy. Histopathology was read as Renal Cell Carcinoma, clear cell type, grade II, tumor measured 11.5 X 10 X 10 cm, tumor emboli seen in renal vein, renal capsule was infiltrated, with extracapsular extension. All the removed 6 lymph nodes were free of disease. Staged as pT3N0Mx. Post opertively she was found to have suspicious lung metastases. Follow up evaluation in October 2007, showed progressive lung metastases. She was started on Sorafenib. She had grade 3 skin and GIT toxicity, and hence dose had to be reduced by 50%. She achieved complete response inspite of receiving half the recommended dose.

Conclusions:

The patient achieved complete response with Sorafenib in this patient with Renal cell cancer, which otherwise has got a dismal prognosis. The dose of Sorafenib had to be reduced by 50% because of side effects, but the complete response could be achieved even with half the recommended dose.

Key Words: Renal cell carcinoma, Sorafenib, Nexavar, Complete remission

Pathology

Category: Graduate (Resident)

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Colonic Diverticula with Tubular Adenomas

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CASE REPORT

Back ground:

Occasionally, colonic diverticula coexist with an adenoma and a carcinoma, but only one study mentioned an adenoma at the outer mouth of a ceecal polyp. We describe a case of colonic diverticula, with tubular adenomas at the mouths of each diverticula.

Case summary:

A 74-years old male patient presented as an emergency case of fresh bleeding per rectum for one day duration. The patient was hypertensive and had had a stroke. Nuclear study confirmed active bleeding at the distal end of the transverse colon. A left hemicolectomy with primary rectocolic anastomosis was performed. The resected colon was 29 cm long. The mucosa showed 9 diverticula with no perforation. At the mouth of all but one diverticulum a polyp was identified, eight in total (6 pedunculated and 2 sessile). Histopathological examination showed multiple diverticula associated with tubular adenomas lined by moderately to severely dysplastic epithelium without stalk invasion.

Conclusion:

A rare case of multiple colonic diverticula with tubular adenomas arising at the mouth of the diverticula. Keywords: diverticular, adenomas.

Key Words: Diverticular; Adenomas; Pathology

Pathology
Category: Clinical

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Intravenous Leiomyomatosis of the Uterus

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CASE REPORT

Background:

Intravenous leiomyomatosis (IVL) is a rare neoplasm characterized by nodular masses of histologically benign looking smooth muscle cells growing within uterine or extrauterine venous system. The exact etiology is unclear and benign histological appearance of neoplastic smooth muscle can be deceptive since IVL might behave in a malignant fashion. Total abdominal hysterectomy and excision of any extrauterine tumor if technically feasible is the cornerstone of treatment.

Case summary:

We report clinical, histological, and immunohistochemical features of a uterine IVL in a 48 year old lady who presented with menorrhagia. The etiopathogenesis and differential diagnosis of this entity are elaborated.

Conclusion:

Knowledge about IVL is essential for adequate treatment and differential diagnosis. Although it imitates a malignant neoplasm regarding its pattern of growth and extension, it must be differentiated from malignant tumors to prevent overtreatment. Long term follow up is recommended in these cases.

Key Words: Intravenous ; Leiomyomatosis; Uterus

Proximal-type Epithelioid Sarcoma in the Groin Presenting as a Diagnostic Dilemma

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CASE REPORT

Background:

Proximal-type epithelioid sarcoma is an uncommon soft tissue sarcoma, which occurs in pelvic and genital area of young adults and tends to behave more aggressively than its conventional counterpart. A correct diagnosis is essential since this tumor often closely resembles other epithelioid lesions such as extrarenal rhabdoid tumor, malignant melanoma or poorly differentiated carcinoma. CASE

Case summary:

A 47-year-old man presented with a painless swelling in the right groin. Local examination revealed a hard, mobile mass that extended to the scrotum. CT scan demonstrated an enhancing mass lesion in the right groin extending to the perineum. A fine needle aspiration of the swelling revealed cellular smear with loosely cohesive tumor cells seen singly, in loose aggregates, at places surrounding fibrovascular connective tissue. The cells were round to oval with moderate to abundant eosinophilic cytoplasm which appeared vacuolated in some cells. The tumor cells stained strongly positive for cytokeratin and CD34. A cytologic diagnosis of a poorly differentiated malignant tumor, possibly an epithelioid sarcoma, was rendered. The tumor was excised. On microscopy, the tumor was composed of sheets of large epithelioid cells with vesicular nuclei, prominent nucleoli and abundant eosinophilic cytoplasm. Many cells had abundant clear cytoplasm. Mitotic rate was low. The cells exhibited strong reactivity for cytokeratin, EMA, vimentin and CD34, while stains for smooth muscle actin, calretinin, S-100 protein, HMB-45, CD31 and CD117 were negative. Based on these morphologic and immunophenotypic profile, a diagnosis of 'proximal-type epithelioid sarcoma' was entertained.

Conclusion:

The present case highlights the difficulty in diagnosing proximal-type epithelioid sarcoma as it has a bewildering array of histologic mimics. Its aggressive behavior underscores the importance of a correct diagnosis, which can be achieved by judicious utilization of a wide panel of immunohistochemical markers.

Key Words: Epithelioid sarcoma; Proximal type; Rhabdoid phenotype

Phyllodes Tumor of the Vulva

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CASE REPORT

Background:

Phyllodes tumor is common in the breast, where it accounts for less than 1% of breast tumors. Extramammary phyllodes tumor has been reported in various ectopic sites, including axilla, prostate and seminal vesicles. We report an extremely rare case of phyllodes tumor of the vulva in an 18-year-old girl.

Case summary:

An 18-year-old girl presented with a slowly growing painless mass in the vulva of one year duration. Local examination revealed a mass in the left labium majus that approximately measured 6 cm. It was nontender, nonulcerated and freely mobile. The lesion was excised and submitted for pathologic examination. Gross examination of the specimen revealed a well-circumscribed globular mass measuring 5.5 cm in diameter. Cut surface showed frond-like masses of firm tissue projecting into small cystic spaces. Microscopic examination showed the lesion to be composed of stromal proliferation lined by epithelium, forming broad leaf-like projections surrounding cystic spaces. The epithelial lining was predominantly secretory type, without any atypia or mitotic activity. The stroma was sparsely cellular, predominantly composed of fibrovascular tissue. Cellular areas were composed of monomorphic spindle shaped cells with vesicular nuclei. There were no mitoses in 50 high power fields. There was no evidence of stromal overgrowth, necrosis or areas of hemorrhage. Immunohistochemistry revealed the epithelial cells to be reactive for estrogen receptor, progesterone receptor and GCDFP-15. Based on these classic morphologic features, a diagnosis of phyllodes tumor of the vulva was made.

Conclusion:

The present case illustrates a very rare example of extramammary phyllodes tumor. Current evidence suggests that such mammary-like lesions are most likely to be derived from 'specialized mammary-like glands' in the anogenital region, rather than arising from ectopic breast tissue derived from the embryonic milk ridge.

Key Words: Phyllodes tumor; Vulva; Aberrant breast tissue

**Lymphoepithelioma-like Carcinoma of the Urinary Bladder
: Report of a Rare Case**

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CASE REPORT

Background:

Lymphoepithelioma is the term used for describing an undifferentiated carcinoma of the nasopharynx, histologically characterized by presence of prominent lymphoid aggregates in the background. Carcinomas with similar histologic features arising outside the nasopharynx are called lymphoepithelioma-like carcinoma (LELC), which are reported in various organs such as thymus, salivary gland, cervix etc. Involvement of the urinary bladder by LELC is uncommon. We present a case of pure LELC of the urinary bladder to highlight the significance of recognizing this unusual tumor.

Case summary:

A 65-year-old man presented with history of recurrent hematuria for several weeks. Computed tomography scan revealed a soft tissue tumor mass in the right posterolateral aspect of the urinary bladder wall. Transurethral resection of the tumor was attempted. The biopsy was reported as LELC with infiltration into the muscularis propria. Subsequently radical cystectomy was performed. Specimen revealed an ulcerated tumor mass measuring 3x3x1.5 cm at the right posterolateral wall of the bladder. On microscopy, the tumor was composed of diffuse sheets and cords of undifferentiated cells having large pleomorphic nuclei with coarse chromatin. Many of the nuclei had prominent nucleoli. The cytoplasm was scant with poorly defined borders. Background showed dense lymphoplasmacytic infiltration. The tumor cells were positive for pan cytokeratin (CK) CK7, CK 8 and epithelial membrane antigen but negative for chromogranin, vimentin and desmin. A diagnosis of pure LELC with evidence of muscular invasion was entertained.

Conclusion:

LELC of the bladder is rare and should be ruled out in bladder biopsies, which show dense lymphoid infiltrate. The differential diagnosis is usually lymphoma, poorly differentiated invasive transitional cell carcinoma with lymphoplasmacytic background. Existing data suggest the pure form responds well to chemotherapy and has better prognosis.

Key Words: Lymphoepithelioma-like carcinoma; Urinary bladder; Cytokeratin

**Extensive Epididymotesticular Malakoplakia:
A Case Associated with Diabetes Mellitus**

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CASE REPORT

Background:

Malakoplakia is an uncommon but distinctive type of chronic granulomatous inflammation, characterized by the presence of sheets of histiocytes with granular cytoplasm (von Hansemann cells) admixed with intracellular and extracellular basophilic laminated inclusions (Michaelis-Gutmann bodies). The disease mainly affects the urinary bladder. We report a case of extensive malakoplakia that involved both testis and epididymis.

Case summary:

A 67-year-old Saudi man with history of poorly controlled diabetes-mellitus presented with pain and swelling of the left testis of 2 weeks duration. Local examination revealed an enlarged, tender left testicular mass that was fixed to the scrotal skin. Ultrasonography of the left testis revealed a well-defined testicular mass of mixed echotexture, which involved the entire testis. Left inguinal orchiectomy was performed. On gross examination of the excised specimen, there was an ill-defined necrotic area measuring 2.5 cm in diameter. The surrounding area appeared fibrotic. On microscopy there was diffuse replacement of testicular parenchyma by large areas of abscess formation, necrosis, areas of fibrosis and dense inflammatory infiltrate, comprising sheets of histiocytes with granular eosinophilic cytoplasm, admixed with neutrophils, lymphocytes and plasma cells. Many of the histiocytes contained small round to oval targetoid structures, morphologically consistent with Michaelis Gutmann bodies. Stains for calcium (von Kossa), iron (Prussian Blue) and periodic acid-Schiff reaction highlighted these targetoid inclusions. These histologic findings were characteristic of malakoplakia.

Conclusion:

The present case highlights the importance of diagnosing malakoplakia when it occurs at unusual locations. Such an extensive malakoplakia occurring at an unusual site in association with systemic illness lends support to the view that a compromised immune status could be etiologically important in malakoplakia.

Key Words: Malakoplakia; Testis; Epididymis

Pathology

Category: Clinical

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Pyomyoma in a Postmenopausal Woman: A Case Report and Review

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CASE REPORT

Background:

Pyomyoma or suppurative leiomyoma is a rare condition since the use of antibiotics began with only 23 cases reported in the past 63 years. Most cases occur in relation to pregnancy or in postmenopausal period. Out of the 7 post menopausal women with pyomyoma, 4 had associated diabetes.

Case summary:

A 61 year old diabetic woman presented to the Surgical Emergency department with abdominal pain and constipation for which she had been investigated. She was found to have a pelvic mass and a normal upper and lower gastrointestinal endoscopy. During her hospital stay, she developed septic shock and acute renal failure for which she was managed conservatively. The Ultrasonic examination of the pelvis revealed a mass of heterogeneous echo pattern in the uterus. CT-scan of the abdomen and pelvis showed heavily calcified uterine mass measuring 14.5 x 17 x 17.5 cm with mild ascites. She was referred to the Gynecology Department and laporatomy was performed on her. During the surgery, multiple intrabdominal adhesions and a 20 week size uterus with a friable uterine wall, mainly at the fundal part, were seen. An iatrogenic opening was made during the manipulation of the fundal part from which purulent and necrotic material came out. A total abdominal hysterectomy with bilateral salphingo-oophorectomy was done and the uterus was sent for frozen section, which revealed a benign smooth muscle tumor with necrotic areas. The permanent H and E stained slides showed benign pyomyoma of the uterus.

Conclusion:

Pregnant/ post partal and post menopausal women with diabetes are vulnerable to develop pyomyoma with its complications and therefore should be treated early. Delaying the surgery for postmenopausal patient with a pelvic mass and a normal gastrointestinal workup would not be in patient's favor. Although mortality in pyomyomas was up to 30 percent before 1945, the overall mortality has shown a declining trend with the early diagnosis and antibiotic treatment.

Key Words: Pyomyoma; Postmenopausal; Review

Pediatrics

Category: Graduate (Resident)

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Spontaneous Chylothorax in a Neonate with Trisomy 21: A Case Report

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CASE REPORT

Background:

Spontaneous Neonatal Chylothorax is a rare but serious and life threatening condition. Chylothorax is an effusion of lymph (chyle) in pleural space. Congenital causes could be due to malformation / disruption of the lymphatic system. We present a Neonate with Trisomy -21, and AV canal defect, who developed spontaneous Chylothorax

Case summary:

A baby boy born to a 45 yrs old mother, by spontaneous vaginal delivery, at 37+5 weeks of gestation with good apgar score. (8-9-10). He showed features of Down's syndrome. Later it was confirmed with Chromosomal analysis. (Trisomy, 21-xy) He developed Congestive Heart failure due to AV canal defect and put on antifailure treatment. (Lasix/Aldactone/Captopril). Umbilical canulation or any other invasive procedures had not been carried out. He developed Pleural effusion spontaneously on day 34, when he was on full feeds, given through Orogastric tube mostly EBM. Thoracosyntesis was carried out and 55 mls. of Pleural fluid aspirated, and kept on continuous chest drainage. Chemical analysis of the fluid showed a very high Triglyceride content, conforming "CHYLOTHORAX" most probably due to congenital malformation of lymphatic system. He continued to drain out about 100 to 125 mls of fluid/day, Somatostatin infusion 3.5 ug/kg/hour commenced on day 44, and MONOGEN formula (containing high MCT fat), feeds were started on day-46. He showed improvement, in the form of reduced pleural fluid drainage, and consistency.

Conclusion:

Chylothorax, collection of lymphatic fluid in the pleural cavity, in neonates is not common but does occur which could be traumatic or Congenital (non traumatic). Congenital Chylothorax (Pulmonary Lymphangiectasia) could be sporadic or genetically determined developmental anomaly of lymphatic system, resulting in pulmonary lymphatic obstruction. It can occur as a part of multiple congenital anomalies in disorders like Down's, Turner and Noonan syndromes.

Key Words: MCT; AV canal; Trisomy-21

**Conservative Management of Early Intracardiac Thrombus
in a Preterm Infant: A Case Report**

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CASE REPORT

Background:

Central venous catheters are commonly used in low birth weight and critically ill infants with increased incidence of thrombotic events.

Case summary:

We are presenting a case of Preterm infant delivered by cesarean section at 29weeks of gestation with a birth weight of 750 gms. The baby had been actively resuscitated with intubation and put on ventilation for RDS followed by administration of Surfactant. the umbilical lines were introduced and well positioned soon after birth (fig1). He developed right sided pneumothorax which has been drained successfully. On day 3 of life during the routine echocardiography (ECHO) study a thrombus of size 10 x 5 mm (fig2). in the right atrium had been noted. The thrombus was not attached to the tip of the catheter. It was therefore decided that the catheter should be removed to avoid dislodgement. It was then decided to have a conservative approach for the management of this thrombus based on reports and to avoid the side effects of the thrombolytic agents. Thrombolytic therapy, was NOT used. A follow up was planned with weekly CardiacEcho. The thrombus was completely resolved in about 43 days (fig3). The infant was discharged at age of 73 days, in good clinical condition and on follow up by (ECHO) no evidence of thrombus noted with good cardiac function.

Conclusion:

The intracardiac thrombus formed as a complication of umbilical catheters in premature neonates can be managed successfully with a conservative approach so as to avoid Side effects of Thrombolytic agents.

Key Words: Fig; Echo; RDS

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Abscess of the Abdominal Wall Resulting from Perforated Ascending Colon Cancer: A Case Report

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CASE REPORT

Background:

Complicated colorectal carcinoma has several symptoms, most commonly being bleeding and obstruction. Occasionally it will cause perforation and rarely as remote abscess in the abdominal wall.

Case summary:

A 62 years old male came to our casualty complaining of painful red swelling over the right loin for 1 month, with history of chronic constipation and significant weight loss. Examination of the trunk showed a firm non-fluctuant tender mass 7×5 cm in diameter located in the right loin with an overlying area of cellulitis. Abdominal exam. revealed a fixed, non tender hard mass in the right iliac fossa. No organomegaly nor any enlarged lymph nodes were palpable. Rectal examination was normal. Stool: positive for occult blood. CBC: Hb of 8.9 g/dl and leucocytosis. CEA: elevated. Abdominal CT: right-sided colonic mass adherent to the lateral abdominal wall with infiltration of the subcutaneous tissue by the tumor, and formation of a subcutaneous abscess. Diagnosis of ascending colonic cancer complicated by an anterior abdominal wall abscess was made. Exploratory laparotomy was performed. Right colonic mass approximately 9×8 cm in diameter was found which was adherent to the lateral abdominal wall, with extension through a fistulous tract into the posterior abdominal wall muscles and subcutaneous tissue. No distant metastases were found. Extended right hemicolectomy and lymph node dissection with en block resection of the involved part of the lateral abdominal wall. Pathology revealed moderately differentiated mucinous adenocarcinoma. Lymph nodes were free [0/13]. The margins of the resected specimen were free of cancer cells. The patient had an uneventful post-op recovery and the abdominal wall cellulitis disappeared fully.

Conclusion:

Abdominal wall cellulitis and abscess should always raise the suspicion of an intra abdominal pathology, especially malignancy. Therefore a complete abdominal examination including rectal examination and stool for occult blood and CT of the abdomen should be done.

Key Words: Perforated colon cancer; Abdominal wall cellulitis; CT scan

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Injury to the Abdominal Aorta During Laparoscopic Cholecystectomy: A Case Report

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CASE REPORT

Background:

Laparoscopic cholecystectomy has become the gold standard for the treatment of uncomplicated symptomatic cholelithiasis, furthermore, the indications for this minimally invasive procedure for gallbladder removal have been expanded to include acute, chronic and acalculous cholecystitis, mucocoele and empyema of the gallbladder, as well as gallstone pancreatitis. However, this technically demanding procedure has many advantages, but sometimes life-threatening complications. We report a case of injury to the abdominal aorta during laparoscopic cholecystectomy.

Case summary:

A 27 years old woman, was scheduled for an elective laparoscopic cholecystectomy because of recurrent attacks of biliary colic, Ultrasound of the abdomen showed multiple gall bladder stones, she has no previous medical illness. Laparoscopic cholecystectomy started with the patient in supine position. The pneumoperitoneum was created by insufflation of carbon dioxide via an easy inserted Verres needle through infra-umbilical puncture, A disposable sheathed 10-mm trocar was inserted straight into the peritoneal cavity while grasping the skin, initially there was moderate resistance at the fascial layer, followed by sudden plunging of the trocar into the abdominal cavity. Upon removing the stylet from the trocar a moderate amount of blood was noted in the sheath. A laparoscope was introduced and a large amount of blood was noted to be pooling around the omentum. At this point the patient became hypotensive, the procedure is immediately converted to a midline vertical laparotomy. The source of hemorrhage was identified after meticulous suctioning and irrigation and controlled. The aorta was found to have 6-mm defect in the anterior wall, few millimeters above the origin of renal arteries, the posterior wall was intact, the anterior defect was then closed.

Conclusions:

The case is presented because of its rare complication.

Key Words: Aortic Injury; Laparoscopic Cholecystectomy

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Squamous Cell Carcinoma of the Gall Bladder Masquerading as a Liver

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CASE REPORT

Background:

Gall bladder cancer is usually discovered after cholecystectomy as the usual clinical presentation is that of gall stone disease. Its more common in females (F:M 3:1). It is the 5th most common malignancy of G.I tract. Most commonly it is an adenocarcinoma (85%). Only 3% are squamous cell carcinoma and 1.5% are adeno-squamous carcinomas. An elevation of CA-19.9 level is the most helpful diagnostic test. We present a case which presented with signs and symptoms of a big liver abscess with normal CA-19.9 levels.

Case summary:

A 35 years old, Bangladeshi lady was admitted to the medical ward as a case of non-biliary acute pancreatitis complicated by bilateral pleural effusion. CT-Scan showed a hypodense gallbladder bed lesion 3.7 x 4 cm suspected as small abscess. She improved and was discharged home. She presented to the emergency room a year later with fever and leukocytosis and a very tender mass in the right Hypochondrium. She was admitted to the surgical ward as a suspected case of liver abscess. LFT were abnormal and CT scan suggested a big liver lesion with central liquefaction and necrosis in continuity with the GB, highly suggestive of a liver abscess. Tumour markers, CA-19.9 was normal and serology for amebiasis and hydatid disease were negative. FNAC revealed only necrotic tissue. Percutaneous drainage produced turbid fluid of about 150 ml/day. Cytology from fluid was negative for malignancy. She remained septic despite drainage and i.v. antibiotics. After 2 weeks an exploratory laparotomy revealed a big tumour originating from GB and involving the whole right liver lobe, it was inoperable. Biopsy from the lesion later showed squamous cell carcinoma of GB. The patient remained septic and died after 2 weeks.

Conclusion:

A case of primary squamous cell carcinoma of G.B. presenting as liver abscess.

Key Words: Gall bladder; Squamous cell carcinoma; Liver abscess

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Renal Allograft Dysfunction Due to Graft Sarcoidosis

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CASE REPORT

Background:

There are only very few case reports of sarcoidosis with graft granulomatous interstitial nephritis. We describe a case of graft dysfunction which presented with granulomatous interstitial nephritis due to sarcoidosis.

Case summary:

The patient was a 58 year old-Kuwaiti lady who underwent live related renal transplantation on May 2005 in USA. She had received kidney from her son, with Alemtuzumab (Campath 1H) as induction therapy. She was maintained on tacrolimus monotherapy with stable graft function until May 2008 and her baseline serum creatinine was 90 to 100 $\mu\text{mol/L}$. On May 2008 she presented with graft dysfunction with serum creatinine 190 $\mu\text{mol/L}$. She had past history of a cerebrovascular accident, deep venous thrombosis and mesenteric vascular occlusion with protein C and protein S deficiency. Later during the year 2005, she developed end stage renal disease. Her native kidney disease was unknown. In the same year she went to USA for a live related transplantation from there. During the time of pretransplant workup, they detected a nodular opacity in the right lung apex. The biopsy report showed giant cell infiltration. She had multiple mediastinal lymphadenopathy and elevated liver enzymes. The liver biopsy showed noncaseating granuloma. She underwent successful renal transplantation. Her urinalysis and complete blood counts were normal. Present CT chest was normal except a small calcified strand at apex of right lung. The graft biopsy revealed multiple non caseating epithelioid granulomas with mononuclear infiltration in the interstitium. We excluded the possibility of tuberculosis by negative tuberculin test, non reactive TB spot and negative sputum AFB and urine AFB culture. We diagnosed this case as sarcoidosis and treated her with prednisolone 40 mg daily. After 5 weeks of treatment her serum creatinine came down to 89 $\mu\text{mol/L}$.

Conclusion:

Sarcoidosis in graft kidney is an unusual and treatable cause for graft dysfunction

Key Words: Graft dysfunction; Sarcoidosis; Interstitial Nephritis

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One Patient, Two Lymphomas, Three Primaries: A Collision Tumor of Marginal Zone Lymphoma and Adenocarcinoma of Ascending Colon with Simultaneous Primary Follicular Lymphoma in the Terminal Ileum: A Case Report

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CASE REPORT

Background:

Concomitant adenocarcinoma and non-Hodgkin's lymphoma(NHL),both located in the intestinal tract,are unusual.Moreover,collision tumors of the colon are extremely rare neoplasms.A case of true collision tumor of a marginal zone lymphoma and a moderately differentiated adenocarcinoma of the ascending colon (hepatic flexure) and a follicular lymphoma involving the terminal ileum is reported.

Case summary:

A 67 years old Egyptian male admitted with adhesive intestinal obstruction and successfully treated conservatively.Patient gave a history of laparotomy in Egypt in 2003 with no report available.Investigations:Stool occult blood +ve,Hb 12.2g/dl,albumin 25g/l.Ultimately CT abdomen showed: irregular thickening of ascending colon and hepatic flexure with multiple adjacent enlarged lymph nodes + thickening of the terminal ileum wall and ileocecal valve and dilated ileum.Tumor markers:normalrange.Colonoscopy:obstructing mass at the hepatic flexure and the ascending colon.Patient underwent exploratory laparotomy.Intraoperative findings:mass in hepatic flexure,palpable mesenteric lymph nodes, 3 anastomoses from previous surgery.Extended right hemicolectomy with lymph node dissection was performed with end to end ileocolic anastomosis.Final pathology report:adenocarcinoma lying on a NHL.7 mesenteric lymph nodes were identified and normal.The terminal ileum also demonstrated the presence of another type NHL.Immunohistochemistry of the lymphomas indicated that the terminal ileum displayed BC I2 +ve follicular lymphoma; colon showed marginal zone lymphoma that was BC I2 -ve.Both types of NHL were CD20 +ve.The patient had an uneventful postoperative recovery and he was referred to KCC for further adjuvant therapy.

Conclusion:

Accurate identification and recognition of both components of the collision neoplasm is important in guiding decisions regarding overall prognosis,adjuvant therapeutic options,and survival which may be dependent on either of the components.

Key Words: Collision tumor; Adenocarcinoma; Lymphoma

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Fulminant Wound Infection Due to Group A Streptococcus with Multi-Organ Dysfunction Occurring After Thyroid Gland Lobectomy.

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CASE REPORT

Background:

Group A streptococcus (GAS) can lead to severe infection of subcutaneous and deep tissues post surgery resulting in high morbidity and mortality secondary to necrotizing fasciitis and toxic shock syndrome. These conditions are rare after clean surgeries but may develop in patients with pre-existing co-morbid conditions. In order to reduce the severity of infection aggressive therapy including antibiotics and surgical intervention should be instituted without delay. We report a case of fulminant wound infection with multi-organ dysfunction developing in a healthy patient after thyroid lobectomy.

Case summary:

A 39-year-old male patient underwent right lobectomy for a solitary follicular thyroid lesion without any preoperative antibiotic prophylaxis. 48 h after surgery he developed neck pain and fever. Examination revealed swelling and cellulitis in the neck with pleural effusion and deranged renal function tests. Clindamycin was started and an immediate neck exploration with evacuation of infected hematoma and sloughed superficial and deep tissues was done followed by irrigation of wound with normal saline every 4 h. Pus culture yielded growth of GAS and treatment with penicillin was initiated but when defervescence was not achieved after 48 h it was replaced with tigecycline. Patient improved and was discharged after 21 days of hospital stay with good healing of wound and no residual renal or respiratory dysfunction.

Conclusion:

To the best of our knowledge this is the first case of post-thyroidectomy GAS fulminant wound infection in Kuwait. Although few cases have been reported in the literature with mortality of >50% despite intensive care and aggressive surgical treatment, there is no consensus on appropriate surgical therapy. Tissue desloughing by frequent irrigation of the wound has not been described before. The importance of close clinical and laboratory monitoring and appropriate antibiotic therapy in the management can't be overemphasized.

Key Words: Group A streptococcus (GAS); Thyroidectomy; Wound infection

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Double Appendix

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CASE REPORT

Background:

Double appendix is a rare disease of gastrointestinal tract which is mostly discovered incidentally during surgery and may be associated with other congenital diseases. Duplication of vermiform appendix is reported to have an incidence of 0.004%. The majority of them are diagnosed at surgery or on postmortem examination.

Case summary:

A 30 years old female patient presented to Al- Jahra hospital in Kuwait on 10th of July 2008 with right lower abdominal pain of one day duration associated with vomiting. Examination showed multiple pigmentation of skin especially in the abdomen . also accessory nipple (polythelia) is noted & scoliosis of the vertebral column,localized tenderness and rigidity with positive rebound tenderness in right iliac fossa . WBC 24.800 Ultrasound abdomen showed fibroid uterus with localized collection in right iliac fossa & appendix measuring 6 mm .diagnostic laparoscopy was done on the day of admission which revealed minimal fluid in the pelvis with one blind ended structure in continuity with caecum (appendix) , dissection of appendix & clipping at base was performed & during dissection of mesoappendix another blind structure which also in continuity with the caecum was incidentally discovered and diagnosed as double appendix and laparoscopic appendectomy was performed. Histopathological diagnosis was vermiform appendix duplex, with features of appendicitis & periappendicitis .

Conclusion:

Double appendix is a rare finding and may associated with other congenital anomalies, further researches should be performed to discover associated anomalies.

Key Words: Double appendix; Appendecitis; Conginital anomaly

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