Anatomy
Category: Undergraduate

1

Prevelance, knowledge and use of diet pills among Kuwait University students

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Introduction:
To determine the prevalence of using diet pills, evaluate the knowledge and study the perceived adverse effects of using diet pills among Kuwait University female students.

Methods:
Cross-sectional sample survey conducted in September 2006 including 426 female students from Kuwait University. Faculties of Medicine, Education, Science, and Sharea were chosen to be involved in the study. Data were collected using a self-administered questionnaire including sociodemographic characteristics, knowledge about diet pills, and use of diet pills.

Results:
The prevalence of using diet pills among Kuwait University female students was found to be 12.6 %. Socioeconomic status was significantly associated with the use of diet pills, $p < 0.001$. One third of diet pills' users belong to high social class compared to18.6 % of non-users. The study found that herbal diet pills were the most popular type as 65.5 % of respondents reported awareness about them. Friends and relatives were the most reported source of obtaining information about diet pills (73.5 %). Significantly higher proportion of diet pills' users reported mass media, physicians and pharmacist as source of information than non-users ($p=0.002$ and <0.001 respectively). Gastrointestinal adverse effects were mainly among Xenical users and herbal diet pills users. Half of both appetite suppressants' users and fat burners' users reported cardiovascular adverse effects. More over, appetite suppressants' users reported respiratory, nervous, and psychological adverse effects. Nausea and headache were significantly associated with longer duration of diet pills' use, $p=0.04$ and 0.036 respectively. In Medicine, 24 % of responding female students were on diet pills compared to 12 % in both Science and Education, while 11.6 % of Sharea female students were on diet pills. Most of users got their pills Over-The- Counter (53.7 %) followed by "prescription" (44.4 %).

Conclusions:
The prevalence of using diet pills among Kuwait University female students was similar to other countries. There is a need to conduct a larger study to estimate the prevalence of using diet pills in the general population.

Funding Agency: None

Anatomy
Category: Clinical

2

The impact of bilateral nephrectomy in blood pressure pattern and control in renal transplant patients.

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Introduction:
Severe hypertension prior to renal transplantation has traditionally been an indication for bilateral nephrectomy (BN). Nevertheless the impact of BN on the prevalence of hypertension after successful renal transplantation has not been will documented. Purpose: to clarify the effect of bilateral nephrectomy on blood pressure pattern and control in renal transplant patients.

Methods:
We retrospectively reviewed 24 patients who underwent bilateral native nephrectomy between November 97 and January 06, 22 of them were under treatment with antihypertensive medications according to the international guidelines. Out of the 24 cases 15 operated for resistant hypertension as group 1 (G1), 9 patients with indications other than hypertension collected in-group 2 (G2). Nephrectomy was done either simultaneous, before or after transplantation. All patients received triple immunosuppresion according to the local protocol, calcinurein (CNI), mycofinolate mofetil (MMF) or azathioprine, and prednisolone. Antihypertensive therapy was evaluated before and after BN. Acute rejections (ACR) as will as CNI nephrotoxicity episodes were recorded.

Results:
In G1 mean age was 30.2 years (range 10 to 62), 5 patients had acute rejection episodes (33.3%) and 3 episodes of CNI nephrotoxicity (20%); in G2 mean age was 33.67 years (range 11 to 61), 2 patients had ACR episodes (22%), and two had CNI nephrotoxicity (22%). Patients in the G1 used (3.6+1.05) (Mean+SD) antihypertensive drug/day before BN., which is significantly higher than in the G2, (2.0+1.65) drugs/day (p=0.02). Three months after nephrectomy it came down to (2.69+0.94) drugs/day in G1, and remained (2.0+1.29) drugs/day in G2. After BN in G1 the difference is sustained at one year with further reduction of the antihypertensives at three years (1.46+1.33) drugs/day. Statistical significance difference between figures before and after BN in G1 was found only at three years (p=0.008). No Statistical significance between G1 and G2 after BN. In G2 Number of drugs shows an insignificant difference of (2.2+1.49) at one year, and (1.62+1.30) drugs/day at three years.

Conclusions:
We concluded that BN in renal transplant patients could result in better control of resistant hypertension, and its complications are within acceptable ranges.

Key Words: Bilaterla nephrectomy; Hypertension; Kidney transplantation
Funding Agency: None

Anatomy
Category: Clinical

3

Blue rhino single dilative percutaneous tracheostomy

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Introduction:
Amongst the percutaneous dilative techniques, Blue Rhino dilative tracheostomy is most popular, safe and efficient technique performed in ICU. It is a modification of Ciaglia sequential dilator technique involving a single step, curved hydrophilic coating dilator.When softened with water coating becomes lubricious, greatly reducing friction. This prospective randomized study was carried out to evaluate how much this technique would be easy, safe and cost-effective one when performed at the bed side of the patients on ventilator in ICU.

Methods:
10 adult patients free from fracture of cervical vertebrae, enlarged thyroid, short neck and abnormal coagulopathy were selected and consent was obtained.Under constant monitor of vital signs, endotracheal tube was deflated and withdrawn 1cm under fibreoptic bronchoscope and monitor until the puncture site below cricoid cartilage was freely accessible. The patient in thyroidectomy position, 1.5 cm horizontal skin incision was made aseptically over 2^{nd}-3^{rd} tracheal rings. 14Gcannula was inserted vertically and caudally through the center of incision till the tip of cannula could be seen through monitor.After removing stylet, seldinger wire was passed through cannula inside the trachea.The introducing 14French dilator was advanced over the wire in twisting motion to dilate initial access site and removed. Placing Blue Rhino over guiding catheter, its distal tip was positioned at safety ridge on the catheter. Blue Rhino with water for hydrophilic action and catheter as a unit was advanced over the wire under constant vision. Whilst maintaining correct alignment to dilation assembly, gradual dilatation of the tracheal stoma was started by advancing unit as a whole in downward and caudal direction inside trachea till the broad black skin line on it was level with skin. After 30 sec it was withdrawn leaving catheter and wire in situ. The lubricated tracheostomy tube 8mm which snagged tightly over loading dilator was advanced over catheter and wire advancing into the trachea. Loading dilator, catheter and wire were withdrawn.The tracheostomy tube was placed in position and confirmed endoscopically. It was inflated, fixed and anchored firmly.

Results:
Patient's age was in the range of 27-86yrs. Nine patients were male and one was female. The procedure was quick, easy and took about 4-8 min (puncture of trachea to insertion of tracheostomy tube). All patients underwent percutaneous tracheostomy successfully (100%) without any serious complication.

Conclusions:
Percutaneous dilator tracheostomy with Blue Rhino is quick, safe, cost-effective and easy to perform at the bed side alternative to surgical tracheostomy with minimal complications.

Key Words: Ciaglia Blue Rhino dilator; Prolonged intubated (ICU)patients, fibre-optic
Funding Agency: None

Anatomy
Category: Clinical

4

Awake fibreoptic bronchoscopic nasotracheal intubation for predicted difficult intubation patients.

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Introduction:
Over the last 4decades anaesthesia related morbidity and mortality have declined but airway catastrophes continue to be represented in most anaesthesia deaths.Airway maintenance is fundamental to safe anaesthetic practice.Preventive crisis management should be the objective. Difficult or failed intubation may lead to hypoxia, aspiration, trauma or death.Awake FOBNI is one of the safest techniques for difficult intubation.

Methods:
Twenty five patients (ASA I-II) gave consent for the study. During preanaesthesia checkup these patieints were assessed and predicted as Difficult Intubation. Tab.dormicum 7.5mg was given orally 2h before procedure.In OT after getting I/V access with18G, patient's vital signs were monitored. Patient's nostrils were instilled with Xylometazoline (0.1%) lying supine with extension of head. Lignocaine (10%) was sprayed into nostrils and oropharynx. Preoxygenation was carried out for 3min.The patient was sedated with dormicum 3mg I/V. An Olympus FOB 3C10 or F1 loaded with ETT 7mm, fixed at its proximal part. It was inserted gently into right nasal passage till epiglottis and vocal cords were visualized. Three ml of 2%xylocaine was instilled through the suction port into the glottis during deep inspiration. After 20s it was advanced into the trachea instilling 3ml 2% lignocaine into the trachea till it reached carina. Patient was sedated with propofol 50 mgI/V.ETT was released and threaded over it into the trachea in an anticlockwise fashion till it reached above the carina and anchored it firmly. ETT was connected with Magill's circuit.

Results:
Patient's age was 24-58yrs. Time taken from bronchoscopy to connection of ETT with Magill's circuit was 2-3min. There were no marked changes in pulse and BP.None of the patients developed hypoxaemia during the procedure SaO2 being 96- 98%.

Conclusions:
Skill of FOBNI will enable the anaesthetist to overcome expected or unexpected difficult airway. Every anaesthetist should try to acquire this technique by learning first in Mannequin, then in normal patients. So if any difficult intubation occurs, it can be solved in time.

Key Words: Difficult intubation; FOB and Technique; Nasotracheal intubation
Funding Agency: None

Anatomy
Category: Undergraduate

5

Student application of selective outcomes measures and psychomotor skills related to the shoulder conditions for clinical orthopedic training in physical therapy

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Introduction:
Evidence based practice is important to improve the quality of patient care and for a practitioner to attain fine clinical skills in order to make critical decision in everyday health care practice. Evidence based practice is currently implied in the training of the physical therapy (PT) students' at Kuwait University. The aim of this study was to determine the ability of PT students' enrolled in basic clinical orthopedic education, to utilize selected outcome measures and psychomotor skills learned in practical sessions to manage patients with shoulder joint pathologies.

Methods:
The clinical orthopedic education booklets of PT students' over a six year period were reviewed. Students' application of psychomotor skills such as peripheral joint mobilizations (PJM), proprioceptive neuromuscular facilitation (PNF) techniques, therapeutic exercises, as well as utilization of basic outcome measures such as range of motion (ROM) and pain were analyzed using SPSS.

Results:
Descriptive statistics show that the majority of students' used PJM techniques (78.57%) and PNF techniques (58.57%). At the same time all the students' used therapeutic exercises following PNF and PJM. The most common comparable joint sign is shoulder abduction, which accounted for 44% of patients seen by the students.

Conclusions:
Emphasizing evidence-based practice in the PT curriculum has been extremely useful in the way students' solve problems during the patient encounter in the treatment of shoulder conditions.

Key Words: Evidence based practice; Outcome; Treatment of shoulder pathologies
Funding Agency: None

Anatomy
Category: Basic Sciences

6

Immunohistochemical localization of adrenergic receptors in the rat organ of Corti

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Introduction:
We previously reported the existence of nerve fibers in the organ of Corti (OC) containing dopamine beta-hydroxylase, an adrenergic marker (ARO Abstr. 28: 226, 2005), and the presence in the OC of norepinephrine itself (ARO Abstr. 26: 12, 2003). However, the identity and localization of adrenergic receptors (ARs) in the cochlea are uncertain.

Methods:
In the current study, we present the immunolocalization of alpha1, beta1, and beta2 AR subtypes in the cochlea of the adult ACI Black Agouti rat.

Results:
For the alpha1 AR subtype, immunoreactivity was detected overlapping apical and basal sites of the inner hair cells (IHCs) in the basal turn, but no immunoreactivity was detected in relation to the IHCs in the middle and apical turns. Immunoreactivity was observed in close association with the outer hair cells (OHCs) in middle and apical turns, occasionally overlapping Deiters' cells. For the beta1 AR subtype, immunoreactivity was detected in close association with the IHCs in all turns. The immunoreactivity was also present in presumed nerve fibers at the base of the OHCs, overlapping Deiters' cells, but the OHCs themselves appeared devoid of immunoreactivity. Immunoreactivity for the beta2 AR subtype was strongly associated with IHCs. Immunoreactivity was detected around the basal poles of the OHCs in the middle and apical turns, possibly associated with nerve fibers, and in the region of Deiters' cells in all three turns. Within the spiral ganglion, type I afferent cell bodies were immunoreactive for alpha1 and beta1 ARs, whereas a subpopulation of the cell bodies was immunoreactive for the beta2 AR.

Conclusions:
The possible roles for ARs in the auditory periphery may be the modulation of afferent neural activity, control of OHC contractility, monitoring of intracellular Ca^{2+}, and K^{+} transport.

Key Words: Organ of corti (OC); Adrenergic receptors; Modulation of neural activity
Funding Agency: Supported by NIH RO1 grants # DC000156, DC004076

Anatomy
Category: Graduate (MSc: Basic Sciences)

7

Low Carbohydrate Ketogenic Diet Prevents the Induction of Diabetes Using Streptozotocin in Rats

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Introduction:
Diabetes mellitus is a complex endocrine disorder that leads to nephropathy, neuropathy and retinopathy. It is found that effective management of body weight and changes to nutritional habits with regard to the carbohydrate content and glycaemic index of the diet have beneficial effects in glucose intolerance. Previously we have shown that low carbohydrate ketogenic diet (LCKD) is quite effective in reducing body weight in humans and was cardio-protective following global ischemic injury in rats. This preliminary study is aimed at understanding the protective effects of LCKD from experimental induction of diabetes in rats.

Methods:
Rats weighing 190-250 g were divided into Normal Diet (ND), LCKD and High carbohydrate diet (HCD) groups and specific diets ad libitum were given to each group for a period of 8 weeks. Each group was further subdivided into normal control, sham control and diabetic groups. Animals in the diabetic group were given a single intraperitoneal injection of streptozotocin (55mg/Kg in saline) for inducing diabetes. The animals in the sham control group were given saline only while the animals belonging to the control group were untreated. The rats were monitored weekly for diet intake, water intake, body weight, urine output and blood sugar. The animals were sacrificed after four weeks.

Results:
The results showed that the rats on LCKD had remarkable tolerance to streptozotocin as indicated by the blood glucose analysis. Urine output level and polyurea condition reflected the diabetic status of each animal. There was a significant decrease in the weight gain of the animals that were fed on a LCKD diet as compared to other groups.

Conclusions:
This study, therefore, suggests that LCKD prevents the development of streptozotocin induced diabetes in rats. The underlying protective mechanism of LCKD needs to be elucidated. Further studies on the therapeutic role LCKD in diabetic rats are in progress in our laboratory.

Key Words: Diabetes; Low carbohydrate ketogenic diet; Streptozotocin
Funding Agency: None

Anatomy
Category: Clinical

8

The outcome of renal allografts with multiple arteries

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Introduction:
Renal allograft transplantation with multiple arteries (MA) was always avoided as much as possible as it is technically demanding and carries higher complication risk. Purpose: to determine patient and graft outcome of live and cadaveric kidney transplantation with multiple renal arteries.

Methods:
We reviewed total number of 646 cases were transplanted between November 1993 and December 2005, 185 (28%) from cadaveric donors (CAD. Thirty-five allografts with MA, 18 CAD, 9 LRD, 8 LURD. We analyzed surgical techniques, number and type of anastomosis, serum creatinine, arterial thrombosis and stenosis, hypertension, graft and patient survival.

Results:
Out of 35 grafts, 30 had double arteries, 21 of them transplanted with 2 separate end to side anastomosis to external iliac arteries, 9 had single (conjoined or cuff anastomosis). Five grafts had 3 arteries, with double or multiple anastomosis, and all were end to side to external iliac artery. Two patients developed perigraft hematoma 5%, compared to 4.5 % in the single artery (SA) group. Serum creatinine of MA group at one month recorded (122.3+44.5) (Mean+SD), (139+86) at one-year and (156+151.5) at 5 years. One case showed renal artery stenosis presented with resistant hypertension. Six grafts 17% were lost in MA group, in 10 years, compared to 15.6 % in SA group. We had 5 patients lost in 10 years in MA group 14%. Three in cadaveric group 16%, one with pulmonary embolism, two with septicemia, compared to 12% in SA group, and one in each of LRD and LURD groups.

Conclusions:
Although MA renal allografts might carry a higher relative risk for complications, but it gives comparable results in graft and patient outcomes justifies its use.

Key Words: kidney transplantation; multiple arteries
Funding Agency: None

Anatomy
Category: Basic Sciences

9

Autophagy in hypertrophic C6 astrocytic cells surviving cisplatin treatment in Culture

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Introduction:
We have reported earlier that C6 glioma cells surviving an acute phase of Cisplatin treatment performed phagocytosis of apoptotic debris and grew into large cells with lobulated nuclei and excessive amount of smooth endoplasmic membranes and lipid droplets. As a feature of their atypical apoptotic demise some of these cells also underwent autophagy that is the object of investigation in this paper.

Methods:
Cultures of astrocyte-like C6 cells were treated with a 90 min pulse of Cisplatin (5-10 mg/ml) and examined by TEM at 9 and 10 days later. For electron microscopy the cultures on coverslips were fixed in 2.5 % phosphate-buffered glutaraldehyde, than postfixed in 2% buffered OsO4, dehydrated in ethanol, and embedded in Araldite CY212. Semithin, 1 µm-thick sections were stained with 1% toluidine blue and used for targeting the cells. Ultrathin sections were double stained with uranyl acetate and lead citrate and examined in a transmission electron microscope JEM-1200EXII (JEOL, Tokyo, Japan) at 80 kV.

Results:
Multiple autophagic foci were observed in the cytoplasm of hypertrophic glial cells in the form of concentric arrangements of long cisterns of endoplasmic reticulum devoid of bound ribosomes. In their core, they contained sequestered cytoplasm with various organelles like monoribosomes, mitochodria or lipid droplets. Lysosomal bodies were also found around and within large autophagosomes.

Conclusions:
Autophagy is evolutionary conserved way of controlled degradation of organelles in cells under stress or dying, which is not usually observed in cells performing apoptosis. Together with our earlier reports of micronucleation in cisplatin treatment survivng cells, the presence of autophagy in some of these hypertrophic surviving cells indicates that they may overcome the damage caused by this cytotoxic drug by elimination of the damaged parts of their nucleus (micronuclei) and cytoplasmic organells (autophagosomes). This indicates that an atypical or incomplete apoptosis takes place under these conditions and shows a possible way though which the tumor cells may reoccur in failed cisplatin treatments.

Key Words: Glioma cells; Apoptosis; Autophagocytosis
Funding Agency: Supported by the Academy of Science

Anatomy
Category: Undergraduate

10

Bone Mass Density In Diabetic Women: Is There A Detrimental Effect?

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Introduction:
The aim of this study was to assess bone mass density (BMD) values in diabetic Kuwaiti female patients and to determine the prevalence of osteoporosis among them.

Methods:
A convenience sample of 210 Kuwaiti females with type 2 diabetes mellitus aged 40-79 years were selected after excluding those with current of previous histories of any condition that can advert the BMD values. An age matched group of 655 non-diabetic healthy ambulatory Kuwaiti women after confirming the same exclusion criteria represented the control group. Bone mass measurements were performed by dual-energy X-ray absorptiometry (DXA) machine at the lumber spine (L2-L4) and femur (neck and total hip). Body size measurements and a questionnaire on past medical and gynecologic history and lifestyle issues were administered to both groups.

Results:
There were no significant differences of the BMD values or the prevalence of osteoporosis between the diabetic and the non-diabetic women. on multivariate analysis, weight showed a dominant significant constructive effect in the non diabetic group as each kg of body weight had a change of 0.6% of the spine BMD, 0.5% of neck BMD and 0.7% of total hip BMD. In the diabetic group, each kg of body weight showed a significant change by 0.2% and 0.3% in the femur region (neck and total hip respectively) only. Parity and lactation proved a significant detrimental effect on BMD more apparent in the diabetic group. Duration of diabetes had a harmful influence on the BMD on the level of univariate analysis only.

Conclusions:
Women with type 2 DM showed no significant difference either in BMD values or osteoporosis prevalence from non-diabetic women. The aggravating factors of BMD were more apparent among the diabetic women than the non-diabetic group and vise versa.

Key Words: Bone Mineral Density; Diabetes Mellitus; Osteoporosis
Funding Agency: None

Anatomy
Category: Clinical

11

Diagnostic Accuracy of Urinary Creatinine Concentration in the Estimation of Differential Renal Function in Patients with Obstructive Uropathy

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Introduction:
To determine the diagnostic accuracy of spot urine creatinine concentration (UCC) as a new test for the evaluation of differential renal function in obstructed kidneys (DRFok) drained by percutaneous nephrostomy tube (PCNT).

Methods:
Patients with obstructed kidneys drained by PCNT, DRFok was derived from UCC by comparing the value of urine creatinine concentration in the obstructed kidney to the value in the contralateral kidney and was derived from DMSA and CC using standard methods. Subsequently, the results of UCC were compared to the results of DMSA and CC.

Results:
Sixty one patients were enrolled. When compared to DMSA, UCC evaluation of DRF correlated significantly (r=0.96). Bland-Altman plot showed that the upper limit of agreement was 14.8% (95% CI 10.7 to 18. 5) and the lower limit was -19.9 % (95% CI -23.8 to -16.1). The sensitivity and specificity of detecting DMSA DRFok $\leq$35% using UCC was 85.2 % and 91.2% respectively. When compared to CC, UCC evaluation of DRF revealed excellent correlation (r=0.99). Bland Altman test gave upper limit of agreement of 10.4% (95% CI 7.9 to 12.8) and lower limit of agreement of -11.3% (95% CI -13.8 to -8.9).

Conclusions:
UCC is accurate in the estimation of DRFok. Given the nature of UCC, it may be more convenient as it allows rapid results unlike those obtained from DMSA or CC.

Key Words: Ureteral Obstruction; Technetium Tc 99m Dimercaptosuccinic Acid.; Kidney
Funding Agency: None

Anatomy
Category: Clinical

12

A Prospective Study of Transperineal Urethrosphincteric Block (TUSB) for Visual Internal Urethrotomy in Patients with Anterior Urethral Strictures

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Introduction:
To evaluate the feasibility and effectiveness of transperineal urethrosphincteric block (TUSB) in providing analgesia during visual internal urethrotomy for patients with anterior urethral strictures.

Methods:
A total of 26 consecutive patients posted for elective visual internal urethrotomy for symptomatic urethral stricture were considered for this prospective study. Twenty four patients agreed to participate in the study. Their demographics and medical conditions were recorded. Patient's mean age was 43.5 years (range 26 - 71). Twenty five percent (25%) of the patients had co-morbid conditions which would have put them at high risk for general anesthesia All patients had TUSB as the main method of analgesia, using 1% lidocaine. Post operatively, patients were asked to score the severity of the pain experienced during TUSB and during the transurethral surgery, on a scale from 0 to 10. Post operative adverse effects and the need for sedation or additional analgesia were recorded. All patients rated their overall satisfaction with the analgesia.

Results:
Mean pain score during instillation of the transperineal block was 1.9 (range 0 - 3) and 1 (range 0 - 5) for visual internal urethrotomy. No sedation, narcotic or additional analgesia were required. No post operative adverse effects were encountered. Ninety two percent (92%) of the patients were very satisfied with the method of analgesia.

Conclusions:
TUSB is an effective, satisfactory and safe method of local analgesia for visual internal urethrotomy in patients with anterior urethral strictures and is particularly suitable for those at high risk of anesthesia.

Key Words: Nerve block; Lidocaine; Urethral stricture
Funding Agency: None

Anatomy
Category: Undergraduate

13

Profiles in Lung Cancer in Kuwait

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Introduction:
The study was designed to evaluate the outcome of treatment in patients with lung cancer presenting to K.C.C.C in the period between 1998-2004.

Methods:
We retrospectively studied the epidemiology, treatment and it's outcomes in 269 patients with lung cancer seen in KCCC.

Results:
Lung cancer is the 5th most common cancer in Kuwait with a frequency of 7.4% in Males and 2.4% in Females.The majority of patients were males 82.5% (222) and 17.5% were females (47) of them 42% were Kuwaiti patients and 58% were non Kuwaiti. The mean age of diagnosis was 60.18% years (range 28-90 years). 78.8% of the patients were smokers. Cough and chest pain were the main symptom at presentation representing *(*65% and 35%, respectively). Most of the patients presented with advanced stage of disease 30.5% of cases received radical treatment, 50.2% of patients treated with a Palliative aim, and 5.6% of cases treated with best supportive case. Surgery as a radical treatment was performed in 17.5% of patients in the form of either lobectomy in 14.1% of cases or Pneumonectomy in 3% cases, while radical radiotherapy was given to 44 patients (16.4%). Chemotherapy was given to 116 patients. The most commonly used combination chemotherapy was platinum and gemzar given to 58 patients

Conclusions:
Our results suggest that lung cancer is one of the most common cancer in males in Kuwait. Smoking is the main risk factor. Most of the patients with lung cancer are diagnosed at advanced stages and overall survival is poor. New controlled clinical trials are needed to improve the poor outcome of the disease.

Key Words: Lung Cancer; Profile; Kuwait
Funding Agency: None

Anesthesia and Critical Care
Category: Clinical

14

Levosimendan loading on CBS start in high risk cardiac surgical patients: prospective case series

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Introduction:
The heart is exposed to many stressors while undergoing cardiac surgery. The end result can be myocardial injury and dysfunction. The signaling mechanisms that are involved with ischemia/reperfusion injuries are being identified. Myocardial adenosine triphosphate-dependent potassium (KATP) channels activation was described as myocardial protective mechanism against myocardial ischemia/reperfusion injuries. Therefore, we loaded high risk cardiac surgical patients with levosimendan before conduction of ischemia and continued with in fusion at reperfusion, and reported the myocardial injury and dysfunction.

Methods:
In this prospective series, we loaded high risk cardiac patients, undergoing high risk and complex cardiac surgical procedures with levosimendan upon the start of cardiopulmonary bypass (CPS), and continued with infusion after de-clamping the aortas. The postoperative myocardial hemodynamic performance, biochemical markers of efficient myocardial function along with the myocardial ischemia marker troponin I (Tn I) were measured and immediate post operative complications were reported.

Results:
Thirty seven patients were recruited in this investigation. In the first twenty four hours after surgery there were two myocardial injuries (6.6 %). The total mean postoperative serum Tn I of 6.1$\pm$21 ng /l. The hemodynamic profiles of the study population showedstatistically significant improvement when compared with the pretreatment measurement values. The mean arterial lactate concentration was 1.8$\pm$1.0 mmol/l.

Conclusions:
Loading high risk cardiac surgical patients with levosimendan, upon commencing CBP before induction of ischemia, to be followed with infusion at the time of reperfusion has useful myocardial protective effects against ischemia and post operative myocardial dysfunction.

Key Words: Levosimendan; Ischemia; Myocardial Protection
Funding Agency: None

Biochemistry
Category: Graduate (MSc: Basic Sciences)

15

Adrenal availability of ligands for retinoid-X-receptor: Mass spectrometric approaches

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Introduction:
Retinoid-X-Receptor (RXR) is a nuclear receptor implicated in regulation of lipid metabolism, cell differentiation and apoptosis. Unlike retinoic acid receptor, RXR does not recognize all-trans retinoic acid. It has been shown that 9-cis-retinoic acid (9-RA) and certain very long-chain polyunsaturated fatty acids (PUFAs): cervonic acid, adrenic acid and arachidonic acid are possibleligands to activate RXR in vivo (in an order of binding-specificity). Human and rat adrenals store cholesterol esters (CEs), in whose composition these PUFAs predominate. Adrenal CEs are hydrolyzed to free cholesterol for steroidogenesis, but role of these PUFAs after liberation remains unknown. We had recently found that the rat adrenals express RXR. The objective was to qualitatively investigate the type of RXR-ligand(s) available in the gland.

Methods:
Adrenals were harvested from Wistar male rats and extracted with acidified hexane. 9-RA was determined by (a) RP-HPLC (UV340), and (b) LC/MS using the positive ion mode and a SIM method (m/z=301). Free PUFAs were determined as methyl esters by GC/MS using pentadecanoic acid as an internal standard.

Results:
9-RA was not detected in the adrenal extracts by RP-HPLC or LC/MS approach. Failure of finding 9-RA was not due to a technical deficiency, because both techniques detected 9-RA from the adrenals fortified with this compound before extraction. Adrenic acid and arachidonic acid were confirmed in the adrenal extracts; cervonic acid was not detectable.

Conclusions:
Adrenic acid and arachidonic acid are plausible ligands for RXR in rat adrenals. Biochemically, the former has a better binding-specificity comparing to, and is also the elongation-product from, the latter. It appears that both elongation and CE metabolism can regulate the glandular availability of ligands for RXR, with respect to their quality and quantity. (The authors thank Dr.T. S. Srikuma for handling of rats.)

Key Words: Adrenal steroidogenesis; Retinoid-x-receptor; Mass spectrometry
Funding Agency: Collage of Graduate Studies

Biochemistry
Category: Basic Sciences

16

Resveratrol as a potential cancer chemotherapeutic/chemopreventive drug: Evidence from in vitro studies

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Introduction:
Resveratrol (3, 4', 5-trans-trihydroxystilbene), a nontoxic natural compound found in a wide variety of plants with known antioxidant property, is emerging as a potent chemopreventive and anti-cancer drug. However, the cellular and molecular basis of its chemopreventive activity has been largely undefined. The objective of this study was to examine the mechanism of cell death induced by Resveratrol in several human cancer cell lines.

Methods:
Apoptosis was quantified by flow cytometry and DAPI staining. Differentially regulated genes by resveratrol were identified by using two cDNA arrays representing genes of the PI3K/AKT (96 genes), the human apoptosis and cell cycle (267 genes) signaling pathways and one oligo array of the human cancer pathway consisting of 461 genes. The expression and activation of genes were analyzed by western blotting and colorimetric assay.

Results:
We report here that the growth inhibitory effect of Resveratol on these cells is due to the induction of apoptosis and is associated with activation of the tumor suppressor protein p53 and other proteins (caspase-3, PARP and Erk1/2) that are involved in apoptosis. Gene expression profile in response to resveratrol treatment will be presented.

Conclusions:
Collectively, the data suggest that caspase-3, p53 and Erk1/2 activation by resveratrol are required for PARP degradation and induction of apoptosis in cancer cells, and provide additional insights into the action of resveratrol, thus substantiating a chemopreventive potential against human cancer.

Key Words: Cancer; Resveratrol; Natural drug
Funding Agency: Kuwait University grants # MB 04/04 and YM 03/05

Biochemistry
Category: Graduate (MSc: Basic Sciences)

17

A Mn porphyrin antioxidant fails to protect against hyperglycemia – induced kidney damage

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Introduction:
Oxidative stress due to hyperglycemia has been implicated in diabetic complications. Diabetic nephropathy is among the major complications of diabetes. Studies of the animal models of diabetes revealed that some of the functional and morphological abnormalities caused by hyperglycemia could be prevented by antioxidants. The aim of this study was to investigate whether a synthetic antioxidant, Mn(III) 5, 10, 15, 20-tetrakis (N-methylpyridinium-2-yl) porphyrin (MnTM-2-PyP) can protect kidneys against hyperglycemia-induced oxidative damage.

Methods:
Hyperglycemic was induces in male Wistar rats by a single ip injection of STZ (60 mg/kg). Rats which maintained blood glucose concentrations above 15 mM in the first week were divided into 2 groups designated as "HG" and "HG + MnTM-2-PyP". The animals in the second group received sc injection of sterile MnTM-2-PyP solution, 1 mg/kg/day for two months. Blood samples were taken for the determination of glucose and glycosylated hemoglobin (HbA1C). Oxidative damage was determined by an HPLC based MDA assay in whole kidney homogenates.

Results:
Blood Glucose and HbA1C level were higher in the diabetic rats and remained unaffected by the antioxidant treatment. Kidney MDA was significantly elevated in the hyperglycemic rats, compared to the controls. MnTM-2-PyP treatment did not suppress MDA production.

Conclusions:
Irrespective of its antioxidant activity in vitro and in vivo, MnTM-2-PyP failed to protect diabetic kidneys against hyperglycemia-induced oxidative damage. Possible reasons include insufficient dose, inability to accumulate in the targeted tissue, or fast metabolism.

Key Words: Diabetes; Oxidative stress; Antioxidant
Funding Agency: Grant # MB 07/04 from Kuwait University

Biochemistry
Category: Graduate (MSc: Basic Sciences)

18

Effect of a Mn porphyrin on antioxidant enzymes in diabetic rat kidney

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Introduction:
Diabetic nephropathy is the single most common disorder leading to renal failure. Recent data suggest that diabetic nephropathy is a consequence of hyperglycemia-induced oxidative stress. Under normal circumstances, the kidney generates reactive oxygen species (ROS), which are efficiently eliminated by superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPX). Oxidative stress occurs when ROS production overrides the capacity of the antioxidant defense. The aim of this study was to investigate the effect of a Mn porphyrin SOD mimic, MnTMPyP, on the activities of the anti-oxidant enzymes SOD, catalase, GPX, and glutathione reductase (GR) in the kidneys of streptozotocin (STZ) hyperglycemic (HG) rats.

Methods:
Female Wistar rats were injected ip with STZ (60 mg/kg). Rats which maintained blood glucose concentrations above 15 mM in the first week were divided into 2 groups designated as "HG" and "HG + MnTMPyP". The animals in the second group received sc injection of sterile MnTMPyP solution, 1 mg/kg/day for two months. After 2 months rats were sacrificed, and kidney homogenates were used for determination of SOD, catalase, GPX and GR activities.

Results:
Compared to the normoglycemic controls, SOD and GPX were markedly elevated in the STZ rats, while catalase and GR remained unaffected. Treatment with MnTMPyP further elevated the SOD (statistically insignificant), GR and catalase activities, but had no effect on GPX.

Conclusions:
The increase in the activities of the antioxidant enzymes is a physiological response aimed at protecting the tissues against hyperglycemia-induced oxidative stress. The effect of MnTMPyP can be interpreted in different ways: a) it protects the enzymes against hyperglycemia-induced inactivation; b) in the assays, the intrinsic MnTMPyP catalytic activity adds to the activities of the rat enzymes; c) MnTMPyP acts as a pro-oxidant. Further, detailed studies are needed to distinguish between those possibilities.

Key Words: Hyperglycemia; Oxidative stress; Antioxidant
Funding Agency: Grant # MB 07/04 from Kuwait University

Biochemistry
Category: Basic Sciences

19

Is inactivation of thiol-containing enzymes a sensitive marker of oxidative stress?

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Introduction:
Oxidative stress (OS) has been implicated in various deceases. Assessment of OS, however, is hampered by the lack of reliable parameters that can be easily measured. Thiols are easily oxidized by reactive oxygen species (ROS), and therefore loss of thiols can serve as a sensitive marker of OS. Thiols play a variety of important functions in cells. Essential -SH groups in enzymes are involved in catalysis and their loss leads to inactivation of these enzymes. Among the enzymes containing essential -SH groups are isocitrate dehydrogenase (ICD), glyceraldehyde-3-phosphate dehydrogenase (GAPDH), and rhodanese (RHO). The aim of this study was to find if inactivation of -SH containing enzymes can be used as a sensitive marker of oxidative stress.

Methods:
Two *E. coli* strains, AB1157 (parental, low [ROS]), and JI132 (SOD-deficient, high [ROS]) were used to model different levels of oxidative stress. Paraquat was used to further increase ROS production. For enzymes and GSH assays, the cells were grown to mid-log phase, harvested, and disrupted by sonication. ICD, GAPDH, and RHO were assayed in fresh cell-free extracts.

Results:
No inactivation of ICD, GAPDH, or RHO was observed in growing AB1157 and JI132 cultures. When protein synthesis was blocked, ICD was much faster inactivated in JI132 than in AB1157 cells. The inactivation was further accelerated by paraquat. Rapid loss of -SH groups and enzymes activities took place when cell-free extracts of JI132 were incubated in air or under a flux of superoxide. In all cases, no inactivation occurred before GSH pool was exhausted.

Conclusions:
Inactivation of -SH containing enzymes cannot be used as a sensitive marker of oxidative stress, since in vivo it depends on de novo protein synthesis, the ability of the cells to regenerate GSH, and the accessibility of the -SH groups for ROS

Key Words: Oxidative stress; Thiol-containing enzymes; Glutathione
Funding Agency: Grant # MB07/04 from Kuwait University

Biochemistry
Category: Basic Sciences

20

Na-H exchanger: Role in human inflammatory bowel diseases

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Introduction:
Na-H exchanger (NHE) is responsible for an electro neutral exchange of Na and H across the cell membrane. At present 10 different NHE isoforms have been reported to express in a cell-tissue selective manner. However, NHE-1 and -3 isoforms have been the most extensively studied ones. NHE-1 is located on basolateral, while NHE-3 is present on the apical domain on the epithelial cells. Both NHE-1 and -3 isoforms regulate intracellular concentration of electrolyte and water, cell volume and size which are altered in human inflammatory bowel disease conditions (IBD). However, the roles of NHE-1 and -3 isoforms are not fully understood in IBD.Objective: The aim of this study was to investigate the role of NHE-1 and -3 isoforms in human IBD.

Methods:
The level of NHE-1 and NHE-3 proteins was examined using ECL western blot analysis. NHE-3 mRNA levels were measured using RT-PCR using actin as an internal control. Sodium pump which provides a driving force for NHE activity was estimated by measuring the ouabain sensitive and K-stimulated p-nitrophenyl phosphatase (PNPase) activity in human colonic biopsies.

Results:
There was a significant induction of myeloperoxidase (MPO) activity, marker of inflammation in the biopsies from Crohn's disease (CD) and Ulcerative colitis (UC). NHE-1 and NHE-3 protein levels as well PNPase activity were suppressed significantly in both CD (n=12) and UC (n=13) as compared to normal IBS control (n=13). NHE-3 mRNA level was also decreased significantly in CD, but not in the UC.

Conclusions:
These findings demonstrate down regulation of NHE-1 and NHE-3 isoforms, which together with a suppression of PNPase activity could contribute to electrolyte disbalance and pathogenesis of IBD.

Key Words: Na-H Exchanger; Colitis; Sodium pump
Funding Agency: Kuwait University Research Administration (Grant # MB05/04)

Biochemistry
Category: Undergraduate

21

Beyond the PSA era: molecular markers for non-invasive detection of prostate cancer

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Introduction:
The search for better prostate cancer diagnostic tools is driven in part by uncertain outcomes of needle biopsies and the limitations of the PSA test, both of which are invasive and uncomfortable. Thus, there is an urgent need for developing markers that can enhance the diagnostic accuracy.Here we compared the gene expression of three molecular markers to show their accuracy and predictability in ýdetecting benign prostatic hyperplasia (BPH), BPH and prostatitis, and cancer tumors.

Methods:
Gene expression of three molecular markers: DD3, E2F and survivin was quantified in voided urine samples after digital rectal examination from 36 patients with: benign prostatic hyperplasia (BPH) (n=18), BPH with prostatitis (n=11), and prostate cancer (n=7). Total RNA was purified from cells shed in the urine and reversely transcribed into cDNA. Gene-specific primers and TaqMan probes were used. cDNA-specific real-time quantitative polymerase chain reaction (PCR) assay was performed using ABI 7000 sequence detection system.

Results:
All three markers showed significant overexpression in cancer patients. DD3 had the highest mRNA expression in prostate cells compared to E2F and survivin. The gene expression ratio of cancerous to BPH was significantly higher for all three genes. The fold increase in the gene expression for DD3, E2F and survivin was: $1.5x10^{19}$ ($p<0.001$), $2.5x10^{2}$ ($p<0.001$) and 12.6, respectively. Unlike DD3 and E2F, survivin mRNA levels were similar in both BPH and BPH and Prostatitis patients. DD3 and E2F showed a $1.7x10^{9}$ and 12.6 fold increase, respectively.

Conclusions:
DD3 and E2F proved effective in identifying the three different conditions of the prostate. Overall, these genes could be excellent candidates for the development of molecular probes for non-invasive early detection of prostate cancer and as potential drug targets.

Key Words: Prostate cancer; Molecular markers; Real-time PCR
Funding Agency: Kuwait University- Research Administration- Grant # MB 01/05

Biochemistry
Category: Graduate (Resident)

22

Molecular characterization of apoptotic effects of Torsion of Testis

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Introduction:
Testicular torsion is associated with damage to the testicular tissue as a result of ischemia-reperfusion (I-R) injury of the testis caused by the twisted spermatic cord and its release. Although necrotic cell death has been thought to be the predominant type of cell death after I-R of the testis, evidence has shown the involvement of apoptotic cell death. Thus, we aim to investigate the molecular survival pathway following acute ischemia in the germ cells of the rabbit testis.

Methods:
The left testes of 6-12 months old NZW rabbits were subjected to 1 hour of ischemia-inducing torsion by cross-clamping the left spermatic cord followed by reperfusion. The right testes servedas internal control. Both testes were excised after 6 months. Germ cell apoptosis was evaluated by TUNEL assay. Gene expression of the survival genes: survivin, Bcl-2 and Bax was assessed by quantitative reverse transcription-polymerase chain reaction (RT-PCR). Johnsen score was used to assess morphological damage for control and testes undergoing I-R injury.

Results:
After 6 months of torsion induced I-R injury the following changes were observed: 1) The number of TUNEL positive germ cells was increased and 2) quantitative analysis of all three survival genes showed a significant decrease in their gene expression after as compared to control testes.

Conclusions:
We postulate that decreased expression of survivin, an inhibitor of apoptosis, and decreased Bcl-2/Bax ratio in the testes after I-R may accelerate germ cell death by apoptosis.

Key Words: Testicular Torsion; I/R Injury; Apoptosis
Funding Agency: This work was funded by Kuwait University research

Biochemistry
Category: Clinical

23

Genetic Polymorphisms of Human Platelet Antigens (HPA 4 and 5) as risk factors for Coronary Heart Disease in the Arab Population.

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Introduction:
Human platelet antigen (HPA) systems consist of more than 12 bi-allelic antigen polymorphisms which may be important in such disorders as neonatal alloimmune thrombocytopenia, post-transfusion purpura, refractoriness to platelet transfusion therapy as well as coronary and cerebrovascular events. In this study we have compared the frequencies of two HPA antigens, HPA 4 and 5, in 2 groups of Arab subjects in Kuwait with and without diagnosed Coronary Heart Disease (CHD) to determine whether there is an association between HPA (4 and 5) polymorphism and CHD.

Methods:
The 2 groups of subjects were: A: 257 patients, evaluated clinically and biochemically and confirmed with acute coronary syndrome (ACS) within 24 hr of admission; Group B: 165 apparently healthy control subjects recruited from the Central Blood Bank. Genotyping was done for all the subjects by the Polymerase Chain Reaction – Sequence Specific Primer (PCR-SSP) method. For each HPA system, a set of one common primer and two allele specific primers were used. In addition, a pair of positive control primers for the Human Growth Hormone gene (HGH) gene was also included as quality control for the different stages of amplification and detection. Results obtained for patients and controls were compared using Fisher's Exact test.

Results:
The results showed that all the patients and controls investigated were homozygous for HPA4a, a pattern closely resembling observations in Caucasians. For HPA5, the frequencies for patients and controls were respectively: Genotype: 5a5a – 80.5% vs. 77.0%, p ns; 5a5b – 16.8 vs. 23.0%, p ns; 5b5b – 2.7% vs. 0%, p=0.05; Alleles: 5a – 88.9 % vs. 88.5%, p ns; 5b –11.1% vs. 11.5%, p ns. This indicates a significantly higher frequency of the 5b5b genotype in CHD patients. This pattern is again similar to reported observations in Saudi Arabs and in Caucasians and could indicate that genotype 5b5b is a potential risk factor for CHD in Kuwaitis.

Conclusions:
HPA4 polymorphism did not associate with CHD risk while the HPA -5b5b genotype appears to be associated with CHD in the Kuwait population studied. The clinical implications of this observation need to be further evaluated.

Key Words: Human Platelet Antigen 4 and 5; PCR-SSP Method; Coronary Heart disease
Funding Agency: Kuwait # MG 01/03

Biochemistry
Category: Undergraduate

24

Superoxide dismutase protective effect against cadmium posioning

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Introduction:
Exposure to toxic metals has become an increasingly recognized source of illness worldwide. Cadmium, which is used in production of Ni-Cd batteries, stabilizers, pigments, and electronic components, is a common environmental pollutant. Cd has deleterious effect on the human health causing chronic rhintis, osteoporosis, and prostate cancer. Cd cannot produce reactive oxygen species (ROS) directly. Nevertheless, recent data indicate that oxidative stress is involved in Cd toxicity. This suggests that Cd might trigger indirect mechanisms of ROS production and/or impair cellular defenses. Superoxide dismutases (SODs) represent the first line of defense against oxidative stress. The aim of this study was to investigate the importance of SOD in protection against Cd toxicity.

Methods:
E.coli, strains GC4468 (Parental); QC1799, lacking SodA SodB; DJ901, deficient in soxRS; and QC 1817, deficient in SOD and soxRS were used. The strains were grown in M9CA medium supplemented with Cd. Growth was monitored by measuring the A 600 nm, and viability was assessed by counting colonies. Induction of the soxRS regulon was assayed by measuring fumarase C and nitroreductase A.

Results:
The Cd LD_{50} for Cd was 2 μM for the SOD-deficient, and 150 μM for the parental strain. Cell viability was also affected at much lower Cd concentration in the SOD than in the parental strain. The soxSR regulon, which positively controls genes coding for protective enzymes was also important in protection against Cd.

Conclusions:
SOD decreases sensitivity towards Cd toxicity by two orders of magnitude. This together with the importance of the soxRS regulon indicates that increased ROS, particularly superoxide production, plays very important role in Cd toxicity.

Key Words: Superoxide dismutase; Cadmium; soxRS
Funding Agency: Grant # MB 07/04 from Kuwait University

Biochemistry
Category: Graduate (MSc: Basic Sciences)

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Inactivation of Metabolic Enzymes by Photo-Treatment with Zinc Meta N-Methylpyridylporphyrin

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Introduction:
Cell proliferation is dependent on energy supply and generation of reducing equivalents in the form of NADPH for reductive biosynthesis. Blockage of pathways generating energy and reducing equivalents has proved successful for cancer treatment. We have previously reported that isomeric Zn(II) N-methylpyridylporphyrins (ZnTM-2(3, 4)-PyP4+) can act as photosensitizers, preventing cell proliferation and causing cell death. The aim of the present study was to investigate the effect of ZnTM-3-PyP an d its photoactivation on cell metabolism.

Methods:
LS174T adenocarcinoma cells were grown to 80-90% confluency. After the addition of the photosensitizer the cells were illuminated with visible light, harvested, and disrupted by sonication. Freshly prepared cell-free extracts were used for measuring the activities of glycolytic, pentose phosphate pathway, and TCA cycle enzymes.

Results:
Upon illumination, ZnTM-3-PyP inactivated glucose-6-phosphate dehydrogenase, glyceraldehyde-3-phosphate dehydrogenase, lactate dehydrogenase, NADP+ -linked isocitrate dehydrogenase, aconitase, and fumarase in intact cancer cells. In the dark ZnTM-3-PyP did not affect these enzymes. Photoactivated ZnTM-3-PyP was more effective than HpD for inactivation of all enzymes, except aconitase and isocitrate dehydrogenase. Enzyme inactivation was accompanied by aggregation, presumably due to protein cross-linking of the enzymes.

Conclusions:
Inactivation of metabolic enzymes leading to disruption of cancer cells metabolism is one of the major reasons for antiproliferative activity of ZnTM-3-PyP in photodynamic therapy.

Key Words: Photodynamic therapy; Zn meta N-methylpyridylporphyrin; Enzyme inactivation
Funding Agency: Grant # YM02/05 from Kuwait University

Biochemistry
Category: Basic Sciences

26

Molecular mechanisms of Green Tea effects: Altered expression of IGF-1 and RXR-α in Rat Kidney

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Introduction:
Green tea (GT) is one of the most commonly used plant-based nutrients that can inhibit cellular mutagenesis and proliferation. Anti-carcinogenic effects of GT are known to be mediated by its polyphenols, however the underlying molecular mechanisms are still unknown. We conducted this study to evaluate the effect of GT on insulin-like growth factor-1 (IGF-1) and retinoid X receptor-α (RXR-α) which have been implicated in the process of carcinogenesis.

Methods:
Male Wistar rats (250-300g) were divided into four groups, Group 1 served as control (water fed) whereas animals from groups 2, 3 and 4 were given GT (6g /L) for 1, 2 and 4 weeks respectively. Kidneys were isolated from animals of different groups to prepare homogenates for western blot analysis and Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) studies of IGF-1, RXR-α, GAPDH (glyceraldehyde-3-phosphate dehydrogenase) and actin.

Results:
In our study, GT was observed to markedly increase (2 to 3-folds) the expression of RXR-α in rat kidney. Western blot analysis revealed that RXR-α protein was significantly ($p<0.001$) increased following GT treatment for 2 to 4 weeks. GT however was found to have no significant effect on the expression of actin protein. RT-PCR analysis of IGF-1 revealed that GT treatment for 1, 2 and 4 weeks markedly decreased the mRNA levels of IGF-1, however the observed effects of GT were significant ($p<0.001$) following four weeks of treatment (Group 4).

Conclusions:
Increased levels of IGF-1 are known to promote cellular proliferation and carcinogenesis whereas activation of RXR has been suggested to inhibit mutagenesis and tumor formation. Our findings that GT attenuates the expression of IGF-1 and increases the expression of RXR-α, suggest the molecular mechanisms that might be associated with anti-tumor properties of GT.

Key Words: Green tea; IGF-1; RXR-alpha
Funding Agency: None

Cardiac Electrophysiology
Category: Clinical

27

Feasibility of Arrhythmia Mapping and Ablation with a Non-Contact Mapping System.

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Introduction:
Mapping and ablation of some arrhythmia is challenged sometimes by very fast heart rate or non-stability of the tachycardia, i.e. few beats. Advanced mapping system such as, non-contact mapping 3D mapping, can help to facilitate the source of arrhythmia. The procedure is usually performed by placing a basket-mapping catheter (array) in the cardiac chamber of interest. Multiple electrodes on the surface of the array register the electrical geometry of the chamber and then the source of the tachycardia. Aim of our study was to test the feasibility and to assess the safety of non-contact mapping and ablation in our center (Chest diseases Hospital).

Methods:
Twelve patients with various Atrial and ventricular arrhythmia were selected for non-contact mapping and ablation. After achieving the vascular access and proper heparenization, multielectrode catheter (Ensite Arraytrade mark, St. Jude Medical) was advanced through a standard 10F introducer to a stable position in targeted chamber, over a 260 cm length 0.035 J-tip guidewire. An ablation catheter was then inserted through the second 8F introducer. The chamber geometry is drawn with the roving ablation catheter and registered by the balloon array, using the Ensite software 5.2. Tachycardia were induced and ablated based on the 3D activation map.

Results:
The total procedural and fluoroscopy times were 120$\pm$32 min and 15.2$\pm$6.1 min, respectively, acceptable with the traditional map and ablation. No major complication related to the placement of the balloon, were reported. Intermediate success in further follow up was reaching 83%.

Conclusions:
3D non-contact map is a feasible and effective approach for mapping and ablation of challenging arrhythmia. It facilitates the mapping of the hemodynamically unstable tachycardia as will as non-sustained tachycardia.

Key Words: Non-contact mapping; Ablation; EnSite
Funding Agency: None

Community Medicine
Category: Undergraduate

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Patient' Perception of Hygiene Among Surgery Inpatients at Kuwait's General Hospitals

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Introduction:
The objectives of the study are:
1. To assess patients' perception of hospital hygiene.
2. To analyze variations in perception according to socio-demographic characteristics and across different hospitals.

Methods:
The target population consisted of all surgical wards inpatients in four general hospitals in Kuwait. Face to face interviews were conducted on all patients. 269 patients were approached of whom 198 participated in this study yielding a response rate of 74%. Overall hygiene scores were calculated for six different aspects of hygiene, namely, food, linens, toilets, general environment and air, doctors and nursing staff, and porters. Each hygiene score was cross-tabulated with the various socio-demographic characteristics of the patients. Non-parametric, descriptive and analytical statistical techniques were used to test differences.

Results:
About 80% of the respondents reported that soap was not available to them and almost a quarter of the patients rated the cleanliness of the toilets as poor. About 25% of the patients said that the staff did not wear gloves while examining them or changing their dressing, 28% found stains on their linens and 37% said that non-disposable crockery was used to serve their meals. Generally, those with a higher education, a higher income and of Kuwaiti nationality gave lower scores than those with a lower education ($p=0.004$), a lower income ($p<0.001$) and of non-Kuwaiti nationality ($p<0.001$).

Conclusions:
While food, linens, and doctor and nursing staff hygiene were generally rated positively, considerable deficiency was reported in the hygiene of toilets. This needs policy attention, since toilets can be a source of several types of infection.

Key Words: Hygiene; Hospital; Patients
Funding Agency: None

Community Medicine
Category: Undergraduate

29

Addiction profile of male institutionalised drug addicts

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Introduction:
This study aimed to quantify the severity of drug use and its relation to cigarette smoking, identify the most common drugs used and the factors related to initiation and therapy among institutionalised drug addicts in Kuwait. In order to explore the public health dimension of drug addiction, we also assessed the health status of this population. Furthermore, differences between the addiction centre and prison were compared.

Methods:
A cross sectional survey of 243 subjects in the central prison of Kuwait (n=83) and the addiction centre (n=130) was conducted. A pilot tested self administered questionnaire was used to obtain data on the type, severity, duration, factors related to initiation of drug use and smoking, socio-demographic factors and major illnesses.

Results:
Mean age of drug addicts in Kuwait was found to be about 34 years ranging from 21 to 57. Subjects came from varied socio-economic background with a considerable proportion with lower educational levels. About 93% were smokers, the majority began smoking at a young age and inmost cases smoking proceeded drug usage. The majority were found to be using multiple of substances, most commonly alcohol (80.2%), cannabis (77.9%) and heroin (63.1 %).The mean duration of use varied from 10 years, 11.8 years and 9.5 years, respectively. About 23% were found to have hepatitis and were those of increased drug exposure and history of intravenous drug use. There were minimal differences between those in the prison compared to those in the addiction in the majority of these areas.

Conclusions:
We found the extent and severity of the drug use in Kuwait to be similar to that of other middle eastern counter parts and somewhat less milder, and the level of health consequences were considerably lower.Public health intervention particularly in setting up well developed rehabilitation facilities in the prison would be vital in Kuwait.

Key Words: Drug addiction; Kuwait; Smoking
Funding Agency: None

Community Medicine
Category: Undergraduate

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Sleep patterns and sleep disturbances amongst the ministry employees in Kuwait

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Introduction:
The Objectives were to study the sleep patterns and major sleep disturbances and their associated factors amongst Government employees in Kuwait.

Methods:
An anonymous self administered questionnaire was handed out to Government employees during working hours at the Ministries complex in the Kuwaiti capital. Three buildings were chosen at random and every consecutive office on every floor was covered.

Results:
Of the 474 questionnaires handed out, 402 completed ones were included in the study. Thus the response rate was 84.8%. The mean age of the respondents was 33.5 years, 62% were female and about two-thirds were married. Regarding sleep patterns, 77% of the respondents slept for 6 hours or less per night, 72% took a nap during the day, and 72% woke up periodically from sleep at night at least once. About 66% of the respondents reported suffering from a sleep disturbance, and 54% reported suffering from insomnia. Also, 9% reported suffering from nightmares and about 9% reported suffering from restless leg syndrome. Those with higher income and ones who suffered from a heart condition reported to sleep longer. Multiple logistic regression indicated that younger age, female sex, being divorced or widowed, higher frequency of stress, and diabetes increased the risk of sleep disturbance.

Conclusions:
If reported insomnia and sleep disturbance are genuinely as high as indicated in the present study then this calls for public health attention since these disturbances may cause not only personal consequences but may affect productivity of a person which can have social implications

Key Words: Sleep Patterns; Sleep disturbances ; Kuwait Government Employees
Funding Agency: None

Community Medicine
Category: Undergraduate

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Attitude of Single Kuwait University Students Towards Consanguinity, and its Practice Among Their Families

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Introduction:
Consanguinity increases the risk of recessive genetic diseases, and is a relatively common practice in Kuwait. The objectives of this study are 1) to measure the prevalence of consanguineous marriage and attitudes towards consanguinity among single Kuwait University students, and 2) to identify the factors associated with preference for consanguinity and its practice in the student's families.

Methods:
Anonymous self-administered questionnaires were completed by 479 students selected from two faculties of Kuwait University (participation rate, 93.7%). Preference for consanguinity was measured by a single "yes/no" question, and a Consanguinity Advantage Score was calculated by summing 4 advantages (+1 each) and 4 disadvantages (-1 each).

Results:
The overall preference for consanguinity was 27.1% [95%.C.I.23-31%]. After statistical adjustment using multiple logistic regression, there were strong associations with Bedouin ethnicity (AOR, 3.2 [1.9-5.4]), male sex (AOR, 4.7 [2.9-7.9], and the practice of consanguinity among parents (AOR 2.7 [1.6-4.3]) and grandparents (AOR, 4.2 [2.1-8.2]), but was not associated with knowledge of consanguinity health risks. Factors associated with ConsanguinityAdvantage Score included male gender, Bedouin ethnicity, Al-Jahra or Ahmadi governorate, lack of knowledge regarding risk of inherited diseases, student and parental preference for consanguinity, and family practices. Practice of consanguinity was similar among grandparents (39%), parents (36%), and married siblings (42%). Family factors associated with practice included Bedouin ethnicity, Al-Jahra and Al-Ahmadi governorate, lower mother's education, with strong family clustering in consanguinity practice.

Conclusions:
Family characteristics and male sex have the strongest associations with preference for and practice of consanguinity, and knowledge of health risks is not independently associated with consanguinity preference.

Key Words: Consanguinity; Inherited diseases; Bedouin
Funding Agency: None

Community Medicine
Category: Undergraduate

32

Prevalence and risk factors of migraine among working Kuwaiti females

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Introduction:
Migraine is world wide health problem and insufficient data regarding migraine are available in Kuwaiti population. Therefore, we conducted cross-section this study to assess prevalence of migraine and evaluate some potential triggers of migraine.

Methods:
We enrolled woking kuwaiti females from 8 different ministries during December 2006. A pretested and a structured self-administered questionnaire was used to collect the data. The questionnaire included questions on demographic characteristics of participants, characteristics of headache, associated symptoms, warning symptoms, family history, potential triggers for migraine attacks, common co-morbidities. Migraine was diagnosed based on the modified criteria of International Headache Society. Data analysis methods included computation of frequencies, Chi square analyses and logistic regression analysis.

Results:
Of 660 females invited, 631(96%) consented for enrollment in the study. The prevalence of migraine in the study popultion was 11.7%. The subjects aged between 25-34 years have the highest prevalence of migraine (13.8%). Divorced or widowed females tended to have highermigraine prevalence(20%). Of the triggers and co-morbidities considered in this study, pregnancy was the only variable significantly ($p=0.035$) associated with migraine on multiple logistic regression analysis and it had protective effect (adjusted OR=0.47; 95% CI: 0.23 – 0.95). ($p=0.009$). Among the females identified as migrainures, higher frequencies of potential triggers were found for sleeping less hours (89.0%), followed by crying (85.9%), stress (84.2%) and loud noise (76.4%).

Conclusions:
Estimates of migraine prevalence in this study was slightly higher than most of the previously reported prevalence in Middle East. Pregnancy seems to offer some relief against migraine. Anemia had the highest frequency among migraineure. Further studies are needed on larger population on Kuwait.

Key Words: Migraine; Pregnancy; Prevalence
Funding Agency: None

Community Medicine
Category: Undergraduate

33

Physician knowledge, beliefs, and preparedness regarding a potential outbreak of Highly Pathogenic Avian Influenza virus in Kuwait

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Introduction:
One of the public health actions needed to control a potential outbreak of the H5N1 Highly Pathogenic Avian Influenza (HPAI) virus is to educate primary care physicians regarding the virus and its treatment and control prior to any such outbreak. The objectives of this study are 1) to assess the level of knowledge and preparedness among Kuwait's primary care physicians regarding Highly Pathogenic Avian influenza (HPAI), its prevention, diagnosis, treatment and control, and to identify factors associated with physician knowledge of HPAI.

Methods:
This cross-sectional study design enrolled 177 primary care physicians in 33 clinics from Capital, Hawalli, Ahmadi, Farwaniya, and Jahra governorates. Sampling was applied by random cluster sampling of clinics stratified by governorate. Response rate was 85%. A self-administered 3-page questionnaire was composed of 25 questions. A knowledge score (range 0-16) was constructed, and dichotomized for analysis as a binary outcome variable. Statistical analyses were performed using t-test, ANOVA, chi-square, and step-wise binary logistic regression.

Results:
The mean knowledge score (±SD) was 7.4±3.0, out of 16(46%). In unadjusted analyses, male gender, non-Kuwaiti nationality, Al Jahra and Hawalli governorates, and Internists had a significantly higher score compared to females, Kuwaitis, other governorates, and other specialties, respectively. In a step-wise logistic regression model, male gender, non-Kuwaiti nationality, Internal Medicine specialty, and Kuwait location of MD degree were significantly associated with higher score. Only 52% of respondents cited Ministry of Health pamphlets or conferences as a source of information on HPAI.

Conclusions:
50% Although some physician subgroups had significantly higher knowledge scores, their overall knowledge was still low.

Key Words: HPAI H5N1; Polyclinics; Knowledge
Funding Agency: None

Community Medicine
Category: Undergraduate

34

Knowledge, Attitude and Practice of Arabic-Speaking Women towards Breast Cancer screening

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Introduction:
The aim of this research was to investigate the prevalence of screening for breast cancer, and to assess the degree of awarness of breast cancer screening methods, in over thirty years of age, arabic-speaking women, in four governmental hospitals of Kuwait

Methods:
A cross-sectional study was conducted on 849 Arabic speaking women-30 years or above, who were attening the out-patients clinics(certain urban hospitals). A self administered questionnare-of 26 questions was distributed to each participant. The questionnaire assesses the subjects' knowledge, attitude and practice related mammography and breast self examination.

Results:
Of the 849 subjects, 80.2% were Kuwaiti nationals and 25.8% were Bedouin ethnic background. Prevalence of breast self examintaion on a monthly basis was 33.8%, for mammography 26.2%Significant associations were found between history of mammogram and women over the age of 50 (OR=3.07, 95% CI: 2.11-4.46), Non-Bedouin females (OR=1.483, 95% CI: 1.077-2.041), ever married (OR=2.443, 95% CI: 1.349- 4.423), a higher income (OR=1.483 95% CI: 1.0772-2.041) and family history of breast cancer (OR=1.654 95% CI: 1.154-2037. On the other hand, with breast self examination was only significant finding was with the age of women, less than 50 years old (OR=0.441 95% CI=0.241- 0.809) in comparison to older women.

Conclusions:
Those who had a breast condition themselves, had a family member or a friend with breast cancer we more oriented and better informed about the subject than the rest. There was a difference between the practices, and the perception of barriers and benefits of breastr cancer screening modes in terms of socio-demographic characteristics. The most common mode of awarness about breast cancer screening was through media or word of mouth. Relative to global studies, the prevalence of recruitment of screening facilities for breast cancer in women aged 50 and above is low.

Key Words: Breast Cancer; Knowledge Attitude Practice; Awarness
Funding Agency: None

Community Medicine
Category: Undergraduate

35

Prevalence, Attitude and Knowledge about Pap Smear among Women in Kuwait

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Introduction:
This study aimed to estimate the life time prevalence of Pap smear among women in Kuwait and to assess their knowledge and attitude towards Pap smear.

Methods:
The study was designed as a cross sectional survey using multi-stage cluster sampling method. We interviewed 304 women attending polyclinics in Kuwait using self administered questionnaire. Factors related to women's history of having Pap smear and their knowledge level and willingness to participate in a screening programme were evaluated.

Results:
The life time prevalence of Pap smear was found to be 37% (95%CI: 33, 43). About half the women (44%) had it only once in their life. History of having at least one Pap smear was significantly related to factors such as age, total family income, marital status, history of cervical infection and knowledge. The level of knowledge on cervical cancer varied among the participants Most of them were uncertain about the symptoms of cervical cancer. About half the women recognized cervical infection, smoking, and having multiple sexual partners as risk factors for cervical cancer; however, only 10% recognised early sexual intercourse as a risk factor. The willingness to participate in a future screening program varied significantly according to the educational level, employment status and total family income.

Conclusions:
Although cervical cancer incidence and mortality are relatively low in Kuwait, they may be under reported in the absence of screening programme. Moreover, Life time prevalence of having Pap smear was found to be considerably lower in Kuwait compared to developed countries.

Key Words: Pap smear; Prevalence; Cervical cancer
Funding Agency: None

Community Medicine
Category: Basic Sciences

36

Healthy Egg: Study of the Fatty Acids Differeces in Classic and OMEGA-3 Enriched Egg in Kuwait Market

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Introduction:
Omega-3 fatty acids are considered essential fatty acids which can be found in fish and certain plant oils. It is important to maintain an appropriate balance of omega-3 and omega-6 in the diet as these two substances work together to promote health called and play a crucial role in brain function as well as normal growth, development, reduce inflammation and help prevent certain chronic diseases such as heart disease and arthritis. Infants are at risk for developing vision and nerve problems. Production of healthy Omega3 containing eggs carried out by feeding natural diet to the hens which includes extended range of ingredients including pulses, green and oil seeds especially flax seeds to enrich the foundation of wheat and soy.

Methods:
A total of 20 of marketed samples, 15 classic (33.3% imported) and 5 fortified (80% imported), from seven countries origin, collected during a period of January 2006 to November 2006. Screening test for fatty acids were carried out by GC chromatography technique after extraction and dervatization of fate. In fortified egg the ratio of alpha-linolenic acid to linoleic acid closed to 1. Samples retested in duplicate with salmon fish oil and flax seed oil as reference omega control. Cholesterol content also scanned with Spectrophotometric method.

Results:
Fatty acid profiles reveals omga6/omega3 ratio in classic egg ranged between 33-75 and in fortified eggs ranged between 1- 10 of tested samples. The local fortified Kuwaiti egg reached to 3 which confirmed with international results, while the UEA product reached to 10 as well control flax seed oil sample revealed ratio 0.23 and salmon fish oil 0.06. The total cholesterol content remains similar.

Conclusions:
The fortified Feeding control is very important tools to decrease the omega6/omega3 ratio in healthy egg production. The Kuwaiti fortified marketed egg samples are confirmed with the international health egg.

Key Words: Fortified egg; Fatty acid; Omega3 and Omega 6
Funding Agency: None

Community Medicine
Category: Graduate (MSc: Basic Sciences)

37

Reported Experience of child abuse among Kuwait University Freshmen

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Introduction:
A cross-sectional study was conducted to measure the prevalence of child abuse in terms of three aspects: physical, sexual, and emotional and to assess the association of abuse with sociodemographic factors.

Methods:
Data were obtained from Kuwait University freshmen using structured self- completed questionnaire. Of the 625 questionnaires given to students in 18 randomly selected classes, 566 (90.6 %) usable questionnaires were received back.

Results:
About two-thirds of the freshmen reported that they had been hit by hand while one-fifth said they had been hit by belt or stick and 2 % reported intentional burn by hot water or iron. In terms of sexual abuse, 11.1% had been subjected to touching and fondling their private body parts and 4.2% had been subjected to rape. Three sociodemographic features were associated with higher experience of physical abuse: older age group ($p=0.014$), males ($p=0.001$), residence with single parent or other relatives ($p=0.004$). Those with higher total family income reported less emotional abuse ($p=0.011$) as well as those who lived with both parents ($p<0.001$). Experience of fondling or touching private body parts was directly associated with number of brothers ($p=0.024$), and inversely with the mother's educational level ($p=0.027$). There was a strong association between emotional abuse and physical as well as sexual abuse ($p\leq0.001$).

Conclusions:
Self reports by freshmen indicate that different forms of child abuse have been experienced by substantial percentages of Kuwaiti children. This suggests an urgent need for a prevention program. Further studies that might help in gauging the health impacts of the problem on the Kuwaiti society are also needed.

Key Words: Child abuse prevalence; Physical and sexual and emotinal child abuse
Funding Agency: None

Community Medicine
Category: Undergraduate

38

Attitude of female university students towards cosmetic repair of facial wrinkles and its relation to psychological distress

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Introduction:
To study both the attitude of female university students towards facial wrinkles repair and its relationship to psychological distress and to ascertain differences between medical students and science students.

Methods:
A cross-sectional sample survey conducted in September 2006 including 477 female Kuwait university students. Data was collected through a self-administered questionnaire including socio-demographic characteristics, knowledge regarding the risk factors which accelerate wrinkling, knowledge and attitudes towards the management of facial wrinkles as well as symptoms of psychological distress. The attitude of the respondents toward the management of facial wrinkling was determined using a self - designed scoring system, while psychological distress was measured using the Hopkins Symptoms Checklist.

Results:
50.7% of the females were willing to undergo cosmetic repair of facial wrinkles while 36.5% were indifferent and 12.8% were unfavorable. A significant association was found between depression and attitude of females towards wrinkles repair, p=0.006 as well as total emotional distress and attitude p=0.041; however, no significant association was found between anxiety and attitude, p=0.073.

Conclusions:
No significant difference was found between the attitude of medical and science students towards the repair of facial wrinkles. Psychological distress has an impact on the attitude of female students towards facial wrinkles management.

Key Words: Wrinkles; Psychological distress
Funding Agency: None

Critical Care
Category: Clinical

39

A prospective study on management of acute exacerbation of COPD in general ward with Non Invasive Ventilation.

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Introduction:
Hospital admission due to acute exacerbation of COPD is common especially in smokers. Due to lack of ICU beds and need prolonged assistated ventilation we designed the study to manage these patients in general ward with non invasive ventilation. Aim of the study was to find out the mortality rate and failure of non invasive ventilation and ICU admission.

Methods:
Patients with COPD admitted with respiratory rate of >30/minute, active accessory muscle of respiration, Oxygen saturation <90% on Oxygen face mask, PaO_2:FIO_2 ratio <200, and arterial CO2 more than 6Kpa were included in the study. Initially patients were put on Oxygen by venturi mask and arterial blood gases were obtained. Subsequently patients were put on Non Invasive Ventilation. Patients were continuously monitored by ECG and pulse Oxymeter. Pressure Support was increased to obtain respiratory rate of <25/min and the disappearance of accessory muscle activity. PEEP was increased up to 10-12cm of water to obtain peripheral Oxygen Saturation 92% with minimal FIO_2 possible.

Results:
Eighteen patients were included in the study 10 were female and 8 were male between age group of 50 to 80 years. In addition to COPD other associated problems were DM in 15, HTN in 15, previous MI in 15, old Pulmonary TB in 3, End stage renal disease in 1, Carcinoma breast in 1 and 12 patients were obese with BMI >35. Six patients (33.3%) needed ICU admission three needed intubation (16.6%) and mechanical ventilation. Two patients died (11.1%) one with Carcinoma breast because of multiple metastases other with ESRD because of septic shock.

Conclusions:
These patients can be managed with non invasive ventilation at general ward with continuous monitoring of the peripheral Oxygen saturation and other vitals. It also needed training of ward staff. ICU admission and intubation with mechanical ventilation needed if deterioration in consciousness, respiratory acidosis or associated multi organ dysfunction.

Key Words: COPD; Non Invasive Ventilation; Intubation
Funding Agency: None

Dentistry
Category: Undergraduate

40

Does the prescription of antibiotics to diabetic patients by dentists correlate with clinical experience?

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Introduction:
To find out if there is an association between the clinical experience of dentists and prescribing antibiotics to patients with diabetes.

Methods:
Data was collected by means of a structured, anonymous, self-completed questionnaire. Questionnaires were distributed to a convenience sample of 65 general dental practitioners from polyclinics, private clinics and specialized dental centres. The questionnaires were distributed to the dentists and collected the following day.

Results:
Thirty-five percent (n=65) of general dental practitioners prescribe antibiotics for the following clinical procedures: check-up, scaling, operative procedure, endodontic therapy, oral surgery and periodontal surgery. Twenty-nine percent of general dental practitioners with clinical experience less than five years prescribed antibiotics to diabetic patients for simple procedures such as check-up and operative procedures compared to 12.2% of general dentists with clinical experience more than five years (p-value=0.089). Fifty-one percent of general dentists with five or more years of clinical experience prescribed antibiotics when indicated (oral and periodontal surgeries) compared to 25% of general dentists with clinical experience with less than five years (p-value=0.038).

Conclusions:
Antibiotic prescription to diabetic patients by dentists in Kuwait is associated with clinical experience. Educational efforts appear to be needed. These efforts can be put into action in order to attempt to increase compliance of dentists to antibiotic prophylaxis recommendations.

Key Words: Diabetic patients; Antibiotic prescription; Clinical experience
Funding Agency: None

Dentistry
Category: Graduate (Resident)

41

Parent-Child Separation during Dental Care

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Introduction:
The objective of this study was to determine if the parental presence in the clinic during dental treatment -in Kuwait- is preferred (or not) in the perspective of parents and dentists.

Methods:
A total of 227 subjects were included in this study. Group 1 consisted of 152 subjects, who were the parents of children attending the ministry of health dental clinics. A second group consisted of 75 dental care providers. The information obtained from both groups was both demographics and the preference to be or to have the parents inside or outside the dental clinic during child dental treatment in normal situations. Both groups were asked to complete a closed-ended questionnaire.

Results:
The results of this study demonstrated a statistically significant relationship between the child age and parents' preference. There was a statistically significant relationship between dentist specialty, age, and year of graduation and their preference to have the parents inside or outside the dental clinic.

Conclusions:
This study demonstrated that parents preferred to be inside the clinic with younger children, and as age advanced this preference decreased. The pediatric dentists showed an overall preference towards parent's presence inside the clinic during dental treatment. There was a significant relationship between the age and year of graduation of the dentist and their preference to have the parents inside or outside the dental clinic, that most young dentist preferred to have the parents outside the clinic.

Key Words: Separation; Dental care; Pediatrics
Funding Agency: None

Dentistry
Category: Basic Sciences

42

Reasons and pattern in patients demand at casualty dental clinic in Ahmadi Hospital, Kuwait

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Introduction:
Before the commencement of any service or for improving any ongoing service, there must be a demand. This demand reflects the extent of service used, and the user preferences. In Dentistry, meeting these demands is not always easy, as the real need of users is either not known or assessed. To assess this demand, the study was planned to monitor reasons and pattern of initial complaints of out-patients in the casualty dental clinic of Dental Services Division at Ahmadi Hospital, Kuwait.

Methods:
A prospective study was designed, where "reason of visit" was classified into 11 categories and data on out-patient visits was collected over a period of 12 months (5 days a week, 8 hours a day). One-way analysis of variance with Bonferroni test, in SPSS, was applied to compare the mean visits in different demands.

Results:
A total of 26332 visits were recorded during the study period. The most common reason for seeking dental management was "acute symptom" (41.5%), with mean visits as 910 (+126 SD) per month. It was followed by those, seeking "check up" (35.5%) and "follow-up" (5%), with mean visits (776+180) and (113+58) respectively. The least reason mentioned was "need referral for outside clinic" (0.1%). One way ANOVA determined, the mean visits for acute symptom and check-up, were significantly higher ($p < 0.001$) than any other complaint A seasonal pattern in visits was also observed in particular months.

Conclusions:
The pattern in visits and reasons, noticed at our hospital were similar to those found in other studies. The findings observed, will help in planning and management of patient dental care at our hospital.

Key Words: Patients demand; Reason of visit; Pattern
Funding Agency: None

Dentistry
Category: Clinical

43

National survey of caries levels in schoolchildren in Kuwait

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Introduction:
The aim of this national dental survey was to determine the caries-free proportions, caries experience and restorative care among schoolchildren in government schools in the five different governorates (Ahmadi, Farwaniya, Hawally, Jahra, Capital) in Kuwait.

Methods:
A national epidemiologic survey of the 5-14 year-old children (n=4, 588) was conducted in the government schools in Kuwait. A stratified, multistage, probability sample of 2.5% of the target population was drawn from each census region. Eight trained and calibrated dentists examined the children. Dental caries was scored using WHO criteria.

Results:
In the primary dentition, the percentage of 5-and 6-year-old children with dft=0 was 12.6% and 14.4% respectively. The corresponding mean dft/dfs for 5- and 6-year-olds were 4.6/9.7 and 4.6/9.9. The restorative index (RI) was 12.8% for 5-year-olds and 18.4% for 6-year-olds. For the permanent dentition, the percentage of 12- and 14-year-old children with DMFT=0 was 26.4% and 27.7% respectively. The corresponding mean DMFT/DFS figures for 12- and 14-year-olds were 2.6/3.4 and 3.9/4.2. The decayed component was the major contributor to these mean scores. RI was 19.2% for 12-year-olds and 18.8% for 14-year-olds. Poor oral hygiene (OR=2.0; 95% CI=1.7-2.4) and increasing age (OR=1.4; 95% CI=1.3-1.5) were significantly associated with caries risk in the permanent dentition.

Conclusions:
Caries levels are similar to those in neighbouring and other Middle East countries. Preventive services should be given high priority and needs to be at an earlier age to target the primary dentition, and future caries in permanet dentition. There is a clear need for expanding the national school oral health program to reach those children who are not yet receiving systematic preventive and curative services. Further studies are required to monitor the effect of the extensive caries preventive programme now in place in Kuwait.

Key Words: Dental caries; Schoolchildren; Kuwait
Funding Agency: Ministry of Health, Kuwait and the Forsyth Institute

Dentistry
Category: Undergraduate

44

Patient Satisfaction Regarding Orthodontic Treatment Stability

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Introduction:
It is very well documented that relapse after orthodontic treatment is very common. Causes of, factors associated with, and ways of management for relapse after orthodontic treatment has been evaluated by several studies. Despite the relapse factor, the patients' satisfaction at long term after orthodontic treatment could be very acceptable. Only few studies were conducted to evaluate patients' satisfaction with post orthodontic treatment stability. Aim: To evaluate patients' satisfaction regarding stability of their orthodontic treatment and to determine whether patient satisfaction is affected by their compliance with wearing the retainer, attending follow up visits and reasons for stopping wearing the retainer, or by the level of their awareness regarding the possibility of relapse after orthodontic treatment.

Methods:
Cross-sectional survey including 101 Kuwaiti patients treated in government dental centers. Data was collected using a questionnaire answered by phone. Association tests were used to determine the affect of several variables on the satisfaction score.

Results:
The percentage of patients who were satisfied with their orthodontic treatment stability was found to be 64.3%. Retainer ware and different reasons to stop wearing the retainer did not significantly affect the satisfaction score. However, there was highly significant relation between patients' satisfaction score and their compliance with attending follow up visits. Patients' awareness regarding the possibility of relapse after orthodontic treatment significantly enhanced their satisfaction score.

Conclusions:
Follow up visits during the retention period and increasing patients' awareness regarding the possibility of relapse after orthodontic treatment, significantly enhance patients' satisfaction towards orthodontic treatment stability.

Key Words: Orthodontic retention; Orhto patient satisfaction; Orthodontic stability
Funding Agency: None

Dentistry
Category: Clinical

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A combination of alleles 2 of interleukin (IL)-1A-889 and IL-1B+3954 is associated with lower gingival bleeding tendency in plaque-induced gingivitis

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Introduction:
Genetic polymorphisms have attracted considerable attention in the study of inflammatory responses. A distinct combination of alleles 2 of interleukin (IL)-1A at locus -889 and IL-1B at locus +3954 seems to be associated with an increased susceptibility to periodontitis. The aim of this study was to assess the influence of this distinct combination of polymorphisms in the IL-1 cluster on gingival bleeding tendency in young adults with plaque-induced gingivitis.

Methods:
50 otherwise healthy, nonsmoking Arabs, 19-28 yr of age, participated. Clinical examinations included periodontal probing Departmenth, bleeding on probing, plaque index, and presence of calculus. Probing was done with a pressure-controlled probe at about 1.27 MPa. Examinations were repeated after 2 and 4 weeks. Polymorphisms in the IL-1 gene cluster were assessed using a reverse hybridization assay. A subject carrying alleles 2 at IL-1A-889 and IL-1B+3954 gene was designated genotype-positive.

Results:
26 subjects were genotype positive (52%). A repeated measures 2-level (occasion, subject) model of the proportion of sites bleeding on probing which was adjusted for average plaque index revealed a significantly lower proportion of bleeding sites in GT positive subjects (estimate -0.050, standard error 0.025, $p<0.05$). Biserial correlations of bleeding proportions were high (0.72-0.78), confirming the steady-state plaque environment.

Conclusions:
A high prevalence of the specific IL-genotype was found in this Arab population. Inflammatory responses to dental plaque were considerably dampened in genotype-positive, non-smoking young adults, which might be related to a reported increased susceptibility to destructive periodontal disease

Key Words: IL-1 genotype; Gingivitis; Steady-state
Funding Agency: Kuwait University Research Administration Grant # DS0204

Dentistry
Category: Clinical

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Short-term Effect of Triclosan-containing Toothpaste On the Association Between Plaque and Gingival Bleeding - A Randomized Controlled Clinical Trial.

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Introduction:
Triclosan (2, 4, 4'-trichloro-2' hydroxydiphenyl ether)in toothpaste has been shown to reduce plaque and gingivitis levels on a subject basis. Specific aims of this study were (i) to determine site-specific longitudinal associations between supragingival plaque and gingival inflammation; and (ii) to analyze multilevel variance/covariance structures in a steady state plaque environment.

Methods:
A 10-week, randomized, 2-arm, double-masked, controlled clinical trial was conducted in 34 healthy, non-smoking females with plaque-induced gingivitis. Clinical periodontal examinations were repeated every other week. At week 4, test toothpaste containing 0.24% sodium monofluorophosphate, 0.3% triclosan, and 2% polyvinyl-methyl ether maleic acid; or control toothpaste containing 0.76% sodium monofluorophosphate and 0.1% sodium fluoride, were randomly distributed.

Results:
Multivariate multilevel models indicated that, after introducing experimental toothpastes, subject random error was reduced from 0.6 to below 0.2. The odds of bleeding on probing was about 30% less in the test than in the control group ($p<0.01$). At the end of the experiment, odds ratios for bleeding on probing and plaque index scores 1-3 (reference 0) were 2.1 to 2.4 in the control group, but 1.1 to 1.9 in the test group ($p<0.01$). No effects on plaque levels and calculus were observed.

Conclusions:
Multivariate multilevel modeling allows the study of fixed and random effects of experimental toothpastes on gingival inflammation in small sample. Triclosan appears to attenuate the causal association between supragingival plaque and gingival bleeding in gingivitis.

Key Words: Triclosan; Toothpaste; Gingival inflammation
Funding Agency: Kuwait University Research Administration Grant # DS0202

Dentistry
Category: Clinical

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Adult Rampant Caries in Kuwait Dental Clinics

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Introduction:
There is little information about adult rampant caries in Kuwait. The aims of this work were, therefore, to: i) estimate the occurrence of adult rampant caries among patients attending Kuwait dental clinics, ii) investigate salivary gland function and estimate treatment need among the patients with rampant caries.

Methods:
The total number of patients seen in 6 Primary Health polyclinics in 5 randomly selected governorates within one month was recorded. A note was made of the patients with adult rampant caries, i.e. patients aged 16+ years who had at least 8 open carious cavities with at least one anterior tooth carious. A questionnaire was also administered on Kuwait dentists, to inquire into the occurrence of the condition in their clinics.

Results:
Adult rampant caries occurred in 0.26% of 11, 538 patients seen at the polyclinics within 1 month, and the highest proportions were from Jahra and Hawally. In contrast, the questionnaire study revealed that 0.52% of patients had rampant caries. ANOVA showed that cases of rampant caries were significantly higher ($p<0.001$) among patients of lower socio-economic group. Salivary flow rates and buffering capacity among the rampant caries patients were within normal limits and most of the patients required extensive restorative treatment and exodontia.

Conclusions:
i) Less than 0.6% of the patients seen in Kuwait clinics had rampant caries, and most of the cases were from Jahra and Hawally governorates, ii)Adult rampant caries in Kuwait was not due to salivary gland hypofunction iii) The affected patients required extensive treatment.

Key Words: Rampant Caries; Adult; Kuwait
Funding Agency: Kuwait University Research Administration Grant # DR01/05

Dentistry
Category: Graduate (MSc: Basic Sciences)

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Oral health status and dental needs of Autistic children and adolescents in Kuwait

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Introduction:
There is a wide conflict in the literature regarding whether the caries index and periodontal health of autistic children is higher, lower or comparable to normal children. The objective of this study was to assess oral health and dental needs of autistic children and adolescents in Kuwait.

Methods:
This study was designed as a case-control study including 39 autistic patients and 39 matching controls in age and sex. Both study and control groups were subdivided into two age groups: 5-11 and 12-18 years. Participants were examined by one examiner following the World Health Organization (WHO) recommendations. Values including decayed, missing and filled teeth (dmft or DMFT), Community Periodontal Index of Treatment Needs (CPTIN) and trauma were recorded. A questionnaire; evaluating oral hygiene behaviors was distributed to study and control groups.

Results:
There were no statistically significant differences between the study and control groups (ages 5-11 years) in the total dmft (3.42±3.42 and 3.53±2.55 respectively), DMFT (1.21±1.67, 1.87±1.34 respectively) and CPTIN (0.63±0.61, 1.91±0.66 respectively). There was also no statistically significant difference between the study and control groups (age group 12-18 years) in the values of DMFT (4.71±2.71, 3.53±2.76, respectively) and CPTIN (1.91±0.66, 0.64±0.66, respectively). Autoextraction was found in 15.4% of the sample.

Conclusions:
The results of this study indicate that there is no significant difference in the values of dmft, DMFT and CPTIN between cases and controls. There was also no statistically significant difference between the two groups in relation to dental trauma.

Key Words: Autism; Autoextraction; DMFT
Funding Agency: None

Dentistry
Category: Clinical

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Assessment of pain associated with the surgical placement of dental Implants

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Introduction:
Despite increasing popularity, limited information is available on the pain experience associated the surgical placement of dental implants. The aim of this study was to assess patient reported pain during and sfter implant insertion and to evaluate factors a ssocited with this pain

Methods:
510 implants were placed in 234 patients, mean pain score were reevaluated during and 24 hours, 1, 6, and12 weeks after surgery

Results:
Mean pain score were hieghest at 24 hours after surgery and decreased gradually

Conclusions:
Pain experienced during and after the surgical placement of dental implants is generally mild, gradually decreased with time, and is significantly associated with operator experience, female gender, surgical difficulty, and pain at earlier time points.

Key Words: Dental implants; Pain; Surgery
Funding Agency: None

Dentistry
Category: Basic Sciences

50

Third molar root development as an indicator of chronological age in Kuwaiti youths

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Introduction:
Dental findings are an important method to use in assessing chronological age. The aim of this study was to answer the question whether the radiological development of the root of the mandibular third molar can give information for the task of individual age estimation. Thereby, the investigation could contribute to age estimation efforts that are carried out on persons with an unknown age.

Methods:
Orthopantomograms of 100 Kuwaiti patients (46 males and 54 females) were analyzed. The patients were aged 13 to 24 years. The study was based on the evaluation of the developmental progress of 194 third molars in these patients. The observer classified the development of the lower third molars, as seen in a panoramic radiograph, into seven defined stages earlier described by Kullman et al.1992. A general linear model for univariate analysis was used to evaluate differences in mean ages in different developmental stages and gender, as well as to study the interaction effect on age.

Results:
The overall mean age of the study sample was 17.9±2.7 years. The majority of patients (47%) were observed in the age group (15-18) years. The data was normally distributed, p=0.09 (Kolmogorov-Smirnov test).The mineralization of the third molar's root was found to start at the age of 14.8 years with ±1.48 SD and the root was fully formed at about 18.8 years with±1.88 SD. The mean ages were significantly different at different developmental stages ($p<0.001$). There were no significant differences between males and females, but the root development was generally more advanced among males than among females of the same age.

Conclusions:
The developmental stage of the root of the lower third molar as seen in panoramic radiographs might be considered as a valuable indicator of chronological age in this sample of Kuwaiti youths, given the scarcity of other available age indicators.

Key Words: Age estimation; Panoramic radiographs; Forensic Dentistry
Funding Agency: None

Dentistry
Category: Clinical

51

Radiographic study of third molar development in relation to chronological age among Kuwaiti juveniles

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Introduction:
Wisdom tooth development is a valuable tool for age estimation in late adolescence and early adulthood as there are no other reliable indicators available for age estimation. The aim of the present study was to try to establish a Kuwaiti age reference standard on the third molar development of Kuwaiti juveniles and young adults for forensic application.

Methods:
The evaluated material consisted of 629 panoramic radiographs of Kuwaiti patients between the ages of 14.0 to 24.9 years, registered with the Kuwait University Dental Clinic. The development of maxillary and mandibular third molars was evaluated according to Demirjian's schematic definitions of crown root formation and statistical tests were used to compare/assess the differences in development related to age. The samples of panoramic radiographs were scored by two masked observers who were calibrated for intra- and inter-observer reliability (Kappa value=0.9).

Results:
More than 80% of females and more than 95% males have attained crown completion under the age of 17 years and the mean age for root completion was 21.8years. The mean age at each developmental stage was generally lower for males when compared to females, but these differences were significant in only stage. No statistcaly significant differences were found between the right and left side for both males and females.

Conclusions:
Based on the data, the Kuwaiti age reference standard for development of the third molar according to modified Demirjian stages were established. For the Kuwaiti population, third molar crown completion is seen at 15-16 years and then continuously unfolds until the root is fully developed at 21-22 years

Key Words: Age Estimation; Third Molar development; Radiographic Study
Funding Agency: None

Dentistry
Category: Clinical

52

Effect of xylitol candies on plaque and gingival indices in physically disabled school students

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Introduction:
Due to physical limitations and inability to master techniques required for tooth brushing, achievement and maintenance of oral hygiene and gingival health can be extremely difficult and remains as outstanding challenge in the care of physically disabled persons. Xylitol is an alternative sweetener and several studies have suggested that usage of xylitol can improve the status of oral hygiene. This study aimed to evaluate the effectiveness of the regular use of xylitol candies on plaque and gingival indices on physically disabled school students in Kuwait.

Methods:
Altogether 145 students (105 in the xylitol group and 40 in the control group) with age range 10-27 years (mean age=14.7+3.1 years) participated in this 18-month intervention program. The school health nurses distributed xylitol candies to the students three times during the school day. Plaque was scored according to the Silness and Loe plaque index and gingivitis according to the Loe and Silness gingival index.

Results:
The mean plaque index (PI) decreased from 1.73 to 1.14 ($p<0.001$), and the mean gingival index (GI) from 1.74 to 1.16 ($p<0.001$) in the study group. Significant differences were found between the xylitol and the control groups in the reduction of PI ($p=0.037$) and GI ($p=0.008$). The mean PI reduction was 33.5% in the xylitol group compared to 17.9% in the control group. The mean GI reduction was 33.3% in the xylitol group compared to 13.8% in the control group. There was high correlation between the individual PI and GI scores at baseline ($r=0.93$) and final examinations ($r=0.95$).

Conclusions:
Consuming xylitol candies three times during school days seemed to reduce both plaque and gingival scores. This school-based delivery system offered a practical way to distribute and use the xylitol candies among these disabled students. The regular use of xylitol candies may therefore support oral hygiene routines in the disabled students.

Key Words: Xylitol candies; Plaque and gingival indices; Disabled school students
Funding Agency: Ministry of Health and Kuwait University, Kuwait

Dentistry
Category: Clinical

53

Barriers to seeking preventive dental care by Kuwaiti patients

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Introduction:
Understanding barriers to seeking preventive dental care by patients is essential for the appraisal and revision of preventive oral health programs. The aim of this study was to examine the reasons for not seeking preventive dental visits in a sample of Kuwaiti patients.

Methods:
A self-administered, anonymous, structured questionnaire was distributed to a random sample of Kuwaiti nationals 18 years of age or older recruited from all 6 health districts of Kuwait. Altogether 2400 questionnaires were distributed, and 80.2% were completed. Multiple logistic regression analysis was performed to identify factors independently associated with not having a preventive dental visit for more than one year.

Results:
The last dental visit was within the previous 6 months for 32.2% of respondents, between 6 and 12 months for 26.2%, and more than 12 months for the remaining 41.6%. The most common reasons for the last dental visit were pain or a dental emergency, need for restorative treatment, and an exam/prophylaxis. The strongest predictors for not having preventive visits were not using a mouthrinse daily, flossing less than once a day, dental fear, belief that there is no need for visits unless pain was present, brushing the teeth less than twice a day, and believing that appointments are too far ahead. Also respondents with older age (>30 years), female gender, and those having only high school education or less were less likely to visit dentist for preventive reasons.

Conclusions:
More than half of the studied population reported not to have a preventive visit for more than one year. Unfavorable self-care habits, dental fear and belief that visiting a dentist is necessary only for pain relief were the strongest predictors for the non-attendance behavior.

Key Words: Preventive dental visits; Attendance behaviour; Dental services
Funding Agency: None

Dentistry
Category: Graduate (MSc: Basic Sciences)

54

Laboratory evaluation of two ion leachable aesthetic restorative materials

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Introduction:
Stability and success of restorative resin materials are a function of the materials themselves and the oral environment. Consequently, it is felt that, materials undergo progressive deterioration on ageing, with corresponding deterioration of their adaptation and stability of their constituents probably by complex chemical and physical oral environmental factors.
This was a laboratory investigation that aimed to study the properties of two ion leachable aesthetic restorations, (Ariston pHc, Compomer-F2000) through three periods, namely 3, 6, and 9 months and at different pH level.

Methods:
Standardized class V cavities were cut on the labial surfaces of upper premolars, and restored by the tested restorative materials (Ariston pHc and F2000) with control group of Z100 material After curing and finishing of the restorations, they were immersed in known ingredients artificial saliva with different pH (acidic, neutral and alkaline).

Results:
A decrease of the hardness by time that was aggravated by the storage medium (acidic > neutral > alkaline) was recorded. Also, the ions release were significantly affected by storage medium (acidic > neutral > alkaline) and storage time (9 > 6 > 3 months). At the mean time there were changes in pHs of the storage medium during the period of the study and they were significantly related to the restorative materials. Statistical analysis of the variable demonstrated that Z100 > F2000 > Ariston pHc regarding the hardness test.

Conclusions:
Within the limits of this study, the following conclusions were drowns:
1.The amount and types of leached ions were significantly affected by the storage medium and storage time.
2.There was a significant role of the leached ions on the hardness of the tested restorative materials through the different testing periods and storage media of the study.

Key Words: Ariston Phc; Leakage; Hardness
Funding Agency: None

Dentistry
Category: Clinical

55

Carriage rate of Helicobacter pylori in the oral cavity of healthy versus disabled Kuwaiti children using Nested PCR

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Introduction:
Helicobacter pylori is strongly associated with non-dyspepsia gastritis and most cases of gastric and duodenal ulcers. The source of this organism is still unknown. Oral cavity has been suggested as a possible source but this is still largely unresolved. This pilot study was carried out to compare the oral carriage of H. pylori in the healthy versus disabled Kuwaiti children using nested PCR.

Methods:
Dental plaque samples were collected from 50 healthy and 50 disabled Kuwaiti children. DNA was extracted from in-vitro cultured H. pylori and the dental plaques using QIAamp DNA blood mini kit according to the manufacturer's instructions. The extracted DNA (5 µlitre) were used in a two-step nested PCR with primers EHC-U (5'-CCCTCAGCCATCAGTCCCAAAAA-3') and EHC-L (5'-AAGAAGTCAAAAACGCCCCAAAAC-3') in the first step and ET-5U (5'-GGCAAATCATAAGTCCGCGAA-3') and ET-5L (5'-TGAGACTTTCCTAGAAGCGTGTT-3') in the second step using standard procedures. The PCR products were analyzed by agarose gel electrophoresis and visualized by ethidium bromide staining.

Results:
In nested PCR, 230bp DNA was amplified from the genomic DNA of in-vitro cultured H. pylori, as expected. Thus, the amplification of 230bp DNA by nested PCR was considered positive for H. pylori in dental plaque samples. According to this criterion, 24% (12 of 50) of the plaque samples collected from the oral cavity of disabled children were positive for H. pylori; while all the 50 samples collected from the oral cavity of healthy children were negative.

Conclusions:
A higher carriage rate of H. pylori was observed in the oral cavity of disabled children when compared with the healthy children. These are interesting findings worthy of confirmation by studying a larger sample in each group.

Key Words: Dental plaque; Children; Helicobacter pylori
Funding Agency: Kuwait University Grant # DP01/01

Dentistry
Category: Clinical

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A prospective clinical study of mineral trioxide aggregate for partial pulpotomy in cariously exposed permanent teeth

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Introduction:
Dentists have long recognized that traumatic exposures of the dental pulp can be successfully capped with calcium hydroxide preparations that produce calcific bridges across the wound surface. Several investigators have demonstrated that the exposed dental pulp has the capacity to heal when microleakage and bacterial contamination are prevented. An experimental material, mineral trioxide aggregate (MTA) has recently been shown to be biocompatible and to seal pathways of communication between the root canal system and the external surfaces of the teeth. The aim was to evaluate the success of using gray mineral trioxide aggregate for partial pulpotomy in cariously exposed young permanent first molars.

Methods:
Thirty one first permanent molars of 23 patients with carious exposure were treated using partial pulpotomy technique. Age of the patients ranged from 7.2 to 13.1 years (mean=10 years). Clinical and radiographic examination revealed pulpal response within normal limits and normal appearance of the periradicular area, respectively. Following isolation and caries removal, the exposed pulp tissue was removed with a diamond bur to a Departmenth of 2-4 mm. After achieving hemostasis, gray MTA paste was placed against the fresh wound. Floor of the cavity was covered with a base of glass ionomer. The teeth were restored with amalgam or stainless steel crowns. Teeth were reviewed radiographically and clinically at 3, 6, 12 and 24 month intervals.

Results:
Treatment was successful for all teeth (100%). None of the teeth treated showed neither clinical nor radiographic signs of failure during the follow-up evaluation time. Six teeth did not respond to vitality testing at the final follow-up period; however, no radiographic signs of failure or clinical symptoms were detected.

Conclusions:
Partial pulpotomies with gray MTA showed a very high success rate a dressing agent in exposed young permanent first molars

Key Words: Pulpotomy; Teeth; Mineral Trioxide Aggregate
Funding Agency: Jordan University of Science and Technology, Jordan. Grant # 143/01

Dentistry
Category: Undergraduate

57

Students' effectiveness in subgingival scaling in jaw models

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Introduction:
Undergraduate periodontal training involves scaling of artificial calculus in manikins. Here, difficult to clean areas in Zurich plastic models (Frasaco, Germany) were to be identified in order to improve teaching.

Methods:
Probing Departmenth and bone level were assessed with a periodontal probe (KUPCP13b, Hu Friedy, Germany) at 4 sites per tooth in one model. Scaling was done in six 2-hour sessions by 24 fifth-year dental students, 5 males. It was approved by supervisors after each session. After completion, remaining 'calculus' made of shellac, pumice, umbra, agar agar, in jaw models was scored as 1, a spot with an area of less than 1 mm^2; 2: a spot with an area of 1 mm2 or more. Scores were added for each of 4 sites (m, b, d, l). Furcation areas were scored separately.

Results:
Interexaminer reliability of scores was assessed on 5 model pairs comparing the author's scoring with that of an experienced periodontist. Cohen's kappa was 0.527±0.027. Since asymmetry of the table was significant ($p<0.05$), all further scoring was done by the author. The highest median score (1.5) was found at the central upper incisor while lowest values were found at lower 2nd molars (median 0.4). No student achieved total debridement of all stain, 1 student was able to totally clean 75% sites. On the other hand, 1 student did not achieve total debridement in more than 70% sites. Most students left only traces (scores 1 or 2). High scores of 5 or 6 at few sites were found infrequently in a minority of students (about 10% of students). A 2-level (site, model) Poisson model revealed a significant influence of probing Departmenth ($p<0.001$) while bone level and gender did not have an effect. The model identified significant differences of scores in jaw side.

Conclusions:
The present results may be used in refining the teaching regarding specific areas in the model requiring special techniques and instruments.

Key Words: Undergraduate teaching; Periodontology; Scaling;
Funding Agency: None

Dentistry
Category: Undergraduate

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Prevalence of complete and partial edentulism and alveolar bone loss in patients of Kuwait University Dental Center: A pilot study

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Introduction:
Both dental caries and periodontal disease are major diseases of the oral cavity. Knowing the prevalence of these diseases is very important in order to assess preventive and therapeutic strategies. The aim of this pilot study was to examine the prevalence of alveolar bone loss and tooth loss in Kuwait.

Methods:
This was a cross-sectional pilot study reviewing panoramic radiographs of a random sample of patients from Kuwait University Dental Center (KUDC). Radiographs were assessed by one examiner for the presence/absence of all teeth excluding third molars and the presence of radiographically assessed alveolar bone loss using principles of the Schei ruler. Associations of tooth loss and alveolar bone loss with age, gender, and nationality were examined with univariate analysis.

Results:
Sixty-one percent of subjects had one or more missing teeth and 1.3 percent were completely edentulous. Moderate to severe alveolar bone loss in at least one sextant was noted in 38.9 percent of the sample. The prevalence of bone loss in non-Kuwaitis (29.7 percent) was higher than Kuwaitis (11.1 percent; $p<0.05$). This study also showed that males had bone loss (24.7 percent) more commonly than females (15.4 percent; $p=0.018$). Furthermore, the severity of bone loss was found to be increasing significantly with age. The mean number of missing teeth was found to be more in non-Kuwaitis (3.26) than Kuwaitis (2.38). The mean number of missing teeth was found to increase significantly with increasing age.

Conclusions:
A significant proportion of patients attending KUDC are affected by partial edentulism and alveolar bone loss. The prevalence of both tooth loss and alveolar bone loss was found to be higher in non-Kuwaitis, males, and increasing with age.

Key Words: Edentulism; Bone loss; Tooth loss
Funding Agency: None

Dentistry
Category: Clinical

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Evaluation of posterior composite restorations using different modes of LED curing lights

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Introduction:
The aim of the study was compare postoperative sensitivity and marginal discoloration following placement of posterior composite restorations using the fast or step curing mode of LED light.

Methods:
Thirty patients with two homologous contra lateral posterior teeth with class II cavities were included. After cavity preparation, on one of the selected teeth the resin composite restoration was cured using the fast mode of the LED light while the contra lateral homologous tooth was cured using the step mode of the same light. All patients were contacted after 2 and 7 days postoperatively. They were asked about the absence or presence of postoperative sensitivity to cold. The patients were questioned to specify the intensity of the pain using a rating scale from 0-3: 0 for no sensitivity, 1 for slight sensitivity, 2 for moderate sensitivity, and 3 for severe sensitivity. If a patient experienced sensitivity or discomfort 7 days after placement of the restoration, he or she was contacted after 30 days. After 6 months restorations were evaluated for marginal discoloration.

Results:
There was a statistically significant difference in postoperative sensitivity between the two curing modes at days 2 and 7 postoperatively (P=0.014 and 0.046, respectively) but not at days 30 and 90 (P=0.317 and 1.000, respectively). The intensity of sensitivity was also different between the two curing modes at days 2 and 7 postoperatively (P=0.007 and 0.025, respectively) but not at days 30 and 90 (P=0.317 and 1.000, respectively). There was no statistically significant difference between the two curing modes with regard to marginal discoloration (P=0.157).

Conclusions:
Step curing reduced the early incidence of postoperative sensitivity after posterior composite restorations compared to fast curing of the same curing light. There was no difference between the two curing modes regarding marginal discoloration.

Key Words: Postoperative sensitivity; LED Curing Lights; Resin Composites
Funding Agency: This work was supported by Kuwait University Research Grant #.DR 03/05

Dentistry
Category: Clinical

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Healing of experimental soft tissue lacerations following application of topical anesthetics

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Introduction:
Topical anesthetics based on a combination of 2.5% lidocaine and 2.5% prilocaine are efficient in eliminating pain of needle stick when placed on skin and oral mucosa suggesting that they could be used in soft tissue lacerations before suturing to enable pain - free exploration and suturing of traumatic lacerations without prior injection needle stick. The aim of the present study was to investigate the healing of experimental oral lacerations after topical anesthetic substances were placed in the lacerations.

Methods:
Thirty-six (n=36) standardized incisions were made bilaterally in the lower and upper labial mucosa of 9 white New Zealand rabbits. All wounds were intentionally contaminated with saliva to simulate laceration wounds in a trauma situation. EMLA cream (ASTRA, Södertälje Sweden) and Oraqix thermosetting gel (Dentsply Pharmaceutical, York, PA, USA) were applied into 30 lacerations and 6 lacerations were left untreated as control. In some lacerations the topical anesthetic agent was left in the wound, while in others they were rinsed off by saline before suturing the laceration wound. The rabbits were then sacrificed after 3 days, 2 weeks and 4 weeks of healing and the lips were processed for histological evaluation.

Results:
Similar normal histological healing patterns were seen in wounds in which EMLA and Oraqix were applied as compared to control lacerations at all stages of healing. There were neither adverse tissue nor foreign body reactions seen in any of the lacerations.

Conclusions:
We conclude that EMLA and Oraqix can be used in the lacerations in the oral mucosa prior to suturing without the risk of adverse tissue reaction.

Key Words: EMLA; Oraqix; Laceration
Funding Agency: None

Endocrinology
Category: Basic Sciences

61

Iodine status among pregnant women in Kuwait

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Introduction:
Little is known about iodine intake and the prevalence of iodine deficiency, if any, in pregnant women in Kuwait. Therefore, urinary iodine excretion (UIE) and changes in thyroid function during pregnancy were evaluated.

Methods:
Urinary iodide level was measured in random urine samples collected from 326 pregnant women at different gestational trimesters. Blood samples were drawn for thyroid function test (TFT) including free thyroxine (FT4) and thyrotropin (TSH) level determination.

Results:
Median UIE values during trimester 2 indicates iodine deficiency according to the new suggested recommendation for pregnant women which is <140 ug/L. Mean serum TSH levels increased between trimesters 1 and 3 ($p<0.05$). Serum FT4 decreased between first and second trimesters ($p<0.05$) and this reduction was maintained to the third trimester. Furthermore, during the second trimester, TSH levels were significantly higher in women with mild iodine deficiency (MI) as compared to normal individuals ($p<0.05$). On the other hand, FT4 levels were lower in subjects with MI and moderate (MO) iodine deficiency during the first trimester ($p<0.05$).

Conclusions:
These results suggest that 56.8% of pregnant women had median UIE level <145 ug/L, and this is associated with low FT4 and consequently high TSH levels. Therefore, the following data may indicate insufficient iodine intake among pregnant women in Kuwait.

Key Words: Iodine; Pregnancy; TFT
Funding Agency: Kuwait Endowment Fund

Genetics and Molecular Biology
Category: Basic Sciences

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Similarity between Kuwaiti and Tunisian populations in epidermal growth factor receptor intron polymorphism in healthy controls and breast cancer patients

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Introduction:
Epidermal growth factor receptor (EGFR), a tyrosine kinase protein, plays a crucial role in signal transduction which regulates key cellular functions. The first intron of EGFR, which has an important regulatory function, contains a highly polymorphic microsatellite AC sequence close to a downstream enhancer sequence. Aim of this study were to assess and compare the AC allele combinations frequency in Tunisian and Kuwaiti healthy populations, and to screen for potential association with breast cancer from both populations.

Methods:
Genomic DNA was extracted from 69 women breast tumours and 353 normal leukocytes from Tunisian and Kuwaiti populations. EGFR Intron 1 polymorphism was analysed using fluorescent genotyping (ABI 3100 genetic analyzer, version 3.5) confirmed by sequencing.

Results:
AC alleles in both Kuwaiti and Tunisian populations varied from (15-24). There was no difference between the AC allelic polymorphism of healthy Tunisian compared to Kuwaiti population. For the most common alleles 17 and 21 there was no relationship observed between cancer and healthy samples in both populations, as the chi-square was null and 2.07 (p=0.15), respectively.

Conclusions:
This is the first study done on AC repeats in Arab speaking region comparing two populations Kuwaiti, from the Arabian Gulf region and Tunisian, A North African country. There were close similarities between these two ethnically similar populations. No significant difference or relative risk between AC polymorphism in healthy and breast cancer in both populations were observed. Our results provide new data on EGFR microsatellite instability in women breast cancer which may contribute to the understanding of EGFR gene expression regulation.

Key Words: EGFR; Breast Cancer
Funding Agency: None

Genetics and Molecular Biology
Category: Basic Sciences

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Identification of conserved dinucleotide repeats in introns of ERBB genes

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Introduction:
Members of the epidermal growth factor-receptor protein family (ERBBs) play a critical role in the control of many physiological processes. Overexpression or dysfunction in the activity of EGFR and other ErbBs has been reported to be involved in many human cancers. Evenly, it has been shown that the first intron of several genes including ErbBs has an important regulatory transcription function. Particularly, a simple CA repeats (CA-SSR) in intron 1 of EGFR have been found associated in vivo and in vitro to the level of transcription modulation of the EGFR and may be located close to a regulatory element. The aim of the study was to look for conserved CA repeats located in introns of the human ERBB genes.

Methods:
Pairwise blast was used to compare intron 1 of EGFR to ErbB genes (ErbB2, EbbB3 and ErbB4). Dinucleotide Tandem repeats were searched using the Tandem Repeat Finder (TRF) program as well as a Perl script designed to find only dinucleotide simple repeats in nearest homologue to EGFR intron 1. Multiple alignment and motif search using MEME were performed to look for short conserved DNA signals that may reveal the presence of potential regulatory elements near the CA-repeats.

Results:
We identified 23 potential STR in intron 1 of EGFR gene using TRF (8 dinucleotides). ErbB4 shows 67 potential STR, while no CA repeat was found in intron 1 of Erbb2 or Erbb3. Using pairwise blast, we found that the nearest homologs to intron 1 are intron 4, intron 15 and intron 20 respectively for ErbB2, ErbB3 and ErbB4. The comparison files of blast and TRF of ErbB1 and ErbB4 displays the existence of 8 exact matching dinucleotide repeats including the previous described CA repeat D7S2550. The Motif search by MEME shows 3 blocks of Pattern. The TFSEARCH program proved an implication of known transcription factor SP1, which is involved in the transcription regulation of ERbB1 and ERbB2.

Conclusions:
Our results suggest that the transcriptional regulatory role of the CA repeat in EGFR intron 1 might be conserved in other ErbB genes. Experimental validation is needed.

Key Words: EGFR; Breast Cancer
Funding Agency: None

Genetics and Molecular Biology
Category: Clinical

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Methylenetetrahydrofolate reductase A1298C mutation is a risk factor for myocardial infarction in Arabs in Kuwait

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Introduction:
Folate metabolism in human cells needs many enzymes, one of which is methylenetetrahydrofolate reductase (MTHFR). Normal level of MTHFR is needed for conversion of homocysteine into methionine, which is an important step to prevent accumulation of homocysteine in the blood (Hyperhomocysteinaemia; HHC). HHC has cytotoxic effects, and it was found by some studies to be associated with cardiovascular diseases (CVD). Two mutations in the MTHFR gene were found to reduce the level of the enzyme: C677T and A1298C, and therefore may be associated with CVD. The prevalence of these mutations differed in different parts of the world. We have previously studied the C677T mutation in Arabs. This study was conducted to study the A1298C mutation and its possible association with myocardial infarction (MI) in Arabs living in Kuwait.

Methods:
PCR and RFLP techniques were used to test for the presence of MTHFR A1298C mutation in 152 subjects (76 MI patients and 76 healthy controls), all of whom were of Arab ethnicity living in Kuwait.

Results:
The mutation was present in 60 MI patients (78.9%) [33 heterozygous (43.4%) and 27 homozygous (35.5%)] and in 49 healthy controls (64.5%) [29 heterozygous (38.2%) and 20 homozygous (26.3%)]. The prevalence in patients was higher than in controls, which was statistically significant (p-value=0.036).

Conclusions:
Arabs have a high prevalence of MTHFR A1298C mutation (64.5%), which is close to the highest value for the prevalence in Europe (45-65%). This mutation appears to be a risk factor for the development of MI in Arabs in Kuwait (2.1-fold increased risk).

Key Words: MTHFR A1298C; Myocardial Infacrtion; Kuwait
Funding Agency: None

Genetics and Molecular Biology
Category: Graduate (Resident)

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Patient demographics and disease variables correlate with distinct cytokine patterns in peripheral blood mononuclear cells from rheumatoid arthritis patients

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Introduction:
Inflammatory and regulatory cytokines are known to play a critical role in the initiation and perpetuation of rheumatoid synovitis. Aim: To evaluate the levels and ratios of a panel of immunoregulatory cytokines in mitogen-stimulated peripheral blood mononuclear cells (PBMC) from patients with rheumatoid arthritis (RA), and to identify biologically-based subsets of RA by relating cytokine profiles to patient demographics and disease variables.

Methods:
42 seropositive RA patients were studied. The patients were characterized into having early, established or late disease; mild, moderate or severe disease; ACR (American College of Rheumatology) functional class I, II, III or IV; and as being in remission, or being active. Thiry seven age- and sex-matched healthy controls (HC) were also enrolled. The production levels in mitogen-stimulated PBMCs of five pro-inflammatory cytokines (IFN gamma, TNF alpha, TNF beta, IL-8, IL-18) and three anti-inflammatory cytokines (IL-4, IL-10, IL-13) along with the ratio of each pro- to each anti-inflammatory cytokine in RA patients and in HC were studied.

Results:
The female to male ratio was 1.8:1. The cytokine profile in female RA patients showed a distinct T cell helper 2 bias with a general pattern of under-production of pro-inflammatory and over-production of anti-inflammatory cytokines as compared to males. RA patients with disease onset over age 40 had lower levels of IL-18 and IL-4 compared to patients with disease onset under age 40. Also, older present age of RA patients correlated with lower IL-4 and higher TNF beta levels. Arab patients, compared with non-Arabs, had distinct cytokine profiles and ratios. Increasing disease duration of RA correlated with enhanced IL-8 levels. As for disease severity, patients with mild RA exhibited higher levels of IL-4. RA patients with non-erosive disease had higher levels of TNF alpha and IL-8. Importantly, there were no significant differences in cytokine production levels or ratios of pro- to anti-inflammatory cytokines between the active and remission RA groups. As regards the number of disease modifying antirheumatic drugs (DMARDs) the patients are receiving, the levels of IL-10 and the ratios of IFN gamma/IL-4 and IFN gamma/IL-13 were higher in patients on <2 DMARDS, whereas the levels of IL-18 and the ratios of IL-18/IL-10 and IL-8/IL-10 were higher in those receiving >3 DMARDs.

Conclusions:
The cytokine profile in female RA patients shows a distinct Th2 bias. There are several interesting differences in cytokine patterns and ratios with respect to age at onset, current age, ethnicity, disease severity, presence or absence of erosive disease and the number of DMARDs the patients require.

Key Words: Rheumatoid arthritis; Cytokines; Variables
Funding Agency: None

Genetics and Molecular Biology
Category: Clinical

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PCR-based detection of fetal RhD and Y-chromosome-specific DNA in pregnant women during different stages of pregnancy

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Introduction:
Prenatal testing of fetal rhesus D (RhD) status and gender by invasive techniques like amniocentesis carries small yet finite risks to the fetus and mother. The aim of this study was to determine whether a noninvasive procedure utilizing maternal peripheral blood as the source of DNA and polymerase chain reaction (PCR) could be used to detect fetal RhD status as well as fetal gender during different gestational stages of pregnancy.

Methods:
Maternal blood was collected from 54 RhD negative pregnant women during first trimester (6-13 weeks, n=14), second trimester (14-26 weeks, n=26) and third trimester (27-40 weeks, n=14). Genomic DNA was isolated from the whole blood and analyzed by semi-nested/nested PCR for detection of DNA sequences corresponding to RhD (n=54) and Y-chromosome (n=48) using RhD and Y-chromosome-specific oligonucleotide primers, respectively. The semi-nested/nested PCR results were compared with the RhD status and gender of the babies after delivery.

Results:
The sensitivity and specificity of semi-nested PCR for detection of fetal RhD positivity in whole blood of pregnant women were 81% and 100%, respectively, while sensitivity and specificity of nested PCR for detection of male fetuses, using Y-chromosome-specific DNA as a marker, were 96% and 91%, respectively. There were no significant differences in the PCR results with samples obtained from women at different gestational stages of pregnancy.

Conclusions:
Semi-nested and nested PCRs for detection of fetal RhD and gender status, respectively, by using the blood of pregnant women during different gestational stages of pregnancy, are reliable non-invasive procedures with high sensitivity and specificity.

Key Words: Fetal RhD; Fetal Y-chromosome; PCR
Funding Agency: None

Genetics and Molecular Biology
Category: Graduate (Resident)

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Microsatellite instability analysis in colorectal cancer: Why are our patients so young?

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Introduction:
Colorectal Cancer (CRC) is a common disease that affects both men and women. It is the third most common cause of cancer-related death in the Western world. The incidence rate of CRC in Kuwait is 8/100, 000/year. CRC is classified as sporadic or inherited. CRC affects young patients in Kuwait and virtually nothing is known about the role of mismatch repair (MMR) genes (MLH1, MSH2, and MSH6) in CRC in this population. This study aims to evaluate major molecular pathways with particular emphasis on the role of mismatch repair genes and Microsatellite Instability (MSI) on the pathogenesis of CRC in Kuwait.

Methods:
158 colorectal cancer samples were randomly selected from major hospitals in Kuwait and tested for MMR protein expression by immunohistochemistry (IHC) in which prepared paraffin embedded tumor tissue slides were stained with antibodies against three mismatch repair gene proteins (MLH1, MSH2 and MSH6), then scored for the presence or absence of each protein. MSI was determined for tumor samples and their matched normal by amplifying five DNA microsatellite regions (BAT-25, BAT-26, D2S123, D5S346 and D17S250) using PCR. Products were analysed by gel electrophoresis and levels of instability were determined.

Results:
MSI represents a major cause of CRC in this population. We show, for the first time, that loss of MLH1 mismatch repair axis plays a significant role in CRC development in Kuwait. MSI was associated with young age, right sided and poorly differentiated CRCs.

Conclusions:
This is the first and largest study that has been undertaken in the Gulf area. Our results show high prevalence of mismatch repair gene defect in CRC patients, which can explain the young age of onset of this disease in Kuwait. If confirmed, an association with hereditary non-polyposis colorecal cancer (HNPCC) should be determined in the near future.

Key Words: Colorectal Cancer (CRC); Mismatch Repair (MMR) proteins
Funding Agency: Terry Fox Foundation - project no. TFF/04/05 and College of Graduates Studies

Genetics and Molecular Biology
Category: Graduate (MSc: Basic Sciences)

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Evidence of association and gene interaction of MX1, eNOS, and DNASE1 contributes to SLE susceptibility

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Introduction:
Systemic lupus erythematosus is a polygenic systemic autoimmune disease characterized by phenotypic heterogeneity. Genome-wide microarrays have revealed that active SLE has a homogeneous gene expression pattern with overexpression of genes related to various pathways. Here we have selected four candidate genes from different cellular pathways; endothelial nitricoxide synthase(eNOS), interferon-induced protein p78(Mx1) and Deoxyribonuclease (DNase)I and II, to genotype, study their association with SLE and investigate the potential gene interaction using tagged genetic markers of the proven associated genes.

Methods:
DNA of 82Kuwaiti SLE-patients and 95race-age-gender matched healthy controls was obtained. DNASEI and II were screened for polymorphic markers using direct sequencing. Mx1 promoter (G-89T, C-123A) and Intron 6 were screened using RFLP and sequencing, eNOS was screened for; T-786C, Intron4-VNTR(27bp-repeat), and exon7 G894T(Glu298Asp) polymorphisms using RFLP, 3%agarose-gel, and sequencing. $\chi 2$ and odds-ratio were used for data analysis. GenePop-software was used to calculate Hardy-Weinberg p-value. PHASE-software was used to estimate the haplotype frequency and testing for association.

Results:
Novel SNPs were retrieved from screening both DNASEI and DNASEII. Significant association was shown only with DNASEI (56bp-VNTR) and SLE. No significant association with DNASEII was found. Markers G-89T and Intron4 27bp-VNTR of MX1 and eNOS respectively showed a significant association with SLE. Fourteen haplotypes were obtained when constructing the genotypes (G-89T, 27bp-VNTR and 56bp-VNTR) of MX1, eNOS and DNASEI, respectively. Two haplotypes showed a significant association with SLE susceptiblity; C55 and T55 (p-value=0.000001) and (p-value=0.001) respectively, (OR=3.30 and 4.64, respectively). Two haplotypes G44 and G45 were associated with healthy controls and worked as a proactive haplotypes (p-value=0.022) and (p-value=0.031) respectively, (OR=0.31 and 0.60), respectively.

Conclusions:
Our results reflected a significant interaction of MX1, eNOS and DNASEI genotypes in Kuwaiti SLE patients, and yielded a strong association with SLE. This finding will provide a clearer picture on how various genes working in different pathways interaction leads to disease state.

Key Words: Gene Interaction; SLE; Mx1
Funding Agency: Supported by Kuwait University, Research Administration

Health Physics
Category: Basic Sciences

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Inter-comparison between three Radon-222 (Rn-222) detectors

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Introduction:
Various detectors are available to measure Rn-222 concentrations. Scientists and researchers worldwide paid a great concern for testing and modifying techniques and methods to measure Rn-222. The objective of this study is to find the most reliable detector to scan indoor Rn-222 concentrations in Kuwait.

Methods:
Three radon detectors were tested in measuring indoor radon concentrations in this study. These detectors were the active alphaguard radon monitor type PQ2000, the passive activated charcoal canister model RA40VC from AccuStar company and the picorad vial (Plastic vials includes activated charcoal grains and filled by liquid scintillation cocktail produced by Packard company). Detectors were distributed into 50 different houses to scan radon concentration in the bedrooms and at the first floor of these houses. Each room was scanned by one activated charcoal, one picorad vial and the Alphaguard monitor. The exposure time for all the detectors was 48 hours. One hundred fifty Rn-222 concentration measurements were collected in this comparison process. The data of the comparison process was tested by the one way ANOVA test to compare means.

Results:
The measured mean values (- or + standard deviation) of Rn-222 concentrations were 12.0 (- or +) 3.77, 13.4 (- or +) 4.21 and 13.2 (- or +) 4.21 Bq/m3 and the 95% confidence intervals were (10.92, 13.07), (12.17, 14.56) and (12.05, 14.44) for activated charcoal canisters, picorad vials and alphaguard monitor respectively.

Conclusions:
There was no significant difference among the means of the three systems (P=0.215). Any of the three detectors can be used to measure Rn-222 concentrations. However, picorad vials are preferred due to their lower limit of detection (1.7 Bq/m^3).

Key Words: Radon-222 Detectors; Radon-222 Measurements; Radiation Protection
Funding Agency: None

Health Physics
Category: Basic Sciences

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Accuracy of indoor Radon-222 (Rn-222) concentration measurements using activated charcoal canisters in Kuwait

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Introduction:
Activated charcoal canister became one of the most famous Rn-222 detectors because of its simplicity and accuracy. The canister contains activated charcoal grains which adsorb radon from the air. The adsorbed radon is decayed into radon daughters, Lead-214 (Pb-214) and Bismuth-214 (Bi-214), which are gamma ray emitters. The canister is then scanned by gamma ray spectrometer. Calibration processes are done by using standard Raduim-226 (Ra-226)/Radon-222 (Rn-222) source in which the adsorption coefficient (CF) of the canister and the detection efficiency (DE) of the gamma ray spectrometer are determined. CF and DE are two parameters incorporated in equation used to calculate radon concentration values. The objective of this study is to determine the accuracy of activated charcoal canisters in measuring radon concentrations by comparing CF values to the international standards.

Methods:
Four secondary Ra-226 standard sources were carefully prepared from a primary standard source with different activities. These secondary sources were carefully injected into four charcoal canisters. Canisters were then tightly closed and left for one month to get secular equilibrium between the injected Ra-226 and the produced radon daughters (Pb-214 and Bi-214) inside the canisters. Thereafter canisters were scanned with gamma ray spectrometer and DE values were determined. Another group of six activated charcoal canisters were exposed to different amounts of radon concentrations inside calibration chamber in order to determine CF values.

Results:
CF values calculated using the DE measurements were 0.105, 0.098 and 0.080 Liter/min at relative humidities 20 %, 50 % and 80 %, respectively and were in good agreement with values reported in the standard operating procedures for Rn-222 measurements issued by the American Environmental Protection Agency.

Conclusions:
Activated charcoal canisters are accurate and reliable in measuring radon concentrations.

Key Words: Calibration of Radon-222 Detectors; Radon-222 Measurements; Radiation
Funding Agency: None

Health Physics
Category: Basic Sciences

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Annual effective dose for individuals due to exposure to Radon-222 (Rn-222) in selected places in Kuwait

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Introduction:
Life on earth obligates the continuous and unpreventable exposure of human beings to natural ionizing radiation. Rn-222 is one of the radioactive nuclides which are naturally and widely produced in the environment worldwide. It is established that inhalation of Rn-222 and Rn-222 progeny delivers half of the natural ionizing radiation exposure of the general public. This exposure is considered to be the second largest source of lung cancer after cigarette smoking. Accordingly, international radiation protection agencies recommended measuring and analysis of Rn-222 concentration in each country. In this study, random areas in Kuwait were scanned and the annual effective dose due to exposure to radon was calculated in order to be compared with the international levels.

Methods:
70 houses in Salmiyah and Jabriya were scanned to analyze the indoor radon concentration by using picorad vials and liquid scintillation counters. Six vials are distributed in each house with a total of 420 vials used in the study. Picorad vial is a plastic vial covered with a removable cap and contained 1.3 gram of charcoal grains which adsorbs radon gas. Measuring radon is done by opening the vial for 48 hours then 10 ml of liquid scintillation is dropped inside the vial, which is then covered. The vial is then counted using the liquid scintillation counter.

Results:
The mean value of the measured radon concentration was found to be 11.6±4.8 Bq/m^3. The maximum and the minimum values are 25.4 Bq/m^3 and 3.3 Bq/m^3 respectively. The annual effective dose due to exposure to radon concentration from this level equals 0.4 mSv.

Conclusions:
The average annual effective dose due to exposure to Rn-222 calculated in this study (0.4 mSv) is less than the international limits of exposure to the natural background radiation which equals 2.4 mSv/year in which 50% of this value is due to exposure to radon (i.e.: 1.2 mSv/year).

Key Words: Effective Dose; Radon-222 Measurements; Radiation Protection
Funding Agency: None

Imaging / Nuclear Medicine and Radiological Science
Category: Basic Sciences

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^{99m}Tc-HMPAO brain scan for monitoring pathophysiological changes of early diabetes using a rat animal model

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Introduction:
Diabetes can induce vascular changes affecting multiple organs in the body causing coronary artery disease in the heart, retinopathy in the eye and nephropathy in the kidney. The brain can also be affected leading to ischemia, stroke and cognitive dysfuntion. Brain imaging studies may help detect the pathological changes in perfusion early in their development, especially using SPECT brain perfusion tracers such as technetium 99m-hexamethylpropylene amine oxime (^{99m}Tc-HMPAO). The objective of this study was to detect alteration of brain perfusion in early diabetes using ^{99m}Tc-HMPAO brain scan in a rat model.

Methods:
Wistar rats were divided into two groups a control group and a diabetic-induced streptozotocin (STZ) group. Each group contained 20 rats. Rat brain imaging using gamma camera was performed for each group after 0.5 (control), 2, 4, and 24 h post 129.5 MBq injection of ^{99m}Tc-HMPAO. Data processing for brain scan was done by drawing a region of interest (ROI) circulating the brain (B) and a ROI around the soft tissues around the neck of each rat as background (BKG).

Results:
Brain ^{99m}Tc-HMPAO uptake-to-background (B/BKG) ratios in control rats were determined first and expressed as the mean±standard deviation (mean±SD). A significant difference ($P=0.05$) only was demonstrated between control and 24 h B/BKG ratios. The brain uptake of ^{99m}Tc-HMPAO in the control groups at 0.5, 2 and 4 h was constant, and then decreased significantly at 24 h. The same previous procedures were done for diabetic-STZ brain scan. The results of P values were highly significant ($P<0.0001$) compared to control groups at all time points (0.5, 2, 4, and 24 h). The brain uptake of ^{99m}Tc-HMPAO in the diabetic-STZ group was constant, then increased significantly compared to control groups.

Conclusions:
This study showed that in the rat model ^{99m}Tc-HMPAO brain scan is capable of detecting early diabetes changes in the brain very early in the course of the disease.

Key Words: Diabetes; Brain radionuclide imaging.; Rat;
Funding Agency: None.

Imaging / Nuclear Medicine and Radiological Science
Category: Basic Sciences

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Nuclear medicine and diabetes. Role of functional renal imaging in experimental and clinical investigation of diabetes and its complications

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Introduction:
Pathophysiological changes associated with diabetes affect various organs and are usually chronic and insidious leading to loss of function such as cardiac or renal failure. Nuclear medicine testing offering physiological, chemical, and metabolic imaging of various processes in the living body would enable early monitoring of subtle functional changes and institution of appropriate management strategy. The objective of this study was to determine whether nuclear medicine investigation can detect early pathophysiological changes due to diabetes in various organs to be of clinical usefulness in diagnosis and management.

Methods:
In this study: part I (experimental), type I diabetes was induced in experimental rats by intraperitoneal (i.p.) injection of streptozotocin (STZ). Each experimental rat was control itself. Investigation of early pathophysiological diabetic complications in the kidney was done using 99mTc-DTPA renal radionuclide imaging by first establishing the techniques of detecting blood flow and measuring glomerular filtration rate (GFR) in control and experimental rats after one week-duration from the induction of type I diabetes by STZ.

Results:
Among the 8 rats studied with 99mTc-DTPA, the mean clearance in the control group was 1.75±0.23 ml/min/100 g, whilst, the mean clearance in the diabetic group was 1.94±0.32 ml/min/100 g as renal uptake determined by computer 1 to 3 min post injection. Our preliminary results for the diabetes groups after 1 week of diabetes showed significant increase in the blood flow ($P<0.05$) and significant increase in the calculated GFR ($P=0.035$) in both plasma clearances and renal uptake compared to controls.

Conclusions:
Nuclear medicine plays an important role in research and clinical management of diabetes and its complications. Also, our other ongoing NM tests show promise for experimental evaluation of function and detection of earlier pathophysiological changes in diabetes.

Key Words: Diabetes; Renal radionuclide imaging; Glomerular filtration rate
Funding Agency: None.

Imaging / Nuclear Medicine and Radiological Science
Category: Basic Sciences

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Detection of early change in renal glomerular filtration in experimental diabetes mellitus using radiolabeled Tc-DTPA and nuclear imaging

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Introduction:
Nephropathy is an important complication of diabetes mellitus. Monitoring of early subtle renal functional changes in diabetes can help devise appropriate management strategies before full chronic nephropathy develops. The objective of this study was to establish a minimally invasive nuclear medicine technique to detect early renal physiopathological changes in glomerular filtration rate (GFR) that occur associated with diabetes.

Methods:
Glucose levels in plasma and urine were measured and [sup]99m Tc-DTPA i.v.(1 µCurie/Kg) radionuclide was injected for non-invasive renal imaging and GFR deteminations before and one week after induction of diabetes. Experimental diabetes mellitus was induced in rats using 55 mg/kg i.p. streptozotocin. Each rat served as its own control.

Results:
Among the 8 rats studied with 99m Tc-DTPA, the mean GFR before induction of diabetes was 1.75±0.23 ml/min/100 g, whilst, the mean GFR one week after induction of diabetes was 1.94±0.32 ml/min/100 g. ($P<0.05$) GFR was calculated from the renal uptake of radiolabel determined 1 to 3 min post injection. Preliminary data also show a significant increase in the GFR ($P=0.035$) calculated from the plasma clearance of radiolabel and in the renal blood flow one week after induction of diabetes compared to the data observed before induction of diabetes. Renal radionuclide imaging also allowed functional imaging of each separate kidney.

Conclusions:
A nuclear medicine minimally invasive procedure can detect early changes in renal glomerular function that occur in diabetes and preceed development of overt nephropathy. It thus may serve an important role in the prevention of renal complications and in the clinical management of diabetes mellitus.

Key Words: Diabetes; Renal radionuclide imaging; Glomerular filtration rate
Funding Agency: Departments of Nuclear Medicine and Physiology

Imaging / Nuclear Medicine and Radiological Science
Category: Basic Sciences

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Can rat be a model for animal brain scan? finding the best imaging time for brain scan

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Introduction:
Brain scan is one of the most important studies in nuclear medicine. It is helpful for evaluating acute and chronic cerebrovascular diseases, dementia, traumatic brain injury, inflammation, and brain death. Technetium-99m hexamethylpropylene amine oxime (^{99m}Tc-HMPAO) is one of the radiotracers for brain perfusion imaging. It is a lipophilic imaging radiotracer that crosses the blood brain barrier. The most common acquisition time for SPECT and planar brain imaging protocols is to start immediately or at 20 to 30 min after ^{99m}Tc-HMPAO injection. To the best of my knowledge, no study has investigated brain uptake at 0.5, 2, 4, and 24 h after ^{99m}Tc-HMPAO injection and its effect on the quality of the image of the brain using rat as an animal model. Therefore the objective of this study was to establish the optimum time for brain imaging of rat after intravenous administration of ^{99m}Tc-HMPAO.

Methods:
20 Wistar rats (200 g) were used in this study. Rats were anesthetized then ^{99m}Tc-HMPAO was administered intravenously within 30 min of preparation. Rat brain imaging using gamma camera was performed after 0.5 (control), 2, 4, and 24 h post ^{99m}Tc-HMPAO injection. Data processing for brain imaging was done by drawing a region of interest (ROI) over the brain and adjacent neck for background (BKG). Then brain ^{99m}Tc-HMPAO uptake-to-background (B/BKG) ratios were determined at each time point.

Results:
Brain uptake-to-background (B/BKG) ratios at 0.5, 2, 4, and 24 h were as the following: 27.64±3.75, 28.85±6.20, 28.53±4.17, and 24.73±6.46, respectively. The Student's paired t-test (p value) was applied to compare between the control time and 2, 4, and 24 h B/BKG ratios. There was no significant change between the control B/BKG ratios and B/BKG ratios after 2 h ($p=0.41$), 4 h ($p=0.37$), and 24 h ($p=0.5$) post injection of ^{99m}Tc-HMPAO.

Conclusions:
This study showed that rat can be used as an animal model for brain scan and the optimum time for imaging is after 30 min post injection because the imaging along 24 h is not changed.

Key Words: Brain scan; 99mTc-HMPAO; Rat
Funding Agency: None

Imaging / Nuclear Medicine and Radiological Science
Category: Clinical

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MRM BI-RADS classification: A guide for diagnosing breast lesion by MRI for inexperienced readers

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Introduction:
The purpose of this study was to assess whether the descriptive terminology and final assessment categories of the Breast Imaging Reporting and Data System (BI-RADS) lexicon can be used for breast lesions detected on MR imaging and to assess how accuratly the magnetic resonance mammographic (MRM) BI-RADS categories reflect the final histopathological diagnosis of the lesions.

Methods:
In 41 patients, 63 masses were evaluated by magnetic resonance imaging and described by BI-RADS terminology with respect to mass shape, margin, the enhancement pattern and contrast kinetics and defining the MRM BI-RADS final assessment categories. The results were validated by either the histopathology or radiological follow up and the accuracy of the MRM BI-RADS category was evaluated.

Results:
There were 25 carcinomas and 38 benign lesions. The infiltrating carcinomas were described as mostly spiculated in 9 (36%) with homogeneous enhancement pattern in 10 (40%) and rim in 8 (32%). The benign masses were mostly well circumscribed in 33 (87%) and round in 22 (58%) with homogeneous enhancement in 22 (58%) and with Nonenhancing internal septations in 4 (11%).The final impression of the carcinomas was BI-RADS category 5 in 16 (64%), category 4 in 7 (28%), and category 3 in 2 (8%). The final impression of the benign lesions was category 5 in 3 (8%), category 4 in 6 (16%), and category 3 in 3 (8%), category 2 in 14 (37%) and category 1 in 12 (31%). BI-RADS category was consistent with the diagnosis of the malignant lesions in 92% and of the benign lesions in 76%.

Conclusions:
The mammographic BI-RADS lexicon can be applied to diagnose and describe the features of infiltrating carcinoma and benign lesions seen on breast MR imaging.

Key Words: BI-RAD; Breast cancer; MRI breast
Funding Agency: None

Imaging / Nuclear Medicine and Radiological Science
Category: Clinical

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Magnetic resonance imaging of the breast: First experience in Kuwait

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Introduction:
The purpose of this is study was to evaluate the ability of magnetic resonance imaging (MRI) to identify and characterize breast lesions.

Methods:
Dynamic 3D MRI was done for patients diagnosed as having suspicious lesions by mammography and ultrasound (US). Lesions were characterized by MRI as benign or malignant based on the morphology and kinetics of contrast enhancement of the lesion. Findings were validated by tissue sampling or clinical and radiological follow up.

Results:
Seventy breast lesions were identified by MRI in 58 patients. The final diagnosis of the lesions were 25 malignant and 38 benign and 7 lesions were seen by MRI only and could not be validated by tissue sampling under US or stereotactic biopsy. The sensitivity, specificity, positive and negative predictive values of MRI in diagnosing malignant breast lesions were 100%, 74%, 71.4% and 80%, respectively.

Conclusions:
MRI was a valuable tool in identifying and characterizng malignant and benign breast lesions and identifying lesions not seen on mammography and/ or ultrasound and it should be used as an adjunct study with mammography and US in breast examinations.

Key Words: Breast cancer; MRI breast; MR Mammography
Funding Agency: None

Imaging / Nuclear Medicine and Radiological Science
Category: Basic Sciences

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Effect of hyperthermia on kidney function and renal scintigraphy

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Introduction:
Fever is caused by different reasons such as environmental conditions, acute rejection after kidney transplantation and bacterial diseases including kidney and urinary tract infections. The aim of this study was to investigate the effect of hyperthermia on kidney function, and the interpretation of the radionuclide renography.

Methods:
Eighteen New-Zeland White rabbits weighing 3-3.5 kg were used in this study. Renography studies were performed using 55 MBq (1.5 mCi) technetium-99m mercaptoacetyltriglycine (99mTc-MAG-3) and Gamma camera equipped with a low energy high resolution collimator interfaced with a computer. Regions of interest were drawn over the whole kidneys and radioactivity-time curves were generated. Time to peak activity (T max), time from peak to 50% activity (T ½) were calculated from the renograms. The same protocol was repeated for the same animal 3 times at 3 days intervals at 2, 3 and 4°C higher temperature. Blood pressure was measured using a catheter inserted into the femoral artery connected to a recorder and renal blood flow was also measured through renal artery using an electromagnetic blood flow sensor connected to a flowmeter. Creatinine and urea in blood were measured.

Results:
During hyperthermia there was a delayed renal uptake and clearance of radioactivity. This delay was proportional to body temperature. The average of T max were (1.6±0.1, 2.8±0.3, 8.8±1, 30±4 min), T ½ (2.77±0.2, 3±0.4, 8.9±1.1, 20±3.4 min) and perfusion index (190±5, 201±4, 218±7, 224±9) to control and hyperthermic rabbits. Mean arterial pressure and renal blood flow did not significantly change during hyperthermia. Creatinine and urea were proportionally elevated to high temperature, ($n=6$, $n=8$, $n=4$; $P<0.05$) respectively.

Conclusions:
Our preliminary results indicate that radionuclide renography studies are affected by hyperthermia and may only be performed at normothermic temperature to avoid misleading results.

Key Words: Hyperthermia; Kidney function; 99mTc-MAG-3
Funding Agency: None

Imaging / Nuclear Medicine and Radiological Science
Category: Basic Sciences

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Influence of hyperthermia on the radionuclide evaluation of cerebral blood flow

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Introduction:
Changes in regional cerebral blood flow (rCBF) may reflect physiological correlates of the diseased state. In neuroimaging studies, some diseases are associated with reduced or increased rCBF. Radionuclide studies have previously been carried out regardless of the patients body temperature. The aim of this study is to investigate the direct effect of hyperthermia on cerebral blood flow and its effect on the interpretation of the radionuclide studies.

Methods:
Fourteen New-Zeland White rabbits weighing 3.5-4 kg were used in this study. Scintigraphic images were acquired using 115 MBq (3.1 mCi) technetium-99m-hexamethyl-propyleneamineoxime (99mTc-HMPAO) and Gamma camera equipped with a low energy, parallel hole and high resolution collimator interfaced with a computer. The same protocol was repeated for the same animal 3 times at 3 days intervals at 2, 3 and 4°C above basal temperature. Regions of interest were drawn over the cerebral hemispheres, olfactory lobes and cerebellum to determine the count per pixel. Blood pressure was measured using a catheter inserted into the femoral artery connected to a recorder. Carotid blood flow was also measured using an electromagnetic blood flow sensor connected to a flowmeter at normal temperature and during hyperthermia.

Results:
During hyperthermia the uptake of 99mTc-HMPAO in the brain was significantly reduced than control ($n=6$; $P<0.05$). This reduction is proportional to the heating temperature. The decrease in cerebral perfusion is regionally dependent, which is more in the cerebral hemispheres, olfactory lobes than cerebellum. Mean arterial pressure did not significantly change during hyperthermia while carotid blood flow was significantly decreased ($n=8$; $P<0.05$).

Conclusions:
Our results indicate that hyperthermia reduces the cerebral perfusion therefore radionuclide studies should only be performed at normal body temperature to avoid incorrect results.

Key Words: Hyperthermia; Cerebral blood flow; 99mTc-HMPAO
Funding Agency: None

Imaging / Nuclear Medicine and Radiological Science
Category: Clinical

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Bone mineral density in healthy Kuwaiti women

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Introduction:
This study aimed to measure bone mineral density (BMD) of the lumber spine and femur regions in healthy adult Kuwaiti women, and to evaluate the influence of body size on BMD results.

Methods:
Bone mass measurement was performed by dual-energy X-ray absorptiometry at the lumbar spine (L2-L4) and femur (four regions) of healthy ambulatory Kuwaiti females aged between 20 and 80 years. Body size measurements and detailed questionnaire on past medical and gynecologic history and life style factors was administered to all subjects. After excluding those with apparent or suggested abnormalities affecting bone mass, only 805 women from 4887 were included and served as the target subjects.

Results:
The spine BMD values for Kuwaiti women up to 69 years were lower than their US counterparts; the peak value was established in the fifth decade. Femur neck BMD was relatively stable up to menopause. Spine osteoporosis was prevalent among 10% of the subjects compared to 4% in the femoral neck. Regression analysis revealed that each kg of body weight has a change of 0.3% in premenopausal women and 0.5-0.6% in the older group. In Multiple regressions that included the three factors (height, weight and age), the effect of age superseded that of weight in the older group of women where there was a detrimental annual effect on spine and femur (neck and total hip) BMD by 0.9% while each kg body weight had a constructive effect by 0.4 and 0.3%. In the premenopausal women, the positive effect of 1 kg of body weight was equivalent to about 1 year of aging in the trochanter region and half a year in the total hip region.

Conclusions:
The BMD values of healthy Kuwaiti women tend to be lower than the US reference at the lumber spine in all age groups but showed higher values for femur neck only in the age group of late 30s through 60 years. Weight has a stronger effect on BMD than does the height. The prevalence of osteoporosis in the lumber spine was more than double that in the femur neck in post menopausal women.

Key Words: Bone mass density; Osteoporosis; T-score
Funding Agency: None

Imaging / Nuclear Medicine and Radiological Science
Category: Clinical

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The role of CT in the postoperative assessment of acetabular fractures

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Introduction:
Acetabular fractures are common in pelvic injuries. Computed tomography (CT) represents a major contribution to the evaluation of pelvic fractures especially those that involve the acetabulum. Anatomic reduction and internal fixation has become the accepted method of treatment of displaced acetabular fractures. The accuracy of articular reduction as determined by plain radiographs has been correlated with both post-traumatic arthrosis and patient outcome. This study was designed to delineate the value of CT scans, as compared to plain radiographs, in the detection of post-operative residual articular displacement.

Methods:
A Retrospective review of CT and plain radiographic images of 16 patients treated operatively for a displaced acetabular fracture in Al-Razi orthopaedic hospital during the year 2006 was undertaken. Articular reduction was then assessed by the same reviewer in both CT scans and plain films. Images were inspected for residual articular incongruities in the form of step and gap displacement of the femoral head within the acetabulum.

Results:
Using standardized evaluation techniques, more patients were found to have residual articular incongruities on CT scans (9 with step and 7 with gap) than on plain radiographs (1 with step and 5 with gap). A step deformity on CT scan correlated with a gap deformity, and as the size of the step deformity increased so too did the size of the gap deformity.

Conclusions:
An accurate assessment of acetabular fractures (AF's) requires both plain films and CT scans. CT scans can accurately demonstrate the components of AF's and the exact position of the femoral head. Therefore, they are essential and should continue to be used in the preoperative evaluation of displaced AF's. We recommend to use CT scans postoperatively as well, since they improve the evaluation of articular reduction and, therefore, can better evaluate the surgical technique and provide an insight as to the development of future hip arthrosis.

Key Words: Acetabular fracture; Postoperative; Computed tomography
Funding Agency: None

Imaging / Nuclear Medicine and Radiological Science
Category: Clinical

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Unilateral kidney visualization on radionuclide renal studies: Mubarak Hospital experience

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Introduction:
Renal diseases are common in Kuwait. Radionuclide renal studies both dynamic and static are commonly utilized for diagnosis and follow up of such dieases. The objective of this study was to evaluate the frequency of non-visualization of kidney on radionuclide studies and the associated causes.

Methods:
Records of all patients who underwent radionuclide renal studies at Mubarak Hospital between 2001 and 2005 were reviewed. Patients who underwent radionuclide renal renography using Tc99m MAG-3 and renal cortical studies using Tc99m DMSA were included. Studies with visualization of unilateral functioning kidney were identified and their clinical data were found from their medical records.

Results:
Among 5665 patients who underwent renal studies, 58 (1%) showed solitary functioning kidneys on scintigraphic studies. Patients' ages ranged from 45 days to 75 years. Fifty patients had complete clinical records to date. The Congenital causes were the most common (52%). Surgical removal of the kidney for a variety of reasons (24%) was the second most common and the most frequent acquired cause followed by recurrent urinary tract infection (10%). This table summarizes the results

Cause	Number
Congenital causes	26
Congenital absence	19
Conenital agenesis	1
Pelvic kidney	4
Crossed fused ectopia	1
Vater syndrome	1
Recurrent urinary tract infection	5
Obstructive nephropathy	4
Renovascular disease	3
Nephrectomy	12
All causes	50

Conclusions:
Our preliminary results show that among patients with a non-visualized kidney, congenital causes are the most frequent underlying cause. Surgical absence is the most common cause of the acquired condition in our patient population.

Key Words: Renogram; Solitary kidney; Mubarak Hospital
Funding Agency: None

Imaging / Nuclear Medicine and Radiological Science
Category: Clinical

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Age related normal variants of growth plates: scintigraphic appearance

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Introduction:
The skeleton is a dynamic structure that changes during the normal physiological processes of growth and remodeling as well as in response to pathological insult. In infants and children, it is well recognized that bone-seeking tracer, which localizes in direct relationship to metabolic activity and blood supply, accumulates in greater amounts in the growth plates of immature skeleton. Scintigraphic appearance of the normal growth plate changes with age. Full investigation of age-related patterns of growth plates uptake on bone scintigraphy has not been reported.

Methods:
A retrospective analysis of bone scans for pediatric age group performed during last four years in our nuclear medicine department was obtained. Distal femoral and proximal tibial growth plates uptake was visually evaluated.

Results:
Eighty-six patients were found during the specified period.Various patterns of growth plates uptake were recognized in different age groups. In the infants and children below the age of four, the physis appeard thick and oval shaped. Later it becames linear, and in adolescence, it may show biconcave pattern as well before progressive fading of activity.

Conclusions:
Age-related patterns of growth plates uptake on bone scintigraphy have been identified. Awareness of these appearances is important since lack of knowledge of these normal variants may lead to misinterpretation of growth plate abnormalities which are known to be under-recognized.

Key Words: Normal variants; Growth plates; Bone scintigraphy
Funding Agency: None

Imaging / Nuclear Medicine and Radiological Science
Category: Clinical

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Analysis of injury patterns in acidental and intentional falls from height

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Introduction:
Injuries resulting from free falls constitute a significant portion of urban injuries and are common reasons for admission in major trauma centers. Knowledge of the typical patterns of vertical deceleration injuries is important in order to be able to look specifically for these injuries in an emergency unit. The aim of our study was to find out whether there is any difference in the injury patterns after accidental and intentional (suicidal) high falls.

Methods:
One hundred and twenty (120) adult patients, admitted to our trauma center in Al- Razi Orthopedic Hospital after a fall from an average height of 7m between 2006 and 2007, were included in our study. They were classified as either having fallen accidentally or intentionally from a height. The radiographs from the primary survey together with radiographs and computed tomographic studies of specific injury sites were reviewed. The injury patterns were studied and then analyzed in these two groups of patients.

Results:
In 72 patients the fall was accidental and 48 jumped with suicidal intent. The most common injuries in high falls were fractures of the thoracic and lumbar spine (75%) especially of the thoraco-lumbar junction. The pattern of limb injuries was towards a significant preference of the metaphyseal and epiphyseal parts of the bones of the distal joints (wrist, elbow, ankle and subtalar). Fractures of the diaphyseal areas and proximal joints (shoulder, humerus, hip and femur) were lower in frequency.The incidence of thoracic injuries was (12.5%) and pelvis injuries was (30.0%). Head injuries occurred in only 12.5%. Blunt abdominal injury was rare (7.5%) in our patients. In the suicidal jumpers the incidence of lower limb injuries was (62.5%), spine fractures was (83.3%) and pelvis fractures was (35.4%) while in accidental fallers the incidence of lower limb injuries was (48.6%), spine fractures was (69.4%) and pelvic fractures was (33.3%).

Conclusions:
Analysis of the injury patterns sustained in high falls revealed that suicidal jumpers, who have a tendency to land feet first, had more frequent injuries to the lower limbs and spine compared to those who accidentally fell from height.

Key Words: High falls; Intentional; Accidental
Funding Agency: None

Imaging / Nuclear Medicine and Radiological Science
Category: Clinical

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Pediatric Hodgkin's Lymphoma: Role of Gallium-67 scan

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Introduction:
Hodgkin's disease represents about 6% of the childhood tumors. Correct evaluation of the patient is important for achieving good outcome. The purpose of this study was to evaluate the role of Gallium scan in Pediatric Hodgkin's disease.

Methods:
This was a retrospective study of 34 patients (22 males/ 12 females). Average age was 11 years. Gallium and CT scans were performed at diagnosis and after treatment for all patients twenty patients underwent gallium scan during early chemotherapy. The mean follow up period was 54.5 months.

Results:
We evaluated the gallium role in predicting the relapse, early response to therapy and viability of tumor in residual mass on CT. Relapse: After treatment 9% (3/34) patients show relapse (2 normal gallium and CT after treatment, 1 patient disease progressed during therapy). Ninty one % (31/34) patients show no relapse (gallium normal 30, regressive 1, CT normal 18, partial response 13). Early response to therapy: 18/20 (90%) patients show normal gallium scan after 1 to 3 cycles of chemotherapy out of which 1 (5%) patient show lesion after therapy while rest are in complete remission. 2 (10%) patients show regressive disease on early scan with no relapse. Residual mass: 16/34 (53%) patients show residual mass on CT after treatment. Post therapy gallium scan was normal in 14 patients while 2 patients had abnormal scans. one patient showed normal scan after 4 months and is in complete remission and the other patient died with advanced disease.

Conclusions:
These results highlight the role of gallium in management of pediatric HD. Gallium scan in early treatment can predict the outcome of the therapy. Negative post therapy Gallium scan reliably predict long term remission while positive scan guide clinicians for early alternate therapy and/or close follow up. Similarly, gallium scan can reliably predict the viability of CT detected post therapy mass.

Key Words: Pediatric Hodgkin's lymphoma; Gallium-67; Residual mass
Funding Agency: None

Imaging / Nuclear Medicine and Radiological Science
Category: Clinical

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Imaging findings in breast cancer: The Mubarak Al Kabeer hospital experience

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Introduction:
Breast cancer is the commonest female cancer and the highest cause of cancer death in females in Kuwait. This study was performed to evaluate imaging findings of breast cancers and correlation with histological and cytological findings.

Methods:
A total of 3996 patients who had mammography and ultrasound in our Radiology Department between January 2004 and December 2005 were studied. Imaging findings were classified according to the Breast Imaging and Reporting Data System (BI-RADS). BIRADS Category 4, (suspicious for malignancy); BIRADS 5, (highly suggestive of malignancy) and indeterminate findings at ultrasound were referred for cytological evaluation. Histology was performed on core biopsies and post-operative surgical specimens.

Results:
Complete data was available for 105 out 203 patients with category 4 or 5 BIRADS. Seventy (66.7) were BIRADS 5, 33 (31.4) BIRADS 4 and 2 indeterminate. Of these, 62 (59%) were Kuwaitis, 28 (26.7%) non-Kuwaiti Arabs, 14 (13.3 %) Asians. Their age range was 13 to 83 years with a mean of 48.9 years. Clinical presentation was mass in 80 (76.2 %), bloody nipple discharge 6 (5.7 %), asymptomatic.12 (11.4 %). Sixty-six (62.9%) patients had cytology alone, 18 (17.1 %) histology alone and 21 (20%) both cytology and histology. Imaging features demonstrated mass lesion in 78 (74.8%) patients, mass with calcification 23 (21.9%) and calcification alone in 3. About 17% of the cancers were multifocal, 10.5 % multicentric, and 2.9% bilateral. The upper outer quadrants and retroareolar areas were the most common locations.

Conclusions:
Approximately 89% of the cancers in this study were symptomatic. One-in-4 had malignant calcification. The demonstration of extent of disease through breast imaging is obligatory for optimum pre-operative planning. Breast screening is recommended for early detection of breast cancer.

Key Words: Breast cancer; Mammography; Breast Imaging and Reporting Data System (BI-
Funding Agency: None

Imaging / Nuclear Medicine and Radiological Science
Category: Graduate (Resident)

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The role of gallium-67 citrate imaging in Graves ophthalmopathy

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Introduction:
Graves ophthalmopathy (GO) is a serious inflammatory condition of the eye in Graves disease. GO is characterized by an early active congestive phase, requiring aggressive anti-inflammatory therapy and a fibrotic phase, that may need surgical management. The objective of this study was to evaluate gallium-67 citrate imaging as indicator of disease activity to predict at an early stage the severity of eye involvement in view of institution of effective treatment.

Methods:
Twenty five patients with Grave's disease presenting with mild to severe GO and 10 controls with no history of thyroid and eye disease were included. GO was classified according to the Clinical Activity Eye Score (CAS) based on 7 test items related to presence of inflammation, such that a CAS $\geq$4 denotes activity. Ga-67 citrate, commonly applied as tracer for inflammation, is used to monitor any degree of eye involvement. Imaging involved single photon emission computed tomography (SPECT) around the head at 24 and 72 hours after intravenous injection of 4-6 mCi Ga-67. Analysis included drawing regions of interest around the orbits and temporal-occipital bone on a reframed trans-axial slice. The maximum count ratios in orbit/skull bone (O/B) were calculated after correction for background activity.

Results:
CAS showed 5 clinically active GO. Visual inspection of 24 hr images showed intense tracer uptake in the orbits of the affected patients. Quantitative analysis performed on 35 patients showed the median O/B ratio in the 24 hr images to be 1.7 GO - 1.3 controls. The interquartile range (IQR) was 0.69 GO - 0.49 controls. The data for the 72hr images: median 1.5 GO - 1.4 controls, IQR 0.55 GO - 0.33 controls. Mann-Whitney test of the O/B ratio in 24hr image was significantly different ($p=0.001$) from 72hr image ($p=0.104$).

Conclusions:
Orbital Ga-67 citrate imaging is a sensitive method for predicting early inflammatory eye involvement and gauging the severity of GO.

Key Words: Ophthalmopathy; Gallium; Graves
Funding Agency: College of Graduate Studies, Kuwait University

Imaging / Nuclear Medicine and Radiological Science
Category: Clinical

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Radiation dose measurement for paediatrics with degenerative dysplasia of the hip (DDH)

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Introduction:
During the treatment course followed for the degenerative dysplasia of the Hip (DDH) paediatric patients, their most radiosensitive area of the body (i.e. the gonads) is being subjected to several radiations exposures. This is due to the periodically performed X-ray images of the hips and the use of the fluoroscopy screening during their hip fixation operation. As dose accumulation during childhood leads to an increased risk of radiation - induced cancers 1, radiation protection measures are especially important in paediatric patients. Thus, the general objective of this study was to investigate the radiation doses delivered to DDH patience in the course of their treatment in Kuwait.

Methods:
Dose measurements during 60 pelvis X-rays and in 40 hip fixation surgeries were performed.

Results:
The data for the accumulative effective doses (E) for each surgery ranged from 16 to 42 μSv. (± 6 to 4). While entrance skin dose (ESD) associated with a pelvis image ranged from 106 to 232 μGy. Therefore, the established values are within the recommended dose ranges of values reported in literature (i.e. (E)=66 μSv/ min, and ESD for a paediatric pelvis X-ray=900 μGy). Using published risk factors for the development of childhood cancers from child exposure [2], the estimated upper limit of this risk was=0.64×10^6 /surgery. Thus, the risk of developing childhood cancer from each surgery is less than six / million, whereas that for each pelvis X-ray was found to be much lower than that value.

Conclusions:
In conclusion, the estimated radiation doses for DID patients fall within the acceptable data 2-5, hence the benefits of using fluoroscopy screening and assessments and pelvis X-rays for these cases are greater than the associated radiation risks.

Key Words: Paediatric; Radiation protection; Radiation dose measurements
Funding Agency: University of Kuwait, # ZN08/04

Imaging / Nuclear Medicine and Radiological Science
Category: Graduate (Resident)

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Semiquantitative methods for characterization of breast lesions on Tc-99m sestamibi scintimammography

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Introduction:
Breast cancer is the commonest cancer with the highest mortality in women. Mammography is currently the most effective screening modality for detecting early cancer which is not clinically palpable. However, it has limited sensitivity in patient with dense breasts or patients who have implants or surgical intervention. Scintimammography has been recently found useful in such cases. The objectives of our study were to optimize the performance of scintimammography using semiquantitative methods thereby improving its sensitivity and specificity for differentiation of benign and malignant breast lesions.

Methods:
This was a prospective study over 6 months of patients who had equivocal findings on mammography perfomed for suspicion of a breast mass. Scintimammography was done after iv injection of 25 mCi of ^{99m} technetium sestamibi. Imaging involved anterior, lateral and posterior oblique views at 20 min. The images were analyzed using Standard and Scaled Visual system by alteration of the intensity of the image display. Semiquantitation was done by BiLinear Interpolative Background Subtraction (BLIBS) to improve contrast and lesion detectability. Comparison was done with the results of histocytology as reference test.

Results:
A total of 45 masses complete with histo/cytological diagnosis were included in the study. The sensitivity, specificity, positive and negative predictive values using standard visual analysis were: 73%, 57%, 56% and 75% respectively. The sensitivity increased to 78.9% using BLIBS analysis, however, at the expense of reduced specificity, positive and negative predictive values (42%, 50%, and 44%, respectively).

Conclusions:
The use of a semiquantitative method for analysis of scintimammography was of some benefit in our study giving an objective means of characterization of breast lesions on scintimammography. However, further evaluation of the method would be warranted.

Key Words: Breast Cancer; Tc sestamibi; Scintimammography
Funding Agency: None

Medical Education
Category: Graduate (Resident)

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Interns' confidence of performing clinical skills

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Introduction:
Several surveys suggest the under-emphasis of the learning of practical skills during internship training. This study aimed to assess the confidence that interns who completed training possessed in performing core clinical skills.

Methods:
Interns who completed rotations in Surgery, Medicine, Obstetrics and Gynecology, and Pediatrics during 2005/06 responded to a questionnaire that listed 48 core clinical skills. Out of the 124 eligible for the study, 85 responded. The respondents indicated their confidence to perform the skills in future and the number of times they had been performed during training.

Results:
The majority of the interns felt confident to perform basic ECG interpretation, basic X-ray interpretation, inserting and intravenous line, inserting urethral catheter and nasogastric feeding. Approximately half felt confident in administering cardio-pulmonary resuscitation or securing airway, and in performing irrigation of the ear, lumbar puncture, pericardiocentesis, insertion of thoracic drainage, insertion of central venous catheter, indirect laryngoscopy, or venous cut-down. A third felt confident in performing artificial ventilation or endotracheal intubation. Only about a third of trainees, with no significant gender variation, felt confident to perform common skills in obstetrics and gynecology such as high vaginal swab, collection of cervical smear, conducting normal deliveries, repair of episiotomy, artificial rupture of membranes, or application of fetal electrodes.

Conclusions:
Although interns were confident in performing some of the core clinical skills, lack of confidence was observed in relation to some of the other basic skills. Interns who may not acquire competency in the core clinical skills need to be identified early and corrective measures taken. This may have implications in the review of the medical undergraduate curriculum as well as in internship training.

Key Words: Clinical skills; Internship training; Kuwait
Funding Agency: KIMS

Medical Education
Category: Clinical

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The impact of a short educational course and clinical practice guidelines on knowledge and attitude of primary care physicians toward diabetes

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Introduction:
Studies demonstrate shortfalls in the quality of care provided by primary care physicians (PCPs) for diabetic patients. CME that addresses provider attitudes toward diabetes and updating knowledge to promote adherence to standards of care may be helpful. The aim of this study was to evaluate the a impact of short educational course and clinical practice guidelines (CPG) on knowledge and attitude of PCPs toward diabetes.

Methods:
We enrolled 80 PCPs attending a five-day course (15 hours), supplemented with CPG on diabetes care. We also surveyed the participants to assess their attitudes toward diabetes. Knowledge was assessed by multiple choice questions and short assay questions. Attitudes were assessed using the Diabetes Attitudes Scale-3 (DAS-3). Data were collected for the participants before and after the interventional course.

Results:
Mean baseline knowledge score was 73.28+10.13 %. The score increased significantly to 88.16+6.97 % ($p<0.0001$) following the intervention. Regarding the attitude, only 67 and 56 participated in the pre- and post-course questionnaire and 41 answered both. Overall, PCPs had a positive attitude toward all the five subscales in the pre- and post-course. Following the course, PCPs had significantly more positive attitudes on three of five DAS subscales, with a statistically significant improvement in attitude regarding seriousness of DM ($P=0.001$), need for special training ($p<0.05$), and patient autonomy ($p<0.05$). There was no improvement in value of tight glucose control and psychosocial impact of diabetes subscales.

Conclusions:
A short educational course and clinical practice guidelines for diabetes care resulted in an improvement in knowledge and attitude of PCPs toward diabetes. These findings demonstrate that these interventions have the potential to improve the quality of care provided by PCPs for diabetic patients.

Key Words: Diabetes; Knowledge; Attitude
Funding Agency: None

Medical Education
Category: Clinical

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Study of in-vitro determination of the periodontal attachment levels in teeth extracted for periodontal reasons in Kuwait

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Introduction:
There is a clear connection between oral health status and the well-being of a person. In view of the changed understanding of the natural history of periodontal disease and the lack of empirical knowledge of the forceps level in the treatment of periodontal disease in Kuwait, investigation into the level of periodontal attachment loss at which dentists decide to extract teeth for periodontal reasons would provide insight into the decision-making process. The aim of this study was to compare the periodontal reasons for extraction of teeth by dentists' in Kuwait to the in-vitro periodontal status of extracted teeth.

Methods:
Dentists, of six dental centres from six governorates across Kuwait were requested to record the reasons for tooth extraction and collect the extracted teeth over a period of 1 month. Of the 342 extracted teeth returned, 293 teeth satisfied the criteria for assessment of periodontal attachment. The root length and 4 linear measurements for stained periodontal ligament were recorded for each tooth using a (10X) dissection microscope.

Results:
Ninety-eight teeth(33%) were identified by the dentists as having been extracted for periodontal reasons. The periodontal attachment loss in these teeth ranged from 10% to 80%. Only 27% (n=26) of the teeth had a site of maximum attachment loss of greater than 40%. A weak, but positive correlation was found between in-vitro measurements of the degree of attachment loss and the dentists' reasons for tooth extraction with Spearman's rank correlation coefficient (Rs=0.36). Eighty percent of the dentists set the forceps level for removal of teeth for periodontal reasons, at a relatively early stage of the disease (i.e. less than 40% of attachment loss).

Conclusions:
The threshold for periodontal extractions in Kuwait seems to be low and undifferentiated, which calls for an improvement in knowledge of periodontal diagnosis and treatment.

Key Words: Tooth extraction; Periodontal; Attachment loss
Funding Agency: None

Medical Education
Category: Clinical

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Knowledge and attitudes of dental care workers towards cross infection control measures in a dental practice in Jahra, Kuwait

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Introduction:
Although adherence to universal precautions and routine use of appropriate barriers provide protection against most microorganisms, health care workers (HCW) including dental care personnel are still at risk of infection. Preventive practices documented include: Hepatitis B vaccination, careful handling of sharp instruments, use of rubber dams to minimize blood spattering, hand washing, and use of protective barriers (e.g. gloves, masks, Protective eyewear, and gowns). Objectives: to assess the level of awareness of occupational hazards among clinical dental staff at Al-Jahra Health Area. This was done by identifying hazards and making recommendations to prevent them.

Methods:
This study was conducted among clinical dental staff in both general and specialized dental clinics in Jahra Health Area. The study population consisted of dentists, nurses,, and technicians. Data was obtained through the use of self-administrated questionnaire (We used only one questionnaire-Arabic-English done by one author) that included questions on personal data, awareness to occupational hazards, seminar attendance, safety measures practiced, and experience of occupational hazard while in practice. Data was analyzed by SPSS Program V.11 using frequency tables to display the responses of the dental staff. Where necessary, cross tabulations were carried out to determine the significant difference between variables.

Results:
The study included 118 (dentists, nurses and technicians). Sixty per cent of them were male. Subject ages ranged from 21 to 60 years with more than half of them are in the age group (31 – 40) years. Most of the staff were aware of the occupational infectious hazards as 83% of doctors attended seminars/workshops on the subject. Only 69% of staff members completed 3 doses of HB vaccination, while intake of the vaccine is lesser among technicians and nurses (60.6% and 61.3%) respectively. Twenty members (16.9%) could recall a sharp injury in the past six months. Only two members are not washing their hands regularly during work, and one member is not wearing gloves between patients. Washing hands before wearing gloves is an important issue in preventing cross infection. Only 67.8% of the study subject performs this measure.66.1% of the study personnel are wearing eye goggles or eye shield during work, while most of them are wearing face mask.

Conclusions:
This study showed that although there is a high level of awareness regarding occupational cross infection control measures among dental care workers in Kuwait, the practical steps for prevention are still inadequate.

Key Words: Knowledge; Dental; Cross infection
Funding Agency: None

Medicine
Category: Clinical

94

Kuwaiti subjects with type 2 diabetes are at high risk for cardiovascular disease

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Introduction:
Type 2 diabetes is associated with a marked increased risk of cardiovascular disease (CVD). The UKPD Study has shown several modifiable risk factors for CVD in patients with type 2 diabetes. These factors are increased concentrations of low density lipoprotein cholesterol (LDL-C), decreased concentrations of high density lipoprotein cholesterol (HDL-C), raised blood pressure, hyperglycaemia, and smoking. The aim of this study was to determine the prevalence of these factors in Kuwaiti subjects with type 2 diabetes.

Methods:
Kuwaiti subjects with type 2 diabetes (n=170) were screened for CVD risk factors at their initial visit to the diabetes unit at Al-Sabah Hospital.

Results:
There were 113 women and 57 men. Mean age was 49.6+10.5 years and mean disease duration 8.0+7.1 years. The mean LDL-C and HDL-C levels were 3.7+1.0, 1.2+0.3 mmol/l respectively. Mean systolic BP was 135.8+22.1and diastolic 81.4+10.4 mmHg. Mean HbA1c was 9.4+2.4%, and 7.2% of the patients were current smoker. Mean BMI was 33.3+7.5 kg/m^2. The mean LDL –C levels for men and women were 3.73 and 3.66 mmol/l, respectively. According to the American Diabetes Association targets, the percentage of patients with HDL-C levels above the target was high (56.5%) and it was more prevalent for women (59.3%) compared to men (50.9%). The mean systolic and diastolic BP was significantly higher in women compared to men (140 vs. 126 and 83 vs. 77 mm Hg, $p<0.0001$) respectively. Although overweight and obesity were prevalent among the studied subjects, the mean BMI for men was 29.4, compared with 35.3 for women ($p<0.0001$). There was no difference in HbA1c levels between both gender, and None of the women were smoker.

Conclusions:
Kuwaiti subjects with type 2 diabetes are at high risk for cardiovascular disease which is the leading cause of death in Kuwait. This indicates a need for interventions to reduce these modifiable risk factors.

Key Words: Diabetes ; Cardiovascular disease; Risk factors
Funding Agency: None

Medicine
Category: Clinical

95

Prevalence of abnormal thyroid function tests in Kuwaiti Arabs with autoimmune diseases

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Introduction:
The prevalence of abnormal thyroid function tests among Kuwaitis is not known. Neither is that of Kuwaitis with autoimmune diseases. The purpose of this study was to examine these issues.

Methods:
We measured serum concentrations of sensitive thyrotropin (sTSH), free thyroxin (FT4) and free triiodotyronine (FT3) in 577 apparently healthy controls, 177 patients with rheumatoid arthritis (RA), 60 patients with systemic lupus erythematosus (SLE) and 25 patients with primary Sjogren's syndrome (pSS) using the immunochemiluminiscent assay method on IMMULITE 1000. Serum antimicrosomal autoantibody and antithyroglobulin autoantibodies were also measured by passive haemagglutination assay.

Results:
Categorizing the subjects into 5 functional groups by the concurrent thyroid function test results, the prevalence of subclinical hypothyroidism was 1.7% in the healthy population, 10.2% in patients with RA, 13.3% in patients with SLE and 16% in patients with pSS. Among RA patients, the prevalence of subclinical hypothyroidism in females (11.4%) was significantly higher ($p<0.01$) than among males (5.4%). In SLE and pSS, all the patients with subclinical hypothyroidism were females. The prevalence of biochemical hypothyroidism was 1.4% in controls, 10.2% in RA, 8.3% in SLE and 4% in pSS. Biochemical hyperthyroidism was seen in 0.2% of controls, 4.5% of RA patients, 5% of SLE patients and None in patients with pSS. The euthyroid sick syndrome was seen in 0.4% of controls, 13.6% of RA, 16.7% of SLE and in None of pSS patients. Antithyroid autoantibodies were present in 3.3% of normal controls, 12.4% of RA, 18.3% of SLE and 12% of pSS patients respectively.

Conclusions:
Abnormal thyroid functions occur frequently in Kuwaitis with autoimmune diseases. It is recommended that thyroid function tests including thyroid serology be routinely done in these patients.

Key Words: Abnormal thyroid function; Autoimmune diseases; Thyroid auto-antibodies
Funding Agency: None

Medicine
Category: Clinical

96

Kuwaiti recommendations for prophylaxis and treatment of tuberculosis in patients treated with tumor necrosis factor antagonists.

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Introduction:
TNF antagonists are the most recent advances in the management of rheumatic diseases. However, re-activation of latent TB is the major concern during treatment. Different recommendations have been proposed in various countries each to meet their own population characteristics. No guidelines, however, have been established yet in The Middle East and this practice remains individual among the different rheumatologists in our area. Objectives: To propose recommendations to prevent reactivation of latent TB and for treatment of active TB in patients started on TNF antagonists in Kuwait.

Methods:
A committee was called consisting of two rheumatologists, a gastroenterologist, a TB specialist, a respirologist and an infectious disease specialist. The committee met in Al-Amiri Hospital which is one of the earliest centers to use biological drugs and has one of the biggest biological agents database registry in the Middle East(300 patients).All of the members were expert consultants in their fields. In January 2006, recommendations of the committee were issued and agreed upon for patients starting anti-TNF agents in Kuwait and for patients diagnosed to have active TB during therapy.

Results:
Prior to those recommendations, a total of 200 patients(73% with rheumatoid arthritis and 23% with psoriatic arthritis)were receiving treatment with anti-TNF agents. Two cases of active TB were reported during therapy, one of them expired.95 patients were started on TNF antagonists during the year following recommendations. No patients had TB and no hepatotoxicity was reported with the use of anti-TB prophylaxis.

Conclusions:
Kuwait is the first country in The Middle East to establish guidelines for TB prophylaxis and treatment with anti-TNF agents that match our population characteristics. The absence of cases with active TB and toxicity related to anti-TB agents following these guidelines may suggest the effectiveness and safety of these recommendations for our population in Kuwait.

Key Words: TNF antagonists; Tuberculosis; Recommendations
Funding Agency: None

Medicine
Category: Clinical

97

Impact of antecedent risk factors on the clinical profile and in-hospital outcome of acute myocardial infarction in young Kuwaiti patients

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Introduction:
The aim of the study was to determine antecedent risk factors, clinical profile and in-hospital outcome in young Kuwaiti patients presented with acute myocardial infarction (AMI).

Methods:
The study population (group I) consisted of 146 patients under age of 40 years, (128 males and 18 females) with a mean age 35.46±4.25 years. The control group (group II) included 214 patients, (180 males and 34 females) with a mean age of 56.53±8.39 years were admitted with AMI. All patients were evaluated for antecedent risk factors, clinical features and outcome. Besides in-hospital mortality, the occurrence of reinfarction, development of heart failure, cardiogenic shock, atrial or ventricular arrhythmias and high degree heart block were recorded.

Results:
There was a significant increased number of female patients in older group presented with heart failure, cardiogenic shock, atrial fibrillation, ventricular arrhythmias and type II or III atrioventricular conduction block. There was a significant increase number of younger male patients presented late after 12 hours ($p<0.01$). We found 16% versus 23% of patients had in-hospital heart failure with a significant increased the percentage in the female patients ($p<0.05$) and 5% of our patients developed reinfarction with a significant increased the male patients versus female patients ($P<0.05$). Multivariate logistic analysis revealed that acute myocardial infarction in young Kuwaiti patients is significantly associated with the presence of diabetes mellitus status, hypertension, hypercholesterolemia, family history of IHD and current smoking, ($p<0.05$).

Conclusions:
Family history of IHD, current smoking, high LDL-cholesterol and diabetes mellitus stauts are associated with AMI in young Kuwaiti patients and young patients with AMI have a favorable in-hospital prognosis compared with older patients.

Key Words: Acute myocardial infarction; Risk factors; Young patients
Funding Agency: None

Medicine
Category: Clinical

98

Increased in-hospital mortality and morbidity after acute myocardial infarction in patients with chronic obstructive pulmonary disease

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Introduction:
The aim of the study was to find out causes of increased in-hospital mortality and morbidity rate in patients with chronic obstructive pulmonary disease (COPD) presented with acute myocardial infarction (AMI).

Methods:
Consecutive 139 patients with AMI were stratified into: Group I: 64 patients with COPD and group II:75 age-matched patients without COPD. Electrocardiogram, chest x-ray, routine laboratory investigations, cardiac enzymes, echocardiography were performed on admission and at follow up. Thrombolytic therapy was given only for 50 patients in group I and 63 patients in group II. Besides in-hospital mortality, occurrence of ventricular arrhythmias, reinfarction, development of heart failure, complete heart block with temporary or permanent pacemaker were recorded.

Results:
There was significant increase in JVP and pulmonary artery dimension and pressure in patients of group I compared with group II ($P<0.05$). There was a significant increase in the in-hospital mortality in group I compared with group II (10.4% versus 4.9%, $p<0.05$). Five patients in group I presented with cardiogenic shock due to associated acute inferior MI and sings of right ventricular infarction. There was 15% of our patients developed reinfarction with a significant increase in the male patients versus female patients ($P<0.05$).Stepwise logistic multivariate analysis revealed a significant correlation between the gender, size of infarction, pulmonary hypertension, right ventricular strain, percutaneous coronary intervention, chest pain to thrombolytic therapy, and cardiogenic shock as an independent variables and the cardiac mortality rate in the patients with COPD after AMI (<0.05).

Conclusions:
The in-hospital mortality rate of acute MI among the patients with COPD is 10.4% over 7 years, the patient´s presentation and ECG pattern may mask AMI sings and delay transfer from medical casualty department to CCU for thrombolytic therapy and adjunctive treatment.

Key Words: Chronic obstructive lung disease; Acute myocardial infarction; In-hospital mortality
Funding Agency: None

Medicine
Category: Clinical

99

Serum C-reactive protein level to diagnose bacterial respiratory infection as a cause of acute asthma exacerbations

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Introduction:
Viruses, bacteria, allergens, irritants, environmental factors can cause acute asthma exacerbations. Cough and sputum need not be due to infection. C-reactive protein is a marker of inflammation, infection, and tissue damage. We investigated the role of bacterial infections causing asthma exacerbations and usefulness of serum C reactive Protein level in its diagnosis.

Methods:
Fifty eight patients that attended hospital as emergency with asthma exacerbation were studied. Sputum culture serum CRP were taken. Pneumonia was ruled out by x- ray chest.Patients with FEV1 less than 50% predicted were selected. Fischers exact test was used to find association between CRP level and different demographic and clinical factors.

Results:
Of 58 patients, acute exacerbation occurred in 60% men and 40% women. Kuwaitis (30) and non Kuwaitis (28) were almost equally affected. Serum CRP level ranged between 6-50mg/L, mean serum level 12mg/L. 21(36.2%) cases had increased C-rp level, 13(22.4%) cases had positive culture. It was found that 45(77.6%) of cases of sputum culture, yielded normal flora of which only 11(24.4%)had elevated CRP. Even though only 13 (22.4%) cases had a culture positive with pathological organisms, higher serum C-reactive protein level was found in 10 (76.9%) of these patients ($p< 0.001$) and was statistically significant. This shows serum CRP level was significantly high in sputum culture with pathological organisms.

Conclusions:
Majority of exacerbations were not due to bacterial infections. But it is an important cause and high CRP level can be considered as a valuable tool to diagnose respiratory infection with pathological organisms in acute asthma.

Key Words: bronchial asthma; c-reactive protein; Exacerbation
Funding Agency: None

Medicine
Category: Clinical

100

Deletion polymorphism of angiotensin-converting enzyme gene determines the susceptibility to rheumatoid arthritis

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Introduction:
Only 30% of the genetic susceptibility to rheumatoid arthritis (RA) can be attributed to HLA genes and most likely other non-HLA genes play a role in RA susceptibility. Recently, high levels of Angiotensin converting enzyme (ACE) have been documented in synovial fluid and pleural effusions of RA patients. Since plasma ACE levels are genetically determined, we hypothesized that the genotypes of ACE gene may be a contributing factor in the pathogenesis of RA.

Methods:
Sixty RA patients were recruited and clinically characterized according to disease duration, severity, activity and ACR functional class. 35 healthy controls (HC) were also studied. ACE gene insertion/deletion polymorphism genotypes were determined in patients and HC using polymerase chain reaction.

Results:
There was a significant over-representation of the DD genotype and the D allele in RA patients when compared to HC. Additionally, gender correlated significantly with genotypic and allele frequencies, with RA males exhibiting a higher frequency of the DD genotype and D allele compared to HC males. Furthermore, Arab patients showed a higher frequency of D allele when compared to Arab HCs. The DD genotype confers a relative risk (RR) of 3 for development of RA. Thus, the worst case scenario for the development of RA would be an Arab male with DD genotype. Our results also suggest a possible influence of the ACE gene on the RA disease activity, severity and functional class.

Conclusions:
In this study we report for the first time a strong association between RA and deletion polymorphism of ACE gene. Though a significant association of the I allele has been reported earlier with Juvenile Idiopathic Arthritis, our study concludes that the D allele predisposes to adult rheumatoid, particularly in Arabs.

Key Words: Rheumatoid arthritis; Angiotensin converting enzyme; Gene polymorphism
Funding Agency: None

Medicine
Category: Graduate (Resident)

101

Lipid testing and lipid lowering medication use in stroke patients

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Introduction:
Recent recommendations call for in-hospital initiation of lipid-lowering therapy (LLT) for ischemic stroke (IS) and transient ischemic attack (TIA) survivors; however, little is known about actual use globally and None is known in Middle East countries. This study describes the use of lipid testing and LLT in Mubarak Al-Kabeer Teaching Hospital (MKH) in Kuwait.

Methods:
In this cross-sectional study, 100 IS and TIA patients were randomly included from medical wards in MKH in the year 2006 in Kuwait.

Results:
One hundred subjects (60% males and 40% females) were included. Of which 81% IS and 19% TIA. Lipid profile measurement was most strongly and independently associated with diagnosis of IS (Vs TIA, P=0.007) and Kuwaiti nationality (Vs non-kuwaiti, P=0.04). Only 23% of those not on LLT had profile done. Around 78% didn't receive treatment on discharge. Male gender was significantly (P=0.03) associated with receiving LLT. Mean (95% confidence interval) TC, TG, LDL, and HDL were 4.77(4.37-5.16); 1.78(1.33-2.23); 2.93(2.6-3.27); 1.02(0.77-1.27) mmol/l, respectively. Low HDL was found in 76%, while high LDL was found in 73%. Among those with normal LDL, 44% had HDL/TC<20%.

Conclusions:
Lipid profile and LLT are far beyond underutilized in patients with IS and TIA in MKH in Kuwait. HDL appeared to be more important than LDL as a modifiable risk factor for IS and TIA. More emphasis needs to be put on increasing HDL as a preventive strategy.

Key Words: Stroke; Lipid profile; Lipid lowering medication
Funding Agency: None

Medicine
Category: Graduate (Resident)

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Evaluating stroke management in kuwait: are we taking it seriously?

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Introduction:
Since many years, the seriousness and fatality of ischemic stroke (IS) and transient ischemic attack (TIA) have been well demonstrated. In Kuwait, there are no stroke units; furthermore, no data is available on the management and procedures recommended by guidelines. We assessed to what extent guidelines are appropriately applied after IS and TIA.

Methods:
This is an observational cross-sectional study encompassing 100 patients (60% males, 40% females; 81% IS, 19% TIA) admitted to Mubarak Al-Kabeer Teaching Hospital (MKH) medical wards during 2006 in Kuwait.

Results:
The commonest risk factors found were hypertension (78%), Diabetes Mellitus (54%), history of IS (34%) and ischemic heart disease (30%). CT brain, Aspirin within 48 hrs, and laboratory tests were done for all patients. Carotid Doppler was done in only 25%. Around 75% had not been investigated with echocardiogram. Only 1% had a 24hr ECG monitoring (Holter). Lipid profile done for only 33%. Among patients with hypertension, 24% had carotid Doppler and 29% had echocardiogram. In the IHD group, 30% had carotid Doppler, 33% had echocardiogram and only one patient (3%) had holter monitor. Patients with history of IS had the least chance of been properly investigated with 15% having carotid Doppler and 18% having echocardiogram. Carotid Doppler was not done in 63% TIA and 77% IS, while echocardiogram was not done in 58% TIA and 75% IS.

Conclusions:
Further physician education regarding the importance of promptly and fully evaluating patients with TIA or IS may be warranted, and barriers to implementation of established secondary stroke prevention strategies need to be carefully explored.

Key Words: Stroke; Transient Ischemic Attack; Guidelines
Funding Agency: None

Medicine
Category: Clinical

103

Health facility visits before the diagnosis of Pulmonary Tuberculosis in patients with far advanced disease

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Introduction:
Patients with Pulmonary Tuberculosis often present with far advanced disease even in a country like Kuwait where health care facilities are readily accessible to all. We looked into the pattern of utilization and efficiency of healthcare facilities in this regard.

Methods:
One hundred patients admitted to the TB wards over a period of one year with far advanced disease in the chest x-ray were interviewed.

Results:
There were 69 males and 31 females. Mean age was 35.77±11.18 years. There were only 3 Kuwaitis. Others were in Kuwait from less than a month to a maximum of 28 years. The major symptoms were fever (80%), cough (76%), weight loss (68%), anorexia (54%), night sweats 18%) and hemoptysis (12%). Diabetes was seen in 27%. 50% had 3+ AFB in the sputum whereas two were smear negative. Thirty-four patients were having symptoms for less than a month, 53 for 1to 3 months, 10 for 3 to 6 months and 2 for more than 6 months. 29% of the patients visited a health care facility only once, 37% twice, 18% thrice, 10% four and 4% five times. The number of visits made was related to the duration of symptoms (p=0.037). The frequency of first, second, third, fourth and fifth visits in order are as follows. Government polyclinics: 59 (59%), 28 (41.2%), 15 (45.5%), 4 (28.6%) and 3 (75%); Government hospitals: 32 (32%), 32 (47.1%), 13 (39.4%) and 10(71.4%); Private clinics: 4 (4%), 3 (4.4%) and 1 (3%) ; TB Unit:1(1%), 5 (7.4%)and 4(12%).

Conclusions:
The health facility of initial choice was the government polyclinic. Nearly a third of the patients went straight to a government hospital possibly because they were more sick. The private sector was not frequented probably because of economic reasons. However, only 29% of the patients with advanced disease were diagnosed to have Tuberculosis in the first visit. Doctors in general practice needs more training to suspect and detect tuberculosis early.

Key Words: Tuberculosis; Diagnosis delay; Kuwait
Funding Agency: None

Medicine
Category: Clinical

104

Some transition pecularities of GDM into DM

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Introduction:
Of all pregnancies complicated by Diabetes, gestational diabetes mellitus (GDM) accounts for 90%. The study was performed to determine GDM complications during pregnancy and after delivery.

Methods:
184 pregnant females (aged 18-42) with at least 1 risk factor underwent a 2h 75g OGTT (WHO) at 15-28 week of gestation. Fasting and postprandial blood glucose levels, glycosylated hemoglobin and lipid profile were measured. Patients with GDM proceed to the OGTT 6-9 weeks postpartum.

Results:
GDM was diagnosed in 13 women (7%). Insulintherapy was required for 4 patients. Insulin was prescribed before meals and before bedtime if needed (18-40 U/d). Fasting glucose levels varied from 5, 4 to 6, 0 mm/l, postprandial did 6, 7 – 8, 3 mm/l. HbA1 ranged from 5, 1% to 6, 9%. High levels of total, LDL cholesterol and triglycerids in 5 patients in 2 and 3 trimesters were found, 4 of them being overweighed and 3 requiring insulintherapy. The following pregnancy complications were registered: gestational pyelonephritis, late gestosis, anemia, early amniorrhea, weak delivery activity and large fetus. Pregnancy outcomes: there was a woman experienced cesarian section on 36 gestation week (because of preeclampsia, the newborn weighed 2200g, 5-6 by Apgar score). The rest 12 females had delivered at 39-40 weeks of gestation. The newborns were 3500-4200g, the Apgar score reached 5-8. The complications, such as, chronic intrauterine fetal hypoxia, conjugation jaundice and first-day hypoglycemia were found in infants. Glucose level postpartum became normal in 11 patients.9 of them underwent the OGTT, and hyperglycemia was not detected, 2 patients were absent. Fasting and postprandial hyperglycemia have been registered in 2 examinees. They had the following features: obesity, insulin requirement and high level of lipids.

Conclusions:
Body mass excess before pregnancy, insulin requirement and hyperlipidemia contribute to transition of GDM into diabetes mellitus.

Key Words: Gestational Diabetes; Diabetes Mellitus; Complications
Funding Agency: None

Medicine
Category: Clinical

105

Abnormal cardiovascular risk profile in Arab patients with polycystic ovary syndrome (PCOS)

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Introduction:
Women with PCOS have been reported recently to have increased risk of cardiovascular events such as heart disease and stroke. The mechanism of such finding is not well addressed and no data are reported on Arab subjects. This study aimed to investigate cardiovascular risk profile in Arab PCOS and controls.

Methods:
We studied 54 Arab women with PCOS and 27 normal control matched for age (mean±SEM of patients versus controls, 27±1 vs. 29±2 years) and BMI (27.8±0.8 vs. 28.3±1.7 kg/m^2). Subjects were studied at early follicular phase of their menses. After 12 hours of overnight fasting, blood was collected for the measurement of glucose, insulin, intact proinsulin, total cholesterol, triglycerides, LDL cholesterol, apolipoprotein A (apoA), apolipoprotein B (apoB), non-esterified fatty acids (NEFA), 3-hydroxybutyrate (3-OHB), testosterone and SHBG (to measure free androgen index, FAI). Insulin resistance was calculated using the HOMA-IR formula.

Results:
PCOS women had significantly higher fasting insulin (p=0.0001), intact proinsulin (p=0.0004), total cholesterol (p=0.001), LDL cholesterol (p=0.001), apoB (p=0.002) and FAI (p=0.001) than control women. They were more insulin resistant (IR-HOMA, 3.7±0.3 vs. 1.7±0.3, p=0.0001) than control subjects. However, they had similar levels of fasting glucose, triglycerides, apoA, NEFA and 3-OHB. Insulin levels and IR-HOMA correlated significantly and positively with testosterone level (p=0.003, p=0.003, respectively) and with FAI (p=0.003, p=0.003, respectively)

Conclusions:
In conclusion, PCOS is associated with increased levels of atherogenic lipid profile including raised total and LDL cholesterol and apoB. They have significantly high insulin resistance and hyper-proinsulinemia which correlate with hyperandrogenism (raised FAI). It is therefore possible that this abnormal metabolic profile is responsible for part of the mechanism of increased vascular events in PCOS.

Key Words: PCOS; Lipids; Iinsulin resistance
Funding Agency: None

Medicine
Category: Basic Sciences

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Correlation of meteorological factors, aeroallergen and asthma levels in Kuwait: a 12 month retrospective study.

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Introduction:
The aim was to investigate retrospectively the joint effect of aeroallergen, environment temperature change, humidity levels, wind speed and precipitation on daily asthma admissions.

Methods:
The daily vists to Al-Rashid allergy center for up to one year was taken. Spore and pollen counts were measured hourly. Airborne fungi was monitored using the Burkard spore trap. Functional relationships between aeromycota (air molds), pollen count and meteorological factors were analyzed. The meteorological factors were: mean temperature, minm temperature, and max. temperature, mean wind speed, relative humidity, rain and max. wind speed. For the relation between allergic symptomology and environmental conditions, a time series analysis, utilizing a STATA package was used.

Results:
From January 2003, total count of the files for the people who received asthma treatment from Al-Rashid Allergy Center was 4353 for the 12 month period. The data collected shows that the number of patients were high in the month of the December about 760 (asthma -540, rhinitis -195, asthma and rhinitis -25) the patients effected by asthma is high when compared with rhinitis and asthma and rhinitis. A high number of emergency patients were also admitted. The important factors for the rapid increase in the patient number observed were Max. average temperature is about 19.70c and Min average temperature is about 11.00c. Max relative humidity 66 -100%. High precipitation was ppt - 66.30mm. The average fungal spore -1960.25 /m^3. The highest number of patients in the month of September and October due to the highest number of average pollen grain count compared with other months.

Conclusions:
Analysis using alpha values of 10% for level of significance, found that wind speed do not influence asthma, but temperature and humidity do have a significant influence, with p-value of 0.050 and 0.097 respectively. The confounding effects of pollution and allergen were not studied.I

Key Words: Asthma; Aeroallergen; Climatic factors
Funding Agency: Environment Public Authority

Medicine
Category: Clinical

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One size does not fit all – Anthropometric assessment of the link between obesity, insulin resistance and coronary heart disease in patients with type 2 diabetes

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Introduction:
Adipokines have an impact on glucose and lipid metabolism and contribute to metabolic derangements including insulin resistance (IR), glucose intolerance, dyslipidemia and hypertension that cluster in the metabolic syndrome (MS) and confer increased risk of MS and coronary heart disease (CHD). The aim of this study was to determine, which of : body mass index (BMI), waist to hip ratio (WHR), waist to height ratio (WHtR) and waist circumference (WC) is the most suitable for the assessment of IR, MS and CHD risk.

Methods:
Fasting CRP, adiponectin, leptin, resistin, insulin, glucose, IR (HOMA), HbA1c and lipid profile were measured in 197 patients with Type 2 diabetes classified by gender, IR, MS (IDF criteria) and CHD. Univariate and multivariate regression analyses were used to find the associations of these variables with each other and with IR, MS and CHD. ROC analyses were used to find the best markers of IR, MS and CHD. There are gender differences in the correlations and abilities of BMI, WHR, WHtR and WC to distinguish between patients with IR, MS and CHD; e.g. in males, WHR showed significant correlation with only adiponectin (r=-0.33) whereas in females, it showed significant correlations with only resistin (r=0.30) and leptin (r=0.39).

Results:
In males and females WHR showed the weakest correlations with CRP and the adipokines and BMI showed the highest correlations. Comparison of areas under the ROC curve showed that the BMI had the highest diagnostic values for detection of CHD and MS but WHR had the highest diagnostic value for detection of IR.

Conclusions:
We conclude that there are significant differences in the performance and associations of indices of adiposity in the assessment of the relationships with adipokines, inflammatory markers, IR, MS and CHD. These differences must be borne in mind when performing studies that assess the link between obesity, adipokines and the risk of IR, MS and CHD.

Key Words: Anthropometry; Insulin resistance; Coronary heart disease
Funding Agency: KFAS grant # 2004-07-02

Medicine
Category: Clinical

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Potential significance of plasma resistin estimation in patients with obstructive airways diseases

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Introduction:
Resistin, also called adipose tissue-specific secretory factor (ADSF) or Found in Inflammatory Zone (FIZZ3) is a hormone, which is secreted by adipose tissue cells has been linked to inflammatory lung diseases. We hypothesize that resistin may have effects on pulmonary mechanics and airway inflammation in patients with obstructive airways diseases.

Methods:
We determined fasting resistin in 40 patients with obstructive airways diseases (acute asthma (n=14); stable chronic asthma (n=22) and stable chronic obstructive pulmonary disease (COPD; n=4) mean (SD) age 48.7 (16.2) years. We also determined levels of complements C3 and C4 and pulmonary function tests and correlated the results with resistin levels.

Results:
Mean (SD) resistin in the patients were: acute asthma 5.6 (2.0) ng/ml; stable chronic asthma 5.3 (4.9) ng/ml and stable COPD 2.4 (0.17) ng/ml. The mean resistin was significantly ($p=0.02$) higher in patients with acute asthma compared to patients with COPD and Kruskal-Wallis analysis of variance shows that resistin was significantly ($p=0.019$) higher when patients with acute asthma were compared to those with stable asthma and COPD but the inflammatory markers C3 and C4 were not. Resistin showed significant inverse correlation with FVC predicted (%) only ($r=-0.52$; $p=0.027$).

Conclusions:
Resistin may be a marker of pulmonary inflammation in patients with acute asthma. Further studies are required to determine the significance of resistin in patients with obstructive airways diseases in general and the low resistin in patients with COPD in particular.

Key Words: Resistin; Asthma; Chronic Obstructive airways disease
Funding Agency: None

Medicine
Category: Clinical

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Emotional health in uncontrolled diabetes

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Introduction:
Uncontrolled diabetes may be due to a number of factors like improper diet, absence of exercise, inadequate or inappropriate medication and co morbid conditions. The 'stress hormones' are hyperglycemic. On the other hand diabetes itself may cause emotional distress or depression and this can lead to a vicious circle.

Methods:
The emotional health of the individual is assessed by the MINI Patient Health Survey questionnaire. The forms were in Arabic or English to be easily understood by the patient and where there was a doubt, a person proficient in the language explained and assisted. The survey cards were scored using a scanner developed by HP Design, Holland.100 consequent diabetic patients with uncontrolled diabetes were studied in this pilot survey. They were evaluated for Depression, Generalised anxiety disorder, Panic Disorder and Social anxiety disorder.

Results:
The prevalence of Depression, Generalised Anxiety Disorder and Panic Disorder were significant in patients with uncontrolled diabetes.

Conclusions:
The reason for uncontrolled diabetes may be an emotional problem like depression or anxiety disorder in addition to the well documented factors like diet, exercise, medication and infection.Larger controlled studies are required to assess the magnitude of the problem in the residents of Kuwait.Diabetes treatment and control may be better if the emotional problems are also addressed.

Key Words: Diabetes; Depression; Panic Disorder
Funding Agency: None

Medicine
Category: Clinical

110

Identifying and developing diabetes friendly foods

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Introduction:
An important reason for the high prevalence of diabetes in Kuwait is the culinary habit of enjoying sweet and rich foods which are high in Calories and Glycemic Index (GI). All members of the family, irrespective of whether they are diabetic or not, prefer to sit together and eat the same food. This leads to low compliance to a formal diabetic diet. While respecting these culinary habits it may be possible to identify or develop foods which not only control diabetes better but may also prevent diabetes in the high risk family members.

Methods:
Glycemic Index testing was conducted as per the internationally recognized method. 10 healthy volunteers were selected. The blood glucose value was determined at 0, 15 mins, 30 mins, 45 mins, 60 mins, 90 mins and 120 mins after administering 50grams of Glucose in the fasting state. Tests were carried out in the same way on separate days after administering 50 gram absorbable carbohydrate containing amounts of each test food in fasting state. The incremental area under the curve for each volunteer is determined for the test food and glucose are determined. GI is calculated by dividing the incremental area under the curve for the test food by the incremental area under the curve for glucose and multiplying the product by 100.

Results:
Several low GI foods were identified and some developed by modifying constituents.

Conclusions:
It is possible to identify the diabetes friendly foods in those consumed locally. It is possible to modify the foods with ingredients that lower GI and make them more diabetes friendly. More research into these areas will fulfill the dream of the diabetics to eat tasty food with the family members and still maintain good blood sugar control and avoid complications. Such foods may lead to a decrease in the incidence of diabetes in the future.

Key Words: Diabetes; Therapy; Glycemic Index (GI)
Funding Agency: None

Medicine
Category: Basic Sciences

111

Prediction of Treatment Success in Chronic Hepatitis C Patients Using Artificial Neural Network (ANN)

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Introduction:
More than 2.8% of the world's population is chronically infected with HCV which is nearly five times greater than the number of HIV infected people. The prevalence rate of this disease in Kuwait is 3.3% of its population. The combined therapy of Interferon (IFN) and Ribavirin (RIB) is the only approved treatment for this infection; however, treatment efficacy still doesn't exceed 40-60%. A single 48-weeks treatment course costs more than $20, 000 and is associated with severe adverse effects that may terminate therapy. Therefore, Artificial Neural Network (ANN) was used to predict responders to therapy and save them pointless suffering and high treatment costs. It is information processing computerized system that simulates the human brain in its structure and some of its functions. It is capable to learn from a given set of data and generalize complex phenomena in order to offer solutions to problems where traditional models have failed or are very complicated to build.

Methods:
300 of proven hepatitis C infected patients who had not been treated previously with IFN were retrospectively analyzed by 7 trained neural networks after treatment with IFN plus RIB for 24-48 weeks to predict their response to therapy. Data about age, gender, body weight, HCV genotype, cirrhosis, viremia and duration of infection were used to train the artificial neural networks being used.

Results:
100 patients were responders (33%) and 200 were non responders (67%). The used trained neural networks had a predictive value of treatment response ranging from 57-75% and of no treatment response from 52-71%. The highest diagnostic accuracy that was achieved was 70%.

Conclusions:
These results emphasize that artificial neural network is the promising tool to distinguish between responders and non-responders to IFN plus RIB treatments and to predict possible outcomes of the treatment in chronic hepatitis C patients.

Key Words: Artificial Neural Network; Treatment Response Prediction; Chronic Hepatitis C
Funding Agency: None

Medicine
Category: Clinical

112

Angiotensin Converting Enzyme Gene Insertion-Deletion Polymorphysm in Spondyloarthropthies.

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Introduction:
Low back pain (LBP) is a common medical problem. Interaction between genetic and environmental factors predisposes individuals to LBP even at an early age. Inflammatory back pain or spondyloarthropathies include ankylosing spondylitis (AS), psoriatic arthritis (PSA), reactive arthritis and undifferentiated arthropathies. Recently, angiotensin-converting enzyme(ACE)gene insertion/deletion (I/D)polymorphism has been widely used as a diagnostic tool in inflammatory diseases and studied in different rheumatic diseases, both in adults and children. The objective of this study is to explore whether I/D polymorphisms of ACE gene has a potential role in inflammatory back pain.

Methods:
The prevalence of ACE gene I/D polymorphism genotypes was investigated using polymerase chain reaction in 63 patients with spondyloarthropathy and compared with healthy controls.

Results:
63 patients who entered the study included 44(69.8%) patients with AS, 12(19.0%) with PSA, 3(4.8%) with reactive arthropathy and 1(1.6%) with undifferentiated arthropathy. There were 43 males and 20 females. Mean age of patient was 38.08±11.2 years, age at onset of spondyloarthropathy 28.1±8.1years and disease duration10.56±7.7 months. The control subjects were 111, 59 females and 52 males. The ACE gene polymorphism showed an overall significant difference between patients and controls, p=.05. ID genotype was significantly more in patients than in controls 30.2% vs.16.2%, p=.01, and DDgenotype was more prevalent in controls 66.7% vs.49.2%, p=.01. The allele frequency also was significantly different between patients and controls, p=0.03, I allele more in the patients as compared to controls 37.5% vs.16.7%.

Conclusions:
In this study, ID genotype and I allele showed higher prevalence in patients, which may suggest their contribution in genetic predisposition of spondyloarthropathy. Further studies are necessary to support the association of ACE genotypes in diagnosis, progression and disease outcome in patients with spondyloarthropathy.

Key Words: Spondyloarthropathy; ACE gene polymorphysm; Prevalence
Funding Agency: None

Medicine
Category: Clinical

113

308-nm Excimer Laser for the Treatment of Alopecia Areata in Children

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Introduction:
Alopecia areata is a rapid and complete loss of hair from localized or diffuse areas of hair bearing area of the skin. It is considered to be an autoimmune disease. Recently there are reports of efficacy of the 308-nm excimer radiation for the management of this condition. Our objective was to study the effect of the 308-nm excimer laser in the treatment of alopecia areata in children.

Methods:
Eleven children with 30 recalcitrant patches (including two children with alopecia totalis) that had not responded to different treatment modalities for alopecia areata were enrolled in this study. All of these patients had more than one lesion and at least one lesion was left as a control for comparison. The lesions were treated with the 308-nm excimer laser twice a week for a period of 12 weeks. The patients were evaluated regularly and all patients completed the study.

Results:
There were 7 males and 4 females in this study. Their ages ranged between 4 and 14 years with a mean of 6.4 and the durations of their disease were between 7 and 25 months with a mean of 11.9. Regrowth of hair was observed in 18 (60%) patches. No regrowth of hair was observed in the control patches. Regrowth was observed to begin to appear in the second month in 8 patients. Fourteen of the 22 lesions in scalp showed a complete regrowth of hair. The patchy leasions of alopecia areata over the extremities failed to show a response. Atopic diatheses had an unfavourable effect on the outcome in our patients. All patients tolerated the laser therapy well. At the end of 6 months post-laser therapy, four patients with scalp lesions which had recovered before showed a recurrence of hair loss.

Conclusions:
The 308-nm excimer laser is an effective therapeutic option for patchy alopecia areata of the scalp in children. According to our study it doesn't work for patchy alopecia areata of the extremities. The tolerance to this laser was excellent in our patients.

Key Words: 308-nm excimer laser; Alopecia areata; Children
Funding Agency: None

Medicine
Category: Clinical

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Risk Assessment of Coronary Artery Disease Using Myocardial Perfusion Gated SPECT in Patients Undergoing Non Cardiac Surgery

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Introduction:
Before any major non cardiac surgery, diagnostic evaluation for coronary artery disease (CAD) in patients (pts)with multiple risk factors or previous myocardial infarction(MI)is crucial because of the high risk for morbidity or mortality in the post operative period. Our aim was to evaluate such pts using Tc99m Tetrofosmin myocardial perfusion gated SPECT (G SPECT).

Methods:
Our study comprised 72 consecutive pts(42 men, 30 women mean age 53 years)referred for clearance before general surgery.55 pts had multiple risk factors and17 were known to have CAD. Unstable angina, recent MI or uncontrolled hypertension were excluded. All pts underwent a 2 day stress/rest Tc 99m tetrofosmin GSPECT, using dipyridamole (50 pts)or treadmill test(22 pts).On the basis of a20 segment left ventricle(LV)model analysis, GSPECT evaluated perfusion as stress/rest summed scores(SSS, SRS) and difference scores(SDS)and regional function indexes (RWM, RWT). LVEF was calculated pre and post stress SDS(0-1) was considered normal, SDS(2-6) mild to moderate ischemia and SDS(>6) severe ischemia.

Results:
18 pts showed severe ischemia, transient LV dysfunction and fall of LVEF post stress:angiography of these pts revealed severe CAD which required revascularization prior to their non cardiac surgery; no peri or post operative cardiac event was reported. 20 pts showed moderate ischemia: at angiography 18/20 had significant CAD that needed stenting before going to general surgery and None of them suffered a cardiac event thereafter. The remaining 34 pts had a normal GSPECT :all these pts underwent general surgery without prior coronaroangiography;31 pts did not suffer any cardiac event, 3 pts developed a subendocardial MI and recovered without complications.

Conclusions:
Tc99 m tetrofosmin GSPECT is a useful non invasive technique in the risk stratification for CAD in high risk pts going for general surgery. Its powerful prognostic value lowers the risk for cardiac events in the peri or post operative period.

Key Words: Gated SPECT; Coronary artery disease; General surgery clearance
Funding Agency: None

Medicine
Category: Clinical

115

Clinical spectrum of subclinical hypothyroidism (SH) and role of thyrotropin releasing hormone (TRH) stimulation testing in the diagnosis of SH.

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Introduction:
Subclinical hypothyroidism is biochemically defined as elevated thyrotropin (TSH) level, although the free T4 level is within the normal range.

Methods:
In order to evaluate clinical usefulness of TRH stimulation test, we analyzed 146 patients with subclinical hypothyroidism (mean follow-up 3.6 years). The objective of this study was to determine the contribution of the TRH test; prevalence of exaggerated TRH-TSH response (5 fold or higher) in patients with "high-normal" screening TSH levels.

Results:
The study cohort comprised of adult patients; age range 14-66 years, mostly Kuwaiti nationals (78.2%), women (92.4%), and symptoms duration 3-30months. Many patients with “subclinical” hypothyroidism, in fact had clinical symptoms; menorrhagia-polymenorrhea 47.6%, oligomenorrhea 17.8%, weight gain/ inability to lose weight 66.8%, dry skin 42.5%, scalp hair loss 60.7%, constipation 16.7%, somnolence 32.8%, forgetfulness 18.6% and depression 12.4%. There was clinically palpable goitre 33.4%, positive family history of thyroid illness 45.3% and 32.6% had elevated thyroid autoantibodies. Exaggerated TRH-TSH response was evident in 83% patients of SH and remained unchanged with a higher basal TSH level (4.5mU/L). However the discriminatory value of TRH was less significant with a higher basal TSH (7mU/L). Most patients (88.1%) were started with small dose of thyroxin (25-50mcg OD) but needed higher dose at study completion (52.1%). Euthyroidism were restored in 87.5% but only 11 patients (7.2%) had normalized TFT to discontinue treatment forever.

Conclusions:
Subclinical hypothyroidism needs more attention for its diverse presentation and propensity to develop overt hypothyroidism. The exaggerated TRH-stimulated TSH response is a diagnostically useful supplemental test in SH patients with relatively lower baseline TSH. However the significance of the test is reduced with a higher baseline TSH levels

Funding Agency: None

Medicine
Category: Clinical

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Analysis of a one-month data from the Coronary Angiograms done in the Chest Diseases Hospital of Kuwait.

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Introduction:
Cardiac Catheterization Laboratory of the Chest Diseases Hospital (CDH) in Kuwait is the only facility available for this purpose in Kuwait. Therefore data collected here truly reflects data from the whole State of Kuwait. To analyze the angiographic data of patients undergoing coronary angiography (CAG) over a one month period in this facility.

Methods:
The Catheterization records of all the patients who underwent CAG during the month of September 2006 were retrospectively analyzed using the SPSS data entry and analysis program

Results:
There were 394 records. 291 were men (73.9%) and 103 were women (23.1%). 57.9 % of the patients were Kuwaitis. Other Arabs formed 22.6%. Those from the Indian sub continent and others made up 19.5%. Their mean age was 54.52 years (23 – 86). Normal Coronaries / No significant Coronary artery disease (CAD) was seen in 21.5%. One vessel, 2 vessels and 3 vessels CAD were seen in 19.3 %, 20.8 % and 34.6 % respectively. Left main CAD was present in 2.7 %. Based on the CAG, 36.9 % were continued on Medical management. 37.5 % were referred for percutaneous coronary interventions (PCI) and 19.3 % were sent for Coronary artery bypass surgery. In 6.3 % either of the later two options was given. 126 of the procedures were PCI of which 62 were planned and 64 were adhoc procedures. A mean of 1.73 stents (1 – 5 numbers) were used.

Conclusions:
A large number of coronary Angiograms are done in the CDH every month. Majority of the patients are Kuwaitis. Significant % of patients has two or three vessels CAD. Most patients are managed with PCI or Medical management.

Key Words: Coronary artery disease; Coronary angiogram; Stents
Funding Agency: None

Microbiology and Immunology
Category: Basic Sciences

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Real-time PCR with SyberGreen and species-specific probes for detection and quantitation of Candida albicans DNA

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Introduction:
Infection with *Candida albicans* is a growing problem with high mortality in immunocompromised patients. The sensitive detection and quantitation of *C. albicans* DNA is important for early diagnosis and improved prognosis. This study established a real-time PCR assay to sensitively detect and quantitate *C. albicans* DNA.

Methods:
Genomic DNA was isolated from culture grown *C. albicans* and used to standardize real-time PCR by LightCycler. Two fluorescent detection systems, based on SyberGreen dye and LightCycler probe system (the stimulator probe labeled with fluorescene dye and the acceptor probe labeled with LCRed640 dye) that can specifically detect *C. albicans* were used. The primers used for SyberGreen detection were genus specific, while the primers used with probes were specific for *C. albicans.* The amplification and detection of the PCR products in real-time were carried out in the LightCycler System of the Roche Diagnostics. Melting temperature analysis was performed to determine the specificity of the PCR products and to identify the Candida species.

Results:
The amplifications of *C. albicans*-specific DNA were detected by both SyberGreen and probe detection systems. The probe detection system was 10 to 100 times more sensitive than the SyberGreen detection system. The other advantage of the probe detection was the amplification of an internal control along with the specific DNA, which was useful in detection of inhibitory activity present in clinical samples, thus avoiding false negativity. The improved sensitivity of the probe detection may also overcome the false negativity with the SyberGreen detection due to low sensitivity. However, SyberGreen detection may be useful when the aim is to detect all Candida species.

Conclusions:
While SyberGreen and probe detection systems could be useful in the diagnosis and quantitative detection of *C. albicans* DNA, the probe detection may be preferred due to improved sensitivity and reduced false negativity.

Key Words: Candida albicans; Real-time PCR; DNA detection
Funding Agency: KFAS grant #. 05-1302-2005

Microbiology and Immunology
Category: Clinical

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Evaluation of INNO-LiPA MYCOBACTERIA v2 and DNA AccuProbe assays for specific identification of mycobacteria directly from BACTEC MGIT 960 system tubes

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Introduction:
Specific identification of *mycobacteria* is of clinical relevance since treatment varies according to the species causing infection. This study evaluated INNO-LiPA MYCOBACTERIA v2 (LiPA) and AccuProbe assays for species-specific identification of mycobacterial isolates in Kuwait directly from MGIT 960 system tubes.

Methods:
Clinical specimens (n=75) cultured and flagged positive for mycobacterial growth by MGIT 960 system were evaluated. The LiPA and AccuProbe assays were performed and interpreted according to the manufacturer's instructions. The results were validated by DNA sequencing of 16S-23S internal transcribed spacer region (ITSR).

Results:
Each of 75 tubes grew only one Mycobacterium species. Both AccuProbe and LiPA identified 49 isolates as *Mycobacterium tuberculosis complex* (MTC) members and ITSR sequences of 8 randomly selected isolates were concordant. AccuProbe assay identified 26 isolates as non-tuberculous mycobacteria (NTM) with species-specific identification of 9 isolates. ITSR sequences were concordant with species-specific identification of 7 of 9 isolates and with the NTM status for the remaining 17 isolates. The LiPA identified 21 isolates as NTM with species-specific identification of 19 isolates while no result was obtained for 5 isolates (no amplicons in LiPA). The ITSR sequencing confirmed specific identification by LiPA for 19 isolates while 2 isolates were identified as *M. immunogenum* and *M. lentiflavum*. Further, 4 and 1 of 5 isolates yielding no result in LiPA were identified as *M. kansasii* and *M. chimaera*, respectively.

Conclusions:
All the MTC isolates were correctly identified by LiPA and AccuProbe assays. Although, AccuProbe assay identified only some (9 of 26) while LiPA identified most (19 of 26) NTM isolates to the species level, 4 M. kansasii isolates correctly identified by AccuProbe assay were not even detected by LiPA indicating sequence variations in LiPA target region in some M. kansasii strains in Kuwait.

Key Words: Mycobacterium species identification; AccuProbe assay; Line Probe Assay
Funding Agency: Kuwait University Grant # MI 02/04

Microbiology and Immunology
Category: Clinical

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Neonatal candidemia in Kuwait: A 12 year retrospective study

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Introduction:
Candida species have become an increasingly important cause of late-onset infection in premature neonates.This study was conducted to determine the prevalence of *candidemia* in neonatal intensive care unit(NICU) and to analyze the role of various demographic and nosocomial risk factors in its onset.

Methods:
All episodes of *candidemia* occurring between January 1995 and December 2006 among infants hospitalized in NICU were identified. Data were collected from clinical records of 112 infants.

Results:
Of 4790 neonates admitted to NICU during 1995-2006, 175 cases of *candidemia* were detected with an overall prevalence of 3.7% and crude mortality of 27.7%.The annual rate of *candidemia* per 1000 admission was variable; the highest being in 1997 (80.3 cases) and the minimum in the year 2004and2005 (18 cases).Of the 112 assessable *candidemia* cases, as many as 78 (69.6%)occurred in very low birth weight (<1500g) neonates, 65(58%)of them were born with gestational age of <30 weeks. Ninety seven(86.6%)neonates received treatment with >2 antibiotics, and this appeared to be the main risk factor for *candidemia*. The other risk factors included administration of total parenteral nutrition for >5days (82.1%), presence of central venous catheter (77.7%).The onset of *candidemia* ranged between 7to 132 days, but majority 63(55.3%) of the cases occurred within 3 weeks of life, and 12(13.4%)died within three days.Candida albicans and non-albicans Candida species accounted for 47.5% and 52.5% of *candidemia* cases, respectively. Candida parapsilosis was the second most common species isolated from 63 (36.2%) cases of *candidemia*.No fluconazole resistance was observed in C.albicans and C.parapsilosis isolates by E-test.

Conclusions:
Many risk factors have been implicated in the pathogenesis of *candidemia* in NICU infants.The occurrence of neonatal *candidemia* in NICU could be considerably reduced by proper usage of antibiotics.

Key Words: Neonatal Infections; Candidemia; Risk Factors
Funding Agency: None

Microbiology and Immunology
Category: Clinical

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Acinetobacter spp in the Maternity Hospital: Is there a relation between neonatal and maternal isolates?

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Introduction:
Multi-resistant *Acinetobacter spp* has become an important cause of nosocomial infection worldwide. The purpose of this study was to define and compare the species profile and antibiotic resistance pattern of both neonatal and maternal clinical isolates.

Methods:
All clinical isolates of *Acinetobacter spp* isolated between January, 2001 and December, 2006 were analyzed.

Results:
A total of 343 *Acinetobacter spp* were isolated, 138 (40.2%) were neonatal isolates and majority 102 (74%) were blood isolates. While 184 (90%) of maternal isolates were genitourinary isolates, 85 (41%), 65 (31.7), and 33 (16.1%) were HVS, urine and episiotomy wound isolates respectively. *Acinetobacter baumanni* was the commonest identified special both in neonatal and maternal isolates form 64.7% (185) of species while *Acinetobacter calcoaceticus* form 33.2% (95) of identified species. 77.3%, 86.5%, 45% *Acinetobacter baumanni* were resistant to ampicillin, cefuroxime and cefotaxime respectively and only one isolate was resistant to imipenem and tazocin and no resistance detected to amikacin and meropenem. The *Acinetobacter calcoaceticus* had the same antibiotic profile as *Acinetobacter baumanni*.

Conclusions:
The species profile and the antibiotic resistance pattern for both neonatal and maternal isolates were comparable and may indicate that the neonatal isolates mainly acquired in the hospital may be related to maternal community strains. At the same time we did not elicit the trend of multi-resistant *Acinetobacter spp* that is reported in the literature as main problematic nosocomial isolates during the last six years.

Key Words: Acinetobacter; Resistance pattern; Neonatal Infections
Funding Agency: None

Microbiology and Immunology
Category: Basic Sciences

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Multilocus sequence tTyping of community-associated methicillin-resistant Staphylococcus aureus in Kuwait hospitals suggests a European origin for the Dominant Clones.

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Introduction:
Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is increasingly isolated from inpatients in Kuwait hospitals. The aim of this study was to determine the genotypes of non multiresistant MRSA, previously characterized by SCCmec typing as CA-MRSA, using pulsed-field gel electrophoresis (PFGE) and multilocus sequence typing (MLST) to determine their sequence types (ST).

Methods:
A total of 26 CA-MRSA obtained in six hospitals were studied. PFGE was performed utilizing SmaI digestion of genomic DNA followed by fragment separation in a CHEF DRIII system. MLST was performed according to internationally standardized protocols. Susceptibility to antibacterial agents was determined by disk diffusion.

Results:
Ten isolates were resistant to kanamycin, ten isolates were resistant to tetracycline, 11 isolates were resistant to fusidic acid, two isolates were resistant to erythromycin and clindamycin and one isolate was resistant to trimethoprim. All of them expressed resistance to cadmium acetate. They belonged to five pulsed-field patterns designated types A-E as follows: PFGE type A (12 isolates), type B (8 isolates), type C (3 isolates), type D (1 isolate) and type F (1isolate). MLST revealed the following STs; ST80 (12 isolates), ST30 (8 isolates), ST5 (2 isolates), ST8 (1 isolate), ST97 (1 isolate) and ST361 (1 isolate). Isolates that had PFGE type pattern A belonged to the same ST (ST80). Similarly, isolates with type B PFGE pattern were ST30. The three PFGE type C isolates had three different STs; ST5, ST8 and ST97. Isolates with PFGE types D and E had ST5 and ST361 respectively.

Conclusions:
The results show that two CA-MRSA clones belonging to ST80 and ST30 genotypes similar to those isolated in Europe are the dominant clones in Kuwait hospitals suggesting a European origin for these clones.

Key Words: Multilocus sequence typing; Community-associated MRSA; MRSA
Funding Agency: Kuwait University Research Administration # MI 01/03

Microbiology and Immunology
Category: Basic Sciences

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The prevalence of antibiotic resistance in Enterococcus species isolated in Kuwait hospitals.

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Introduction:
A previous study (1999-2001) revealed that the prevalence of vancomycin resistance was low (2.6%) in *Enterococcus species* isolated in Kuwait hospitals. However, 19% of the isolates expressed high-level gentamicin resistance. The aim of the present study was to compare the prevalence of antibiotic resistance in current enterococcal isolates to those in the previous study to determine any changes in resistance patterns.

Methods:
Between 1 March and 31 July, 2006, 294 *enterococcus isolates* were identified using the Vitek GP card and tested for susceptibilities to antibiotics by disk diffusion and MIC determination by agar dilution or Etest..

Results:
The 294 consisted of 257 (87.4%) *E. faecalis*, 18 (6.1%) *E. faecium*, 6 (2.0%) *E.gallinarum*, 3 (1.0%) *E. avium* and 10 (3.4) unspeciated isolates. They were isolated from urines (94, 32%), blood (19, 6.5%), high vaginal swabs (50, 17.0%), catheter tips (4, 1.3%) and other sources (127, 43.2%). Two hundred (68.0%), 127 (43.2%) and 125 (42.5%) of the isolates were resistant to high level kanamycin (MIC >2000 mg/L), streptomycin (MIC >1000 mg/L) and gentamicin (MIC >500mg/L) respectively. They were also resistant to tetracycline (84.7%), chloramphenicol (31.2%), erythromycin (67.0%) and rifampicin (25.2%). Twenty five isolates (8.5%) were resistant to ampicillin but only four (1.3%) of them produced beta-lactamase. Only two (0.7%) E.faecalis isolates were vancomycin resistant (MIC > 32mg/L).

Conclusions:
The study revealed that *E. faecalis* remained the most common Enterococcus species isolated in Kuwait hospitals. The prevalence of vancomycin resistance remained low. However, the proportion of isolates resistant to high level gentamicin (from 19% to 42.5%), kanamycin (from 20% to 68%), streptomycin (from 20% to 43.2%), and tetracycline (from 60.5% to 84.7%) increased significantly since the last study. Beta-lactamase production was detected for the first time in enterococcus isolated in Kuwait.

Key Words: Vancomycin-resistant enterococci; Aminoglycoside restant enterococcus; Antibiotic
Funding Agency: Kuwait University Research Administration # MI 01/03

Microbiology and Immunology
Category: Clinical

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Enteric adenovirus serotype 41 causes acute gastroenteritis in Kuwait

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Introduction:
Human rotavirus (RV) and *adenovirus* (AdV) infections are major causes of acute outbreaks and sporadic cases of gastroenteritis occurring primarily in children less than 5 years old. The infection might be fatal, and infection control measures are costly. Human AdV species F is represented by two serotypes, 40 and 41 known for their tropism for the gastrointestinal tract, thus termed enteric adenoviruses (EAdV). This group account for 1-20% of acute gastroenteritis in children. Other AdVs, including serotypes 1, 2, 3, 5, 7 and 31 have been detected in human feces. The aim of this study was to identify AdV serotypes associated with acute gastroenteritis in Kuwait.

Methods:
Stool samples were collected from 100 children (<5 years old) admitted with acute gastroenteritis admitted to Kuwaiti hospitals, and proven negative for RV by ELISA. The samples were inoculated into cell line and then tested for AdV by immunofluorescence (IFA). The samples were further tested by two PCR assays to detect and identify AdVs. PCR positive samples were sequenced by dye terminator cycle reaction. Sequences were analyzed using a Beckman Coulter Sequencer and compared to published adenovirus DNA sequences (GenBank).

Results:
Fourteen out of one hundred (14%) RV- negative stool samples were positive for AdV by PCR and culture/IFA. EAdVs (species F) was identified in 11 (79%) positive samples, while respiratory AdVs (species B) were detected in 3 (21%) positive samples. Sequence analysis of PCR products identified all EAdVs as AdV41, while B species were identified as AdV7 (2 samples) and AdV3 (one sample).

Conclusions:
Enteric adenovirus serotype 41 and non-enteric adenovirus serotypes 7 and 3 are important causative agents of acute gastroenteritis in Kuwait.

Key Words: Acute gastroenteritis; Enteric adenovirus; PCR
Funding Agency: Research Administration, Grant #. YM01/04

Microbiology and Immunology
Category: Graduate (MSc: Basic Sciences)

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Typing of adenoviruses associated with human disease in Kuwait by PCR-based sequencing

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Introduction:
PCR-based sequencing is being widely used for typing of viral agents in clinical specimens, and identification of mutations responsible for resistance to antiviral therapy. The known 51 human adenovirus (HAdV) serotypes are divided into strains, genome types and variants. This makes this group a good target for typing by this technology. It is highly recommended since the available culture-based typing assays are slow and labor-intensive. In this study, we applied PCR-based sequencing to detect and type HAdVs associated with human diseases in Kuwait.

Methods:
Five-hundred samples including respiratory specimens, eye swabs and stool samples collected from patients seen/admitted at Kuwaiti hospitals presenting with respiratory infection, conjunctivitis, and gastroenteritis, were screened for HAdVs by culture/immunofluorescence assay (IFA) and by PCR targeting a conserved region of the HAdV hexon protein gene. PCR amplified products of conserved hexon region, and hexon hypervariable region-7 (HVR-7), were sequenced by dye terminator cycle reaction. Viral DNA sequences were analyzed using a Beckman Coulter Sequencer and compared to hexon gene sequences (GenBank).

Results:
Ninety-two out of 500 samples (18%) were positive for HAdVs by PCR. These include 59/139 eye swabs (42%), 18/115 (16%) stool specimens, and 15/246 (6%) respiratory specimens. PCR results showed 97% (485/500) concordance with culture/IFA. Sequence analysis of adenovirus hexon gene was completed in 50 PCR positive samples. Of them, 22 (44%) were serotype 7 (AdV7), 10 (20%) were AdV3, 10 (20%) were AdV41, 5 (10%) were AdV11, 2 (4%) were AdV8, and 1 (2%) was AdV37.

Conclusions:
PCR-based sequencing of the hexon gene has proven effective for the diagnoses of HAdVs at the serotype level enabling the identification of this group of viruses for the first time in Kuwait.

Key Words: PCR; Sequencing; Adenovirus
Funding Agency: Research Administration, Grant #. YM 01/04

Microbiology and Immunology
Category: Graduate (MSc: Basic Sciences)

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Rapid molecular detection of multidrug-resistant clinical Mycobacterium tuberculosis isolates in Kuwait by a line probe assay, Genotype MTBDR

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Introduction:
Rapid detection of multidrug-resistant (defined as resistant at least to rifampin, RIF and isoniazid, INH) *Mycobacterium tuberculosis* (MDR-TB) strains is important for initiation of effective chemotherapy, ensuring successful treatment and preventing further spreading of MDR-TB strains. While >90% RIF-resistant strains contain mutations within RIF-resistance-determining region (RRDR) of rpoB gene, INH-resistant strains carry mutations in four genes but more frequently, from some geographical locations, at katG315. The Genotype MTBDR assay (gMTBDR) is a new and the only commercial test that detects mutations conferring resistance to RIF (rpoB gene) and INH (katG315), simultaneously. This study evaluated the performance of gMTBDR in detecting mutations in rpoB and katG315 genes among MDR-TB strains in Kuwait.

Methods:
The *M. tuberculosis* H37Rv was used as a reference strain and 37 MDR-TB and 19 fully susceptible *M. tuberculosis* strains characterized by phenotypic drug susceptibility testing by BACTEC 460 TB system were analyzed. Mutations in RRDR of rpoB and katG315 were detected by gMTBDR kit (used according to the kit's instructions). The test was completed within 8 hours.

Results:
The gMTBDR correctly identified all susceptible strains. The gMTBDR identified 31 of 37 (84%) MDR-TB strains as RIF-resistant with specific detection of mutations in 23 isolates while 6 (16%) strains were identified as RIF-susceptible. The S531L was the most common (18 of 31, 58%) mutation in the rpoB gene. The gMTBDR also identified 19 of 37 (51%) MDR-TB strains as INH-resistant with specific detection of katG315 mutations in 18 isolates while 18 (49%) strains were detected as INH-susceptible.

Conclusions:
The gMTBDR assay rapidly detects the resistance to RIF in majority (84%) of MDR-TB strains, confirms the MDR-TB status of nearly half of the isolates by detecting mutations at katG315 and is useful for better management of patients infected with MDR-TB strains.

Key Words: Mycobacterium tuberculosis; Multidrug resistance; Rapid detection
Funding Agency: Kuwait University grant # YM 03/06

Microbiology and Immunology
Category: Clinical

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Candida haemulonii: an emerging opportunistic pathogen resistant to amphotericin B and azoles

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Introduction:
Candida haemulonii is rarely reported as a cause of invasive candidiasis. Here, we describe an outbreak of C. haemulonii fungemia in a neonatal intensive care unit (ICU) of a maternity hospital in Kuwait.

Methods:
The diagnosis of *C. haemulonii fungemia* involving four neonates was made by isolating the yeast from blood cultures. Since the phenotypic characteristics of the isolates were not helpful, molecular methods were used for species-specific identification. The amplification of species-specific internally transcribed spacer (ITS)-1 and ITS-2 regions of rDNA and/or D1/D2 regions of 26S rRNA was performed by using panfungal primers and the amplicons were sequenced. The antifungal susceptibility of the isolates was determined by E-test using RPMI 1640 medium supplemented with 2% glucose.

Results:
Of the 4 neonates with *C. haemulonii fungemia*, 3 were born pre-term and one full-term. All the neonates were exposed to risk factors for Candida infections that included use of broad-spectrum antibiotics, administration of total parenteral nutrition and placement of central venous catheters. The 7 isolates obtained from the neonates assimilated trehalose, esculin, and glycerol but did not assimilate cellobiose, melibiose, melezitose and salicin. The ITS and/or D1/D2 region sequences of the isolates matched nearly completely with the corresponding sequences from the reference C. haemulonii strain, thus confirming their identification. They were uniformly resistant to amphotericin B, fluconazole and itraconazole, but susceptible to 5-flucytosine, voriconazole, and caspofungin. Despite antifungal therapy, 2 of the neonates died.

Conclusions:
To the best of our knowledge, this is the first report describing an outbreak of *C. haemulonii fungemia*. The report underscores the emergence of this rare Candida species, resistant to polyenes and azoles, as a cause of invasive candidiasis in neonates.

Key Words: Candida haemulonii; Neonates; Fungemia
Funding Agency: Kuwait University Grant # MI04/05 and Ministry of Health, Kuwait

Microbiology and Immunology
Category: Basic Sciences

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Environmental occurrence of moulds in Intensive Care Unit and Operation Theater of Mubarak Al-Kabeer Hospital: A prospective study

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Introduction:
Nosocomial opportunistic mold infections can be life-threatening in immunocompromised patients. These moulds in the hospital environment normally arise from contaminated outdoor air that infiltrates hospital ventilation system. The objective of this study was to monitor aerial prevalence of moulds in Intensive Care Unit (ICU) and Operation Theater (OT) of Mubarak Al-Kabeer Hospital prospectively.

Methods:
Petridishes containing Sabouraud dextrose agar (SDA) were exposed for 30 minutes at fortnightly intervals in the ICU and OT at fixed sites for 8 months. The SDA plates were incubated at 28 degree C for 3-4 days and the counts for colony forming units (CFU) were made for various fungi to determine their relative prevalence.

Results:
During the monitoring period of 8 months (January to May and September to November), 240 Petridishes were exposed in the ICU yielding 61 colonies of moulds. Of these, 38 were identified as *Aspergillus species* (A. niger 19, A. nidulans 8, A. flavus 7, and A. terreus 4), 5 as *Cladosporium species*, and 9 as *Penicillium species*. Nine of the colonies belonged to other fungal species. In the OT, 142 Petridishes were exposed yielding 24 mould colonies representing *Cladosporium species* (7 colonies), *Aspergillus species* (5 colonies), *Penicillium species* (11 colonies) and *Paecilomyces species* (one colony). Twenty-one mould colonies were isolated from the 60 surface swabs taken from various places in ICU and OT and these were identified as *Aspergillus species* (7 colonies), *Cladosporium species* (8 colonies) and *Penicillium species* (6 colonies).

Conclusions:
The study suggests that prevalence of aerial fungi in ICU and OT was low (< 0.3 cfu/plate), even when an extended period of 30-minute exposure was employed. However, isolation of *A. terreus* and *A. flavus* from ICU environment underscores the need of frequent periodic monitoring for these nosocomial mould pathogens.

Key Words: Aerial Fungi; Prevalence; Intensive Care Unit
Funding Agency: Kuwait University Research Grant #. MDI 257

Microbiology and Immunology
Category: Basic Sciences

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Th1 and Th2 cytokine responses of peripheral blood mononuclear cells in diabetic tuberculosis patients

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Introduction:
Patients with diabetes mellitus (DM) are more susceptible to *pulmonary tuberculosis* (TB) of which the precise mechanisms are not yet fully understood. In general, Th1 (e.g. IFN-g) and Th2 (e.g. IL-10) cytokines are correlated with resistance and susceptibility to TB, respectively. To elucidate the mechanisms of increased susceptibility to TB, we have studied cytokine profiles of non-diabetic and diabetic pulmonary tuberculosis (TB) patients, by quantitation of Th1 (IFN g, IL-2, TNF-b), Th2 (IL-10, IL-4, IL-5) and the pro-inflammatory cytokines (TNF-a, IL-6, IL-8, IL-1b) secreted by peripheral blood mononuclear cells (PBMC).

Methods:
PBMC obtained from non-diabetic pulmonary TB (NDTB, n=12) and type II diabetic TB patients (DTB, n=11) were stimulated in vitro with complex antigens of *M. tuberculosis* (whole cells, culture filtrate and cell walls) and antigens encoded by regions of difference (RD) between *M. tuberculosis* and BCG, i.e. RD1, RD4, RD6 and RD10. Culture supernatants were collected on day 6 and assayed for cytokine secretion using Flow Cytomix kits (BenderMed Systems. The concentrations of each cytokine were expressed as mean pg/ml+SEM. In response to antigenic stimuli, the experimental / control (E/C) >3 were considered a positive response. The concentrations of cytokines secreted by PBMC of both groups were statistically analyzed for significant ($P<0.05$) differences using non-parametric Mann-Whitney U-test.

Results:
All of the complex antigens, except culture filtrate in case of IL-10, induced secretion (E/C>3) of IFN-g, IL-10, and TNF-a by PBMC of both groups of patients with no statistical difference between the DTB and NDTB patients. Except for RD1 antigens which induced secretion of IFN-g, None of the other RD antigens induced IFN-g secretion by both donor groups (Table 1). None of the other cytokines were secreted by PBMC of both donor groups in response to any of the RD antigens. Although, the concentration of IFN-g was significantly higher in DTB patients, as compared to NDTB patients, the IFNg/IL-10 ratios were higher in NDTB that DTB patients.

Conclusions:
Both diabetic and non-diabetic TB patients respond to complex antigens of *M. tuberculosis* by producing cytokines belonging to Th1, Th2 and pro-inflammatory groups. DTB patients produce statistically higher concentrations of Th1 (IFN-g) and Th2 (IL-10), compared to NDTB patients in response to RD antigens. The lower Th1:Th2 ratio in the DTB patients compared to the NDTB patients may account for the hampered resistance to *M. tuberculosis* infection under diabetic conditions.

Key Words: Diabetes; Tuberculosis; Cytokines
Funding Agency: Grant # KFAS-2002-1302-04

Microbiology and Immunology
Category: Clinical

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Inhibition of Th1-type cytokines in kidney transplant recipients with active CMV infection

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Introduction:
Cytomegalovirus (CMV) infection is a major complication after kidney transplantation. It is clear that Th1 and Th2 subsets are of major importance in determining the class of immunoprotective function in infectious diseases. A corollary to this is the conclusion that the type bias either toward Th1-dominance or Th2-dominance can make a difference between effective elimination of the virus or exacerbation of the disease. Given the strong influence exerted by Th1- and Th2-type immunity on the outcome of infections, we felt it important to elucidate Th1- and Th2-type responses to CMV infection in kidney recipients (KR).

Methods:
One hundred twenty KR were inducted in this study. KR were followed up for a period of 6 months after transplantation for CMV infection diagnosed by the antigenemia assay. We investigated PBMC responses to the mitogen phytohemaglutinin (PHA) and 5 CMV-related peptide antigens (pp65, gB, pp150, pp28 and pp38). Stimulation index (S.I.) was determined by radioactive thymidine uptake while the production of Th1-type cytokine (IL-2, IFN-ã, TNF-á) and Th-2 type cytokines (IL-4, IL-10) were measured by ELISA.

Results:
The difference in the stimulation of peripheral blood mononuclear cells (PBMC) with pp65 antigen gave a significant difference between the CMV-negative and CMV-positive KR ($p<0.0001$). The levels of cytokines after PHA stimulation were statistically significant between the two groups in the case of IFN-g ($p<0.05$) and TNF-a ($p<0.5$). As for the stimulation with CMV-related antigens pp28 gave statistically significant differences in the level of IL-10 between the two groups ($p<0.05$).

Conclusions:
Levels of Th1-type cytokines were significantly lower in CMV-positive KR. Low level of Th1-type cytokines seem to correlate well with active CMV infections in kidney recipients.

Key Words: Kidney recipients; Cytomegalovirus; Cytokines
Funding Agency: Office of the Vice Rector for Research, Grant #. MI 03/02, Kuwait University

Microbiology and Immunology
Category: Basic Sciences

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Plasmid- mediated tetracycline resistance in Campylobacter jejuni in Kuwait

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Introduction:
Campylobacter jejuni is a major foodborne pathogen and cause of diarrhoea worldwide. Tetracycline is one of the drugs that can be used to treat serious *C. jejuni* infection. The objective of this study was to investigate the prevalence and mechanism of tetracycline resistance in *C. jejuni* isolates in Kuwait.

Methods:
Single consecutive isolates of *C. jejuni* from 85 diarrhoeal patients at Mubarak Al Kabir Hospital, Kuwait during 2000 to 2005 were studied. Minimum inhibitory concentrations (MICs) of tetracycline were determined by agar plate dilution method. Isolates with MIC $\geq$ 16 μ/ml of the drug was considered resistant. Plasmid analysis of the isolates was carried out by the alkaline lysis method. Plasmid transfer by tetracycline resistant to tetracycline susceptible recipient *C. jejuni* was carried out by filter mating. Tetracycline resistance encoded by tetO gene was determined by PCR. Genetic relationship among the isolates was determined by pulsed-field gel electrophoresis (PFGE).

Results:
Thirty-four isolates (40%) were resistant to tetracycline. All of them produced an amplicon of 559-bp in PCR corresponding to tetO gene. Eighteen of 34 tetracycline resistant isolates (53%) harboured a 35-kb plasmid. In preliminary studies, one resistant *C. jejuni* transferred resistance to a recipient *C. jejuni* which acquired the plasmid and became positive for tetO gene. The tetracycline resistant *C. jejuni* isolates were unrelated to each other as they showed different banding patterns by PFGE.

Conclusions:
A significant proportion of *C. jejuni* isolates in Kuwait carried tetracycline resistance encoded by tetO gene. The preliminary finding suggests that the resistance is transferable. These results support the findings from other parts of the world that plasmid-mediated tetracycline resistance is characteristic of *C. jejuni* isolates. Therefore, empirical treatment with tetracycline is not recommended for *C. jejuni* infection.

Key Words: Campylobacter jejuni; Tetracycline resistance; Plasmid
Funding Agency: Kuwait University (Grant # MI02/01)

Microbiology and Immunology
Category: Graduate (MSc: Basic Sciences)

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Virological Analysis, Genotypes and Mutational Patterns Affecting the Replication Capacity of the Hepatitis B Virus

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Introduction:
Genetic variability of HBV encounters 2 compounding forces: a high viral copy number and the lack of proofreading activity in the HBV polymerase; as a result a large pool of quasispecies is generated under immune and antiviral selection pressures leading to immunoglobulin escape mutants and antiviral resistant variants. Therefore, the aim of this study was to identify the dominant HBV species and to determine the frequency of mutations reported to increase viral replication and result in poor prognosis among HBV-infected patients in Kuwait.

Methods:
Three different genotyping methods were applied INNO-LiPA, PCR-RFLP and DNA-sequencing in samples from 150 HBV-infected patients. Antiviral resistant variants (YMDD mutants) and HBV subtypes were detected based on the amino acid sequences obtained from sequencing polymerase region. Precore/basal core promoter mutants that abolish HBeAg expression and enhanced viral replication were identified at positions 1762, 1764, 1858, 1896 and 1899 by sequencing the entire core gene. Finally, viral replication activity was evaluated using bDNA assay.

Results:
Agreement between LiPA and DNA-sequencing methods was found in all cases and HBV genotype D was the most prevalent strain. Antiviral mutants were detected in only 5.3% of the patients. Viral loads were equally high in HBeAg(+) and HBeAg(-) patients. The most frequently encountered precore mutation was G1896A, and basal core promoter mutations were A1762T and G1764A.

Conclusions:
Genotype D was found to be the dominant infecting strain in all patients with severe hepatic damage. Negativity for HBeAg at commencement of therapy was an important factor for emergence of YMDD mutants. Sequence analysis of the lower stem of the epsilon structure in the precore domain revealed 1896 stop codon mutation dominant among HBeAg(-) patients.

Key Words: HBV quasispecies; YMDD variants; 1896 stop codon mutation
Funding Agency: Supported by Research Administration project grants YM 02/03, Kuwait

Microbiology and Immunology
Category: Graduate (MSc: Basic Sciences)

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Variability in Hepatitis B Virus Core Sequence Associated with Persistence of Viral Replication and Changes in T-cell Responses

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Introduction:
Hepatitis B virus DNA contains four open reading frames. The core gene encodes the 185 amino acid long nucleocapsid protein (HBcAg) and the nonparticulate form identified as HBeAg. HBcAg is immunologic target of CTL that contains helper T cell and humoral epitopes. Different HLA-restricted HBcAg T cell epitopes have been proposed. Recently, substitutions in the amino acid sequence of the HBcAg were reported which are related to viral persistence and active liver disease. The aim of this study was to identify these substitutions and their influence on the progression of liver disease among HBV chronically-infected patients in Kuwait.

Methods:
Sera samples were collected from 100 HBV chronically-infected patients. The complete HBV core gene was amplified and sequenced. Precore and basal core promoter mutations affecting the HBeAg expression and enhancing viral replication were detected. Different CD4 and CD8 T cell epitopes have been characterized. Finally, the phylogenetic relationship was analyzed using Phylip program.

Results:
HBV genotype/subtype-specific nucleotide substitutions were found characterizing genotypes A, D, A+D and C/D hybrids. CD4 T cell epitope (amino acid 147-156) identified a major target in HLADR13 has been examined with a mutation at position 151 essential for T cell recognition. HLA-(A2, A24, A31 and A11) were found restricted to the CD8-epitopes. The most prevalent precore mutation is G1896A and basal core promoter mutations are A1762T and G1764A.

Conclusions:
Most amino acid substitutions involved the HLA-restricted CTL, T helper and B cell epitopes, irrespective of HBV genotype/subtype. Specific precore/basal core promoter mutants and T cell epitopes were found which may affect the severity of the liver disease within the local population.

Key Words: HBV core genetic diversity; HLA-restricted HBcAg T-cell epitopes; Viral persistence
Funding Agency: Supported by Research Administration project grants # YM 02/03, Kuwait

Microbiology and Immunology
Category: Clinical

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Hematological parameters differentiate malaria from nonmalarious in acute febrile illness

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Introduction:
Malaria is a major health problem in the tropics with 300 – 500 million cases of malaria reported annually. In malaria patients a prompt and accurate diagnosis is the key to effective disease management. Malaria is considered as the main differential diagnosis of acute febrile illness in the tropics and change of various hematological parameters has been observed in patients with malaria. The aim was to ascertain which hematological parameters increase the probability of malaria in patients with acute febrile illnesses.

Methods:
All the patients with fever were included in the study. The hematological parameters like, white blood cells (WBC), hemoglobin (Hgb), lymphocytes, Neutrophils, hematocrit (HCV), red blood cells (RBC), with red blood cell indices like, (MCV, MCH, MCHC, RDW), and platelet counts were determined by using automated coulter counter. Giemsa stained peripheral blood smear was taken as gold standard for the diagnosis of malarial.

Results:
A total of 250 patients were included in the study and 100 (40%) had a positive blood smear for malarial parasite. *Plasmodium falciaprum* was identified in 30 (30%), *P. vivax* in 62 (62%) and P. falciaprum and *P. vivax* in 8 (8%) patients. The mean values of WBCs, RBCs, lymphocyte and platelet counts were significantly lower for the infected groups than for the uninfected groups, both in P. falciaprum and P. vivax. Patients with P. falciparum had less than 40, 000/mm^3 platelet counts whereas in normal patients it is more than 150,000/mm^3.

Conclusions:
The finding shows that the presence of thrombocytopenia and decrease in WBCs and hemoglobin in malaria patient with acute febrile illness increases the probability of malarial infection.

Key Words: Hematological; Malaria; Thrombocytopenia
Funding Agency: Ministry of Health, Kuwait

Microbiology and Immunology
Category: Graduate (MSc: Basic Sciences)

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Antifungal susceptibility profile of bloodstream isolates of Candida parapsilosis from Kuwait: Evidence of caspofungin resistance

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Introduction:
Candida parapsilosis is the second most important nosocomial yeast pathogen in Kuwait. The aim of this study was to determine antifungal susceptibility profile of bloodstream isolates of C. parapsilosis.

Methods:
All the *C. parapsilosis* isolates were tested for purity and identified by Vitek2 yeast identification system and by semi-nested PCR amplification of rDNA. Minimum inhibitory concentrations (MICs) were determined by Etest using RPMI 1640 medium, supplemented with 1.5% agar and 2% glucose and buffered to pH 7 with MOPS in accordance with NCCLS M27-A method. An inoculum suspension adjusted to the turbidity of 0.5 McFarland standards was used for inoculation and plates were incubated at 35^{o}C and read at 48 h according to manufacturer's guidelines. The following antifungal agents were tested: amphotericin B (AP), fluconazole (FL), voriconazole (VO), 5-Flucytosine (FC), and caspofungin (CS). The Clinical and Laboratory Standard Institute breakpoints for resistance are: FL ≥64 µg/ml, VO ≥4 µg/ml, and FC ≥32 µg/ml.

Results:
The MIC ranges and MIC90 values of the test isolates were as follows: AP 0.064-1 and 0.5 µg/ml, for VO <0.002-1 and 0.047µg/ml, for FL 0.047≥256 and 1 µg/ml, for FC 0.023≥32 and 0.125 µg/ml and for CS 0.125-4 and1.5 µg/ml, respectively. All the isolates were susceptible to AP and VO. Based on CLSI susceptibility breakpoints criteria, only 2 (1.8%) isolates were resistant to Fl, and 1 (0.9%) to FC. Six (5.3%) isolates demonstrated MIC values of ≥2 µg/ml against CS and were considered as resistant.

Conclusions:
Antifungal resistance among bloodstream isolates of *C. parapsilosis* against VO, FL, AP, and FC is uncommon. However, about 5% isolates of *C. parapsilosis* in Kuwait were found to be intrinsically resistant to caspofungin.

Key Words: Candida parapsilosis; Antifungal agents; Resistance
Funding Agency: Kuwait University Research Grant # YM 04/06

Microbiology and Immunology
Category: Clinical

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In vitro activity of tigecycline against aerobic Gram-positive, Gram-negative and anaerobic bacteria in a tertiary-care hospital

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Introduction:
Tigecyclin, a glycylcycline, has demonstrated in vitro and in vivo activity against a broad spectrum of bacterial pathogens. Objectives: To evaluate the antimicrobial activity of tigecycline against both aerobic (Gram-poistive and -negative) and anaerobic bacteria isolated from both community as well as healthcare-related infections.

Methods:
A total of 251 bacterial isolates (79 Gram-positive, 146 Gram-negative and 26 anaerobes) from various clinical specimens were included in the survey. Antimicrobial susceptibility testing of the isolates against tigecyclin and comperable antibiotics was performed using E test. Extended-spectrum Beta lactamases (ESBL) in Enterobacteriacae were detected using the same.

Results:
The MIC50 and MIC90 of all Gram-negative bacteria, excluding Pseudomonas aeroginosa and Proteus speices, were 0.5 and 2ug/l, respectively. ESBL production in Enterobacteriacae was 27% with 77% susceptibility to tigecycline. Percentage susceptibility of tigecyclin to all the 48 staphylococci tested including MRSA, all the 31 streptococci tested, except for 3 isolates of Enterococcus fecalis, and all anaerobes showed 100% susceptibility.

Conclusions:
Tigecycline is a new and effective antibacterial agent that can be used as a broad spectrum cover for a variety of infections including those due to drug resistant bacteria.

Key Words: Tigecycline; Antimicrobial susceptibility; Broad spectrum
Funding Agency: Wyeth Pharmaceuticals

Microbiology and Immunology
Category: Basic Sciences

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Comparative evaluation of Aspergillus terreus DNA and galactomannan in serum and bronchoalveolar lavage of intravenously infected mice

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Introduction:
Invasive *aspergillosis* is a growing problem in immunocompromised individuals and is associated with high mortality. Although Aspergillus fumigatus is the principal etiologic agent, infections caused by Aspergillus terreus have also increased recently. Since A. terreus is often resistant to amphotericin B, an early diagnosis is imperative for better prognosis. The aim of this study was to develop a sensitive and specific diagnostic protocol of invasive aspergillosis by detecting A. terreus-specific DNA in serum and bronchoalveolar lavage (BAL) specimens of intravenously infected mice and to compare the results with galactomannan (GM) levels.

Methods:
Sixty immunosuppressed BALB/c mice were infected intravenously with 1 X 106 conidia of A. terreus. The mice were sacrificed on day 1, 3, 5, 7 and 9 post-infection in groups of twelve each and their BAL, blood, and lungs were cultured. The A. terreus-specific DNA and GM in serum and BAL were detected by nested PCR (nPCR) and Platelia Aspergillus (BioRad, Marnes-la-Coquette, France), respectively.

Results:
The nPCR developed with primers derived from internally transcribed spacer (ITS)-1 and ITS-2 regions of rDNA was specific for A. terreus as genomic DNA from other Aspergillus species or other fungi was not amplified. The lung homogenates of all the infected mice yielded A. terreus in culture, while the blood and BAL specimens were uniformly negative. The % positivity of serum samples for GM and nPCR were 78% and 73%, respectively. In contrast, among BAL samples, 71% were positive for GM and 81% for A. terreus- specific DNA. The combined detection of A. terreus DNA and/or GM enhanced the positivity to 95% in serum and 98% in BAL.

Conclusions:
The data suggest that GM and A. terreus DNA are easily detected in both, serum and BAL, during the entire course of infection and their combined detection could be useful in the early diagnosis of invasive aspergillosis.

Key Words: Aspergillus terreus; Nested PCR; Galactomannan
Funding Agency: Kuwait University Grant # MI04/02

Microbiology and Immunology
Category: Clinical

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Emergence of isolates of Salmonella spp with reduced susceptibility to ciprofloxacin in Kuwait and the United Arab Emirates: of potential clinical problem?

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Introduction:
Kuwait and UAE are of worldwide significance in the context of global epidemiology of antimicrobial resistance because of a large expatriate population of workers from different parts of the world. Our main objective was to evaluate the antimicrobial susceptibility of clinical isolates of *Salmonella spp*. in these countries over a 2-year period and determine the extent of resistance problem.

Methods:
A total of 410 *Salmonella spp* isolated from symptomatic patients in various hospitals in Kuwait and UAE, were studied. The problem of drug resistance was investigated by determining the antimicrobial susceptibility of 410 Salmonella spp. from both countries by the E-test method. Results were analyzed according to the CLSI interpretative criteria. Reduced susceptibility to ciproflaxicin was determined in accordance with published data.

Results:
The MIC_{90}s of amikacin, cefotaxime, ceftriaxone and ciprofloxacin were 1.9, 0.47, 0.47, and 0.14µg/ml, respectively (Kuwait isolates), and 2.5, 0.22, 0.22, and 0.056µg/ml, respectively (UAE). Resistance rates among Kuwait and UAE isolates to ampicillin were 25.1% and 15.5%, cefotaxime/ceftriaxone 1.6% and 1.6%, ciprofloxacin 1.2% and 0.8%, chloramphenicol 5.6% and 5.7%, and trimethoprim 25.5% and 7.4%, respectively. In Kuwait and UAE, 14.2% and 7.3% of the *non-typhoidal Salmonella*, respectively, and 44% of S. Typhi and 46.7% S. Paratyphi demonstrated reduced susceptibility (MIC; 0.125-0.5µg/ml) to ciprofloxacin.

Conclusions:
A large number of *Salmonella spp*. isolates were resistant to the first-line antibiotics, many of which were multi-drug resistant. High proportions were also with reduced quinolone susceptibility, a phenomenon that appears to be spreading rapidly throughout the world.

Key Words: Salmonella spp; Susceptibility; Kuwait and UAE
Funding Agency: Kuwait University Research Administration: Grant # CM01/04

Microbiology and Immunology
Category: Clinical

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Prevalence of CTX-M type ESBL-producing Salmonella spp. in Kuwait and UAE

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Introduction:
Cefotaximases (CTX-M) are a rapidly spreading class A â-lactamase with high prevalence among Escherichia coli and *Klebsiella spp* in Kuwait. In order to assess the current presence of CTX-M-producing *Salmonella spp*. in our countries, clinical human isolates were screened for the presence of ESBL and bla $_{CTX-M}$ genes.

Methods:
Non-duplicate clinical isolates (284 from Kuwait and 123 from UAE) were tested for their susceptibility to ampicillin and the cephalosporins as well as for ESBL production using the E test methods. Confirmation of the presence of bla $_{CTX-M}$ beta-lactamase gene was performed by PCR with CTX-M universal F and R primers. The PCR products were sequenced using Bigdye Terminator Cycle Sequencing Kit version 3.1. Typing of the CTX-M positive strains was performed by pulsed field gel electropheresis (PFGE).

Results:
Overall, 25% and 1.6% each were resistant to ampicillin and cefotaxime/ceftriaxone, respectively. Of the 407 isolates studied, 69 (17%) were ESBL-producers. Ten (14.5%) of these were CTX-M-producers; 9 isolates from Kuwait, prevalence of 3.2% and one, prevalence of 0.8%, from UAE. Analysis of the DNA sequences showed all the 10 isolates to be CTX-M-15-producers. All strains carried ISEcpIB gene. Clonal relatedness of the 10 strains showed that 4 of the 9 Kuwaiti strains were genetically related but the other 5 were of diverse origin.

Conclusions:
This study reports CTX-M-15-producing Salmonella isolates and the presence of bla $_{CTX-M-15}$ in Salmonella Typhi from Kuwait and UAE for the first time.The finding is worrying as the genes are found in association with the ISEcpIB gene, which may easily facilitate their spread.

Key Words: Prevalence; CTX-M ESBL; Salmonella spp
Funding Agency: Kuwait University Research Administration: Grant # CM01/04

Microbiology and Immunology
Category: Clinical

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Time-related Study of Characteristics of Staphylococcus spp. Colonizing Neonates in a Neonatal Intensive Care Unit

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Introduction:
Staphylococcus spp. (staph), especially coagulase-negative staphylococcus, is the most common organism isolated from blood cultures in neonates. The objective of this study was to examine the surface colonization of neonates with staph at the time of admission to neonatal intensive care unit (NICU), determine their phenotypic and genotypic characteristics, changes observed in the initial colonizing strains during a period of ≥ 4 weeks and impact of such observation on selection of empirical therapy in neonates with clinical suspicion of late-onset septicemia.

Methods:
Specimens were obtained from the axilla, groin and nose of 17 newborns on the day of admission to NICU and weekly thereafter and cultured on blood agar. The neonates under study received ampicillin plus gentamicin after collection of the first set of specimens. Isolates were identified by API (BioMerieux, France) and antimicrobial susceptibility was performed by Kirby-Bauer method using 20 antimicrobial agents. Pulsed-field gel electrophoresis (PFGE) was performed on all isolates to determine their genetic stability.

Results:
A total of 201 staph isolates, which included S.epidermidis (155), S.aureus (19), S.saprophyticus (10), S.scurri (6), S.haemolyticus (4), S.hominis 3, S.simulans 2, S.warneri 1, and S.capitis 1 were identified. The initial isolate was S.epidermidis in 83.2 % cases and continued to colonize ≥ 1 site for ≥ 4 weeks in 35.3 % neonates. Replacement with 1, 2, 3-4 new spp. from ≥ 1 site was observed by the fourth week in 29.4 %, 23.5 %, and 11.8 % cases, respectively. Wide variation in PFGE and antimicrobial resistance patterns was observed in strains isolated each week. Overall resistance to penicillin, methicillin and gentamicin was 91%, 86.5% and 82%, respectively.

Conclusions:
Initial skin surveillance cultures done in neonates may not be helpful in guiding selection of antimicrobial agents, should septicemia occur in the second week or beyond after admission to the NICU.

Key Words: Staphylococcus; Colonization; Neonates
Funding Agency: None

Microbiology and Immunology
Category: Clinical

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Presence of the globally emerging rotavirus genotype, G9 P8 in children in Kuwait

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Introduction:
Group A rotavirus (RV) is the most significant cause of dehydrating diarrhea among 5 years old or younger children worldwide. Within the group there are different sero/genotypes of which G1-G4 and the emerging G9 are the most important ones. They are usually associated with genotype P8. Knowing the distribution of RV sero/genotypes in a country is important for the introduction of RV vaccine. The aims of this study were to: (a) determine the role RV in the causation of diarrhea and (b) identify genotypes present in the country.

Methods:
Stool samples from 347 children (<5 years old) admitted with severe diarrhea in Kuwaiti hospitals were first tested by ELISA for the presence of RV. Positive samples were than processed for G and P typing using RT-PCRs established in the Virology Unit.

Results:
Of the 347 stool samples tested, 123 (35%) were positive in RV-ELISA and 118 (90%) of them could be genotyped. The majority of the strains, 73 (62%) were found to be genotype G1. Genotypes G2, G3, G4 could be detected in 13%, 2.5% and 5%, respectively. The globally emerging genotype G9 was present in 12% of the strains. Among the P types, P8 was the most frequent across all G types.

Conclusions:
The fact that 35% of children with diarrhea suffered from RV infection underlines the importance of RV in Kuwait. Although the majority of severe cases were caused by genotype G1, other types including the globally emerging G9 were also present. Since there is a temporal variation in distribution of sero/genotypes, long-term laboratory surveillance is necessary.

Key Words: Rotavirus diarrhea; Genotypes; Vaccine
Funding Agency: Office of the Vice Rector for Research, Grant #. MK 01/04,

Microbiology and Immunology
Category: Basic Sciences

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Detection of Fusarium oxysporum DNA and (1-3)-beta-D-Glucan in serum and bronchoalveolar lavage specimens of experimentally infected mice

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Introduction:
The diagnosis of invasive *Fusarium* infections is difficult due to non-specific signs and symptoms and similarity in tissue morphology with Aspergillus species. In this study a sensitive diagnostic protocol based on detection of Fusarium oxysporum DNA by nested (n) PCR and (1-3)-beta-D-Glucan (BDG) in serum and bronchoalveolar lavage (BAL) samples obtained from experimentally infected mice was developed.

Methods:
Sixty immunosuppressed mice were infected intravenously with 107 *F. oxysporum* conidia/mouse. Six mice were sacrificed every day post-infection. Blood was used for culture and for obtaining serum. The lung homogenate was used for culture and for direct microscopy. The genomic DNA from the reference strains of *F. oxysporum* and 9 other fungi was isolated and used as template for nPCR specificity. The species-specific primers were derived from the internally transcribed spacer (ITS)-1 and ITS-2 regions of rDNA. The DNA from serum and BAL specimens was extracted using standard procedures. The PCR amplicons were detected by agarose gel electrophoresis. BDG was detected by Fungitell (Cape Cod Inc.).

Results:
The lung homogenates of all the infected animals yielded *F. oxysporum* in culture. The fungus was also discernible in KOH-calcofluor mount of 40 (67%) of the animals. The nPCR was specific for *F. oxysporum* and detected nearly 440 fg of Fusarium DNA which is roughly equivalent to 10 genome copies. BDG was detected in 55/60 (92%) and 9/60 (15%) of serum and BAL samples, respectively. However, *F. oxysporum* DNA was detected in 47/60 (78%) and 59/60 (98%), respectively.

Conclusions:
A sensitive and species-specific nPCR assay has been developed for the detection of *F. oxysporum* DNA in serum and BAL samples of experimentally-infected mice. The data from experimental Fusarium infection suggest that combined detection of *F. oxysporum* DNA and BDG may help in early diagnosis of invasive fusariosis.

Key Words: Fusarium oxysporum; (1-3)-beta-D-glucan; Nested PCR
Funding Agency: Kuwait University Grant # MI 04/02

Microbiology and Immunology
Category: Graduate (PhD: Basic Sciences)

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DNA vaccines constructed to express Mycobacterium tuberculosis-specific antigens induce protective immune responses

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Introduction:
Tuberculosis (TB) is a major local, regional and global infectious disease problem with 8-10 million new cases and 2-3 million deaths each year. Immunization with BCG, the currently available vaccine against TB, compromises the use of tuberculin test for diagnostic and epidemiological purposes due to antigenic crossreactivity of BCG with *M. tuberculosis*. In addition, being a live vaccine capable of causing disease by itself, especially in immuno-compromised subjects, BCG cannot be used in all groups of people. Thus, there is an urgent need to develop *M. tuberculosis*-specific and safer vaccines against TB. In previous studies, we have identified RD1 ORF3, ORF5, ORF6 and ORF7 as *M. tuberculosis*-specific antigens deleted in BCG. The aim of this study was to construct DNA vaccines based on these antigens and evaluate them for induction of protective immune responses in mice.

Methods:
DNA corresponding to RD1 ORF3, ORF5, ORF6, ORF7 and RD903 genes were cloned into pGEMT-Easy vector and sub-cloned into DNA vaccine vectors pUMVC6 and pUMVC7. The identity of each recombinant plasmid construct was confirmed by restriction digestion and DNA sequencing. The recombinant and parent plasmids were purified in large quantities and used to immunize BALB/c mice (6-8 weeks old, 12 groups with 5 mice in each group). After three weeks of immunization, mice were euthanized, spleens removed and spleen cells from each mouse were tested for antigen-induced proliferation with antigens of *M. tuberculosis*, BCG, pure proteins of each ORF and synthetic peptides of RD1 ORF3. IFN-gamma responses were evaluated with synthetic peptides of ORF3.

Results:
A total of 10 recombinant DNA vaccine candidates, corresponding to the five antigens, were successfully constructed in pUMVC6 and pUMVC7. When tested for induction of antigen-specific and protective immune responses by immunization, antigen-specific proliferation responses were observed for a given antigen only with spleen cells of mice immunized with the homologous recombinant DNA vaccine. The mice immunized with the parent plasmids did not show positive immune responses to any of the ORF antigens. Testing with peptides of RD1 ORF3 in antigen-induced proliferation and IFN-gamma assays showed that a broad population of protective T cells recognizing various epitopes was induced in mice immunized with ORF3 DNA vaccine.

Conclusions:
DNA vaccines with *M. tuberculosis*-specific antigens induce antigen-specific but broad immune response to various epitopes. The ability of the DNA vaccines to elicit protective immune responses makes them an attractive weapon as a safer vaccine against TB.

Key Words: Tuberculosis; DNA vaccines; Protective immunity
Funding Agency: Research Administration grant # YM01/03 and the College of Graduate studies

Microbiology and Immunology
Category: Clinical

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Teicoplanin resistant coagulase negative staphylococci causing line associated bacteremia in immunocompromized patients in a Kuwait general hospital

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Introduction:
To report three cases of line associated bacteremia caused by teicoplanin resistant coagulase negative staphylococci from immunocompromized patients.

Methods:
Three coagulas-negative staphylococci (CNS) were isolated from blood cultures of patients with central lines and characterized by cultural characteristics, Gram stain, tube coagulase, catalase test and biochemical reactions (using Vitek GP card) and typed by pulsed field gel electrophoresis (PFGE). Teicoplanin susceptibility was determined by Etest. Resistance to other agents was determined by disk diffusion. Data on teicoplanin consumption was reviewed.

Results:
The three CNS isolates were identified as Staphylococcus epidermidis. They were resistant to teicoplanin (MIC: 24, 24, 48 mg/L). They had vancomycin MIC of 2, 3, 4mg/L. They were also resistant to methicillin. The isolates had different PFGE patterns which suggests that the were not related. An average of 40000 mg of teicoplanin were consumed during the year 2005.

Conclusions:
The present report reveals the emergence of teicoplanin resistance in CNS in our hospital. The major cause of this may be the increased use of teicoplanin in the hospital. A larger study is required to determine the extent of glycopeptide resistance in CNS isolated in our country.

Key Words: Teicoplanin; Staphylococci; Bacteremia
Funding Agency: None

Microbiology and Immunology
Category: Clinical

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Parvovirus B19 DNA in the Blood is an Important Marker of Infection in Immunocompromised Patients

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Introduction:
Diagnosis of uncomplicated cases of acute parvovirus B19 infection (fifth disease or arthropathy) is usually clinically based and can be accomplished by the detection of specific IgM antibodies, except in immunocompromised patients, who are prone to persistent infection and who may generate B19-specific IgM antibodies less reliably. Likewise, specific IgG is not a reliable marker for discriminating a past infection from chronic persistent infection. In the present study, we introduced a sensitive PCR assay for the detection of parvovirus B19 DNA in immunocompromised patients.

Methods:
Immunocompromized patients tested negative for CMV antigenaemia were grouped on the basis of their B19-specific serostatus irrespective of their disease status: IgG and IgM negative (n=32), IgG positive and IgM negative (n=25). The sera had been tested for B19-specific IgM and IgG antibodies by an immunofluorescence assay. The presence of B19 DNA in serum samples was investigated by using nested PCR.

Results:
Six out of 32 patients negative for B19 IgG and IgM were positive for B19 DNA in their blood, even though they had no symptoms suggesting B19 infection. Seven out of 25 patients positive for B19 IgG and negative for B19 IgM, were also positive for B19 DNA in their blood; of those patients, four had no symptoms and three patients only had fever.

Conclusions:
The detection of parvovirus B19 DNA by nested PCR was more sensitive than serology. Our results suggest that the detection of B19 infection by PCR in immunocompromized patients may establish a definite diagnosis and assist therapeutic decision-making.

Key Words: Parvovirus B19; Nested PCR; Immunocompromized
Funding Agency: None

Microbiology and Immunology
Category: Clinical

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Characterisation of extended spectrum beta-lactamases identified by the Vitek system and their subsequent comparison with other commercial ESBL testing systems in strains isolated from Kuwait and the United Kingdom.

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Introduction:
This study was performed to assess the behaviour of ESBLs in clinical strains detected by this system in comparison with two other commercial ESBL detection methods. Screening and confirmation of the test were done following(NCCLS)rules

Methods:
Two hundred and fifty-one unique patient isolates (single isolates from different individuals)of *Klebsiella pneumoniae*(123)and *Escherichia coli*(114), *Klebsiella oxytoca*(7), *Enterobacter cloacae*(5), *Citrobactaer freundii2* flagged as(ESBL)positive by the Vitek system (GNS-526 card), were collected.These strains were isolated from a variety of clinical specimens (swabs, urine and sputum) submitted to the clinical bacteriology laboratories of the Royal Infirmary of Edinburgh, Hairmyers Hospital in Glasgow, Amiri and Farwania Hospital in Kuwait.

Results:
Of the 101 RIE strains tested, 15 E.coli were found to be ESBL-negative by Etest ESBL strips.On re-testing the 15 E.coli with the Vitek GNS-532 card, 14 of these were subsequently found to be ESBL negative despite originally flagging as ESBL positive. The remaining 236 ESBL producing strains were also subjected to the double disc diffusion(DDD)technique for the detection of ESBLs. Of these, two were falsely negative by Etest ESBL test strips and 38 were false negatives by the double disc diffusion method. The Etest false negative ESBL producing strains of K. pneumoniae were positive by DDD.

Conclusions:
The Vitek method was the least demanding method to perform as it is an integral part of the routine susceptibility test card.Etest strips were reliable but the most expensive of all techniques used.The DDD test, while relatively inexpensive was technically subjective and, in our hands, seven of the ESBL positive strains that were confirmed by the other two techniques, were not detected. Despite the false positive ESBL producing *E. coli*, the Vitek susceptibility card with its integral ESBL test offers the clinical laboratory a valuable and quick option to screen for ESBL producing Klebsiella spp. and E.coli as part of the routine laboratory methodology.

Key Words: ESBL; Vitek system; E-test
Funding Agency: None

Microbiology and Immunology
Category: Basic Sciences

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Lymphocyte profiles and serum antibodies to neurofilaments in pre-eclamptic Kuwaiti women

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Introduction:
It is hypothesized that the pathogenesis of preeclampsia (PE) is accompanied by alterations in immunoregulation that may affect normal turnover of peripheral neurons and release of cytoskeletal components (principally neurofilaments). Since this is expected to alter serum levels of antibodies to neurofilament epitopes, the possibility exists to utilize this parameter as a biomarker for intensity of the disorder.

Methods:
Peripheral blood of 23 pregnant women in the third trimester; 13 with PE, 10 healthy pregnant women and 10 non-pregnant controls were evaluated by flow cytometry for major lymphocyte populations and for antibodies to neuronal cytoskeletal elements by Western blot analysis.

Results:
The percentages of CD3+CD16+CD56+, CD4+CD25+, CD8+CD25+, and CD8+HLA-DR populations were significantly increased in normal pregnancy and PE compared to non-pregnant women ($p<0.01$), dramatic increase of CD4+CD54+ but not CD4+CD45RA populations was observed in PE. Concentrations of autoantibodies for the 200-kDa neurofilament (NFH) was decreased but for the 160-kDa (NFM) was significantly increased in PE. Autoantibodies against the 70-kDa neurofilament (NFL) was significantly decreased in normal pregnancy compared to non-pregnant women ($p<0.05$) and further decreased in PE ($p<0.01$).

Conclusions:
The alteration in anti-neurofilament concentration in PE taken in context with shifts in lymphocyte subpopulation frequencies has enormous potential clinical implication of utility as a possible biomarker. More research evaluation is however advocated.

Key Words: Pre-eclampsia; Cytoskeletal proteins; Lymphocytes
Funding Agency: None

Microbiology and Immunology
Category: Clinical

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HPA-1a Typing Can Save The Neonates Life

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Introduction:
Neonatal Allo-immune thrombocytopenia (NAITP) is a case where fetal or neonatal thrombocytopenia results from fetomaternal alloantigen incompatibility and placental transfer of (IgG) antibodies to fetus.This will increase the tendency of bleeding, as a result, intracranial hemorrhage occurs. The most common antigen associated with NAITP is the HPA-1a, reported in up to 83% of the cases. HPA-5b antigen is also responsible for 20% of NAITP cases.

Methods:
Invistigation were done in platelet serology laboratory using ELISA methods.

Results :
Typical results yields when testing the mother and father samples as follows :
Mother HPA-1a typing is negative.
Father HPA-1a typing is positive.
Fetus HPA-1a typing is positive.
Antibody detection test show HPA-1a antiplatelets antibodies positive in mother plasma.X-matching the mother plasma with the father platelets show incompatibility in GP IIb/IIIa.Intrauterine transfusion with HPA-1a negative platelets had saved the newborn`s life.

Conclusion :
Any neonates with suspected NAITP who is bleeding or has a platelet count of $< 30x10^9$ / L should be transfused with compatible platelets to minimize the risk of intracranial hemorrhage.

Key Words: HPA-1a; ELISA; x-matching
Funding Agency: None

Microbiology and Immunology
Category: Basic Sciences

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Confirmation of in vivo expression and identification of major antigenic regions of RD1-ORF14 protein of Mycobacterium tuberculosis recognized by human antibodies

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Introduction:
We have previously shown that a putative protein of *M. tuberculosis* (RD1-ORF14 protein) was recognized by antibodies present in sera of tuberculosis (TB) patients. The RD1-ORF14 protein is not predicted in the published genome sequence of *M. tuberculosis*, but was predicted by us using GeneMark software. The aim of this study was to confirm its in vivo expression and identify the major antigenic regions of the protein by testing sera of TB patients with overlapping synthetic peptides.

Methods:
To cover the sequence of ORF14 protein, a total of 17 synthetic peptides (25-mers and overlapping with neighboring peptides by 10 amino acids) were synthesized by fmoc chemistry and obtained commercially. *M. tuberculosis* cell wall antigens and three peptides of two *M. tuberculosis* proteins (one peptide of Rv3017c and two peptides for RV3905, previously shown to have strong antibody reactivity) were used as positive controls. A peptide of Rv3017c (previously shown to lack antibody reactivity) was used as a negative control. The antigens/peptides were used to coat wells of enzyme-linked immunosorbent assay (ELISA) plates at 1 µgram per ml. The wells were blocked and incubated with sera (diluted 1/100) from TB patients (n=21). The unbound antibodies were washed and the bound antibodies were detected with alkaline phosphatase-conjugated secondary antibodies. After the addition of substrate, the optical density (OD) was read with an ELISA reader at 405 nm. The OD405 values in the presence of a peptide and serum were compared with the serum alone, and were considered positive if the ratio exceeded 1.5.

Results:
All of the sera reacted with cell wall antigens and most of the sera (57 to 100%) reacted with the positive control peptides but None reacted with the negative control peptide. Among the peptides of ORF14, peptides P1 (aa 1-25), P5 (aa61-85), P6 (76-100), P9 (aa121-145) and P10 (aa 136-160) showed antibody reactivity with 48%, 86%, 76%, 71% and 86% of the tested sera, respectively. The reactivity to other peptides of ORF14 was in the range of 0% (P2, P3, P4 and P12) to <5% (P11, P13, P14, P15, P16 and P17).

Conclusions:
The results confirm that RD1-ORF14 protein is expressed in vivo and contains three major antigenic regions (aa 1-25, aa 61-100 and aa 121-160) for antibody recognition.

Key Words: RD1-ORF14 protein; In vivo expression; Antigenic regions
Funding Agency: Kuwait University Research Administration grant # MI 02/02

Microbiology and Immunology
Category: Basic Sciences

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Whole blood infection as a model to determine protective versus non-protective immunity against Mycobacterium tuberculosis in humans

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Introduction:
The efficient development of new vaccines and drugs against tuberculosis is hampered due to to the non-availaibilty of in vitro systems to evaluate the efficacy of potential vaccines and drugs in humans. The clinical trials to determine the efficacy of new candidate vaccines and drugs in humans are extremly complex with time and budget constrains. The aim of the present study was to establish a reproducible in vitro system that can be used for speedy screening of new vaccines and drugs against *M. tuberculosis*, and to study the possible growth inhibitory or enhancing effect of various cellular components and cytokines.

Methods:
Venous blood was collected from healthy humans (n=23) in tubes with anti-coagulants. The whole blood, plasma and purified adherent cells/macrophages were infected with a luciferase reporter construct of *M. tuberculosis*. The infected cultures were incubated at 370C in an atmosphere of 5% CO2 and 95% air. After 24 to 96 h of incubation, the cultures were evaluated for the growth of *M. tuberculosis* by quantitation of luciferase activity (relative light unit [RLU]/ml) using a chemiluminescence assay. The culture supernatants were collected after 48 and96 h of blood culture to determine the concentrations of secreted cytokines IFN-gamma, TNF-alpha, IL-10 and IL-12.

Results:
M. tuberculosis did not grow in cell free plasma and the growth in purified macrophages was not reproducible. However, the growth of *M. tuberculosis* in whole blood was reproducibly determined by estimating the luciferase activity. With whole blood from most donors, the luciferase activity of *M. tuberculosis* was significantly inhibited by 96 h of culture, which suggested the presence of mycobacterial growth inhibitory component(s), whereas in a minority of subjects enhanced growth was observed by the end of 96 h of culture period. The concentrations of IFN-gamma and IL-12 were similar in both the groups, whereas elevated concentrations of TNF-alpha and IL-10 were detected in the supernatants of cultures with enhanced growth.

Conclusions:
Our work demonstrates the use of whole blood infection model for early (in 96 h) assessment of *M. tuberculosis* growth in humans. In addition, it suggests the growth inhibitory and protective effect of IFN-gamma and IL-12, and identifies TNF-alpha and IL-10 as cytokines with growth enhancing effect. The work further suggests that the established system may be used as a first step to evaluate candidate anti-TB vaccines and drugs for their efficacy before embarking on complex, time-consuming (several years) and expensive (millions of KDs/USDs) field trials in humans.

Key Words: Whole blood infection; M. tuberculosis; Growth enhancement/inhibition
Funding Agency: Supported by by KFAS grant #. 2002-1302-04

Microbiology and Immunology
Category: Clinical

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Hepatic cystic echinococcosis and amebic abscess of the liver: a diagnostic dilemma in the Middle East?

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Introduction:
Hepatic cystic echinococcosis (CE) and *amebic liver abscess* (ALA) are both prevalent in Kuwait, the former being endemic while the latter is imported primarily from the Indian sub-continent. Following a clinical examination, imaging studies, usually an ultrasound (US) or computerized tomography (CT), are requested. Both modalities are excellent at identifying space-occupying lesions but there are limitations in establishing their etiology. We explore the clinical and laboratory problems related to the simultaneous request for serodiagnoses for both CE and ALA in the same patient.

Methods:
We first describe 4 patients in whom both tests were requested simultaneously, emphasizing the difficulties and pitfalls in diagnosis. We then elucidate the dilemma faced by physicians requesting both hepatic CE and ALA serodiagnoses concurrently and in substantial numbers.

Results:
Of 232 samples for concurrent CE and ALA serology, 115 (49.5%) were from Arabs. Of the 23 (9.91%) positive for hepatic echinococcosis, 19 (82.6%) were from Arabs but only 3 (13.04%) from the Indian subcontinent ($P < 0.0001$). In contrast 105 (45%) samples for ALA from non-Arabs, the titer was significant in 86 (37%) patients, 54 (62.1%) from the Indian subcontinent and 26 (30.23%) Arabs ($P < 0.0001$).Discussion: Thus apart from the clinical presentations, the origin of the patients is a significant indicator of the possible etiology of the space-occupying lesion. We highlight attendant problems such requests create in terms of the level of the clinical acumen, laboratory time, manpower and the costs involved. We also show that apart from CE and ALA, other clinical conditions give rise to similar hepatic lesions. Bacterial and fungal abscesses and hepatomas were identified and perhaps such a list of differential diagnoses is important in endemic areas.

Conclusions:
We suggest guidelines for physicians to deduce a clinical diagnosis before requesting serologies for both CE and ALA.

Key Words: Hepatic cystic echinococcosis; Amebic liver abscess; Serodiagnosis
Funding Agency: # MI 03/03

Microbiology and Immunology
Category: Clinical

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Blood Culture collection: A study of the efficacy of an in-services training program.

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Introduction:
Blood culture is an important tool in the diagnosis and management of sepsis. The method of collection and the number of sets collected from a patient contribute largely to the successful isolation of the pathogen and correct interpretation of the culture results. We attempted to analyze the results of blood cultures of inpatients admitted to Farwaniya hospital over a two year period and the usefulness of a in-services training program for the nursing staff.

Methods:
Data of the blood cultures performed for inpatients in the various departments in Farwaniya hospital during the period January 2005 to December 2006 was analyzed. A single set or a single bottle received was labeled unacceptable, while a minimum of two sets or more was considered adequate. A revised training program in blood culture collection was conducted for the nursing staff in January 2006 and the effects of such a program were studied.

Results:
A total of 13285 sets of blood cultures were received in the department of microbiology during the two year period of which 4653 sets were received in 2005. A 33% increase was noted in the number of sets received in 2006. However, the positivity rate reduced by 32.6% from 586 in 2005 to 395 in 2006. The number of contaminated sets or those determined as unacceptable were 507 and 237 respectively in 2005. After the in-services training program, these reduced to 503 and 214 respectively, but were not statistically significant. However, the percent benefit achieved in 2006 after the training was statistically significant ($p=0.011$) as also was the reduced percent loss ($p=0.020$) compared to 2005.

Conclusions:
Collection of multiple sets of blood culture is an important factor in interpretation of microbiological findings. Periodic training programs in the correct methodology of collection of blood culture help in reducing losses and improve the efficacy of a septic workup.

Key Words: Blood Culture; In-services Training; Benefit
Funding Agency: None

Microbiology and Immunology
Category: Clinical

152

The recently identified human metapneumovirus causes serious acute lower respiratory infections in children in Kuwait

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Introduction:
The human metapneumovirus (hMPV) has been identified in 2001 as a new respiratory pathogen. The virus is a member of the *Paramyxoviridae* and similar to other *paramyxoviruses* in that, it is an enveloped, RNA virus. The viral genome encodes 2 important proteins; the F (fusion) and N (nucleocapsid) which play a role in the pathogenesis of infection. The hMPV was first detected in samples collected from children with respiratory syncytial (RS) virus-like diseases. Data show that the virus is responsible for about 2-10% of respiratory symptoms. The aim of this study was to investigate the role of this virus in the causation of lower respiratory tract infection in children in Kuwait.

Methods:
In this study 52 children aged less than 10 years, who were admitted to Mubarak Al-Kabir hospital with severe lower respiratory symptoms were investigated for hMPV in their respiratory secretions. These children were tested negative for other respiratory viruses including RSV. These respiratory samples were processed for nucleic acid extraction and the viral genome was amplified by an RT-PCR targeting F and N regions of the virus. Samples, in which the amplification resulted in the formation of characteristic bands for both the F (450 bp) and N region (377 bp), were considered positive for hMPV.

Results:
Of the 52 children tested, 7 (13%) were found to be infected with the hMPV. The age of the children was between 1 and 10 years and they presented with severe lower respiratory symptoms like bronchiolitis, respiratory distress and pneumonia.

Conclusions:
These preliminary findings identifies the importance of hMPV as a new etiological agent causing severe lower respiratory infection in Kuwait. A more detailed study is now underway to determine the impact of this virus on the respiratory infections in Kuwait.

Key Words: Respiratory infection; Human metapneumovirus; Detection
Funding Agency: Office of the Vice Rector for Research, Grant # MI 01/04

Molecular Pathology
Category: Clinical

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Metafer4-PV, the optimal flourescence in situ hybridization (FISH) scoring system for her-2/neu amplification in breast carcinomas

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Introduction:
Twenty to thirty percent of breast cancers show Her-2/neu protein expression and are associated with poor prognosis. A very expensive drug, Herceptin (generic name Trastuzumab) has shown great promise by increasing survival time for women with Her-2/neu overexpressed breast carcinomas. FISH offers most accurate, reliable and reproducible results of Her-2/neu assessment. Discordance between immunohistochemistry (IHC) and FISH is mainly observed in tumours that are moderately positive (2+). Further evaluation by FISH is recommended for such cases before instituting therapy. We developed the first FDA approved Metafer4-PV software for scoring Her-2/neu gene amplification.

Methods:
A total of 37 cases from HMJCSS hospital were received with a median age of 52 years ranging from 31-73 years. 73% (27/37) of the cases received were selected as 2+ by IHC. 5µm thick tumour tissue sections mounted on silanized slides were subjected to FISH assay using Vysis Path Vysion Probe containing a mixture of Spectrum Orange labeled Her-2/neu locus and Spectrum Green labeled CEP17 region. Her-2/neu / CEP17 ratios were determined. Cases were categorized as non-amplified, borderline amplified and amplified if the ratios are below 1.8, between 1.8 and 2.2 and above 2.2 respectively.

Results:
65% (24/37) of the cases were non-amplified, 8% (3/37) borderline amplified and 27% (10/37) amplified for Her-2/neu gene using FISH assay. Among 2+ (IHC) cases, 70% (19/27) proved to be non-amplified, 7% (2/27) were borderline amplified and 22% (6/27) were amplified.

Conclusions:
The use of FDA approved Metafer4-PV system is highly recommended for the optimal scoring of Her-2/neu/CEp17 ratio determination, which do not depend on the subjective assessment of the pathologist. Our results caution against the use of immunohistochemistry for detection of Her-2/neu gene abnormalities.

Key Words: Metafer4-PV; Her-2/neu; FISH
Funding Agency: KFAS # 990707, Ministry of Health

Neuropsychiatry
Category: Clinical

154

The impact of depression, disability and family caregiver attitudes on the quality of life of Kuwaiti patients with multiple sclerosis

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Introduction:
Assessment of subjective quality of life (QOL) in routine care of multiple sclerosis patients (MS) could facilitate the detection of psychosocial aspects of disease that may otherwise go unrecognized. The objectives of the study were to (i) compare the QOL ratings of relapsing remitting (RR) and other MS diagnostic groups with those of a general population group and the impression of their family caregivers (FC); and (ii) assess the association of demographic, clinical and FC variables with patients' QOL.

Methods:
Consecutive MS attendees at Ibn Sina Hospital were assessed with the 26 –item WHOQOL Instrument, Beck's Depression Inventory and Expanded Disability Scale. FC rated their impression of patients' QOL and attitudes to patients' illness.

Results:
170 MS patients (60m, 110f) consisted of 145 RR and 25 others, aged 32.4 SD 8.8. RR group had significantly higher QOL domain scores (e.g., general facet=7.1 SD 1.2 Vs 5.0 SD 2.3) and lower depression and disability scores than the others ($P<0.001$). Patients had significantly lower QOL scores than the control group ($P<0.001$). FC impression was significantly correlated with patients' ratings. Depression was the commonest significant covariate of QOL domains. When we controlled for depression and disability scores, differences between the two MS groups became significant for only one (out of 6) QOL domains. Patients who were younger, better educated, employed, felt less sick and with lesser side effects, had higher QOL. The predictors of patients' QOL were disability score (B=-0.46), FC impression (B=0.32) and FC fear of having MS (B=-0.17).

Conclusions:
Attention to disability and depression, as well as caregiver education and patient and caregiver psychosocial support could help to improve patient's QOL. QOL should be part of routine clinical outcome measures

Key Words: Multiple Sclerosis; Depression-disability; Family-quality-of-life
Funding Agency: Biogene Algorithm, USA

Neuroscience
Category: Basic Sciences

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Minocycline modulates CD200 receptor expression in the brain during *Trypanosoma brucei* infection

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Introduction:
Microglia activation during the meningoencephalitic stage of African trypanosomiasis, caused by subspecies of *Trypanosoma brucei* (Tb), contributes to the neuroinflammation of the disease. Recently we have reported that minocycline reduces microglial activation in mice infected with Tb brucei (Masocha et al., 2006). Microglia are constitutively maintained in a quiescent state by neurons through neuronal CD200 and microglial CD200 receptor interactions. Our objective in this project was to study the effect of minocycline on the expression of CD200 and its receptors (CD200R) in the brain during *Trypanosoma brucei* infection.

Methods:
C57BL/6 mice were infected intraperitoneally with 2, 000 -3, 000 Tb brucei parasites. Mice were treated i.p. daily with minocycline or its vehicle (PBS), commencing on the day of parasite inoculation. Mice were sacrificed and brains and spleens sampled for analyses. Gene transcripts of CD200, CD200R1, CD200R2, CD200R3 and CD200R4 were quantified in brains from minocycline-treated and PBS-treated uninfected and infected mice by real time PCR.

Results:
The levels of CD200 mRNA in the brain were not altered significantly by Tb brucei infection or treatment with minocycline. Infection induced an elevation of CD200R4 transcripts in the brain, which was inhibited by minocycline treatment. On the other hand, infection alone did not alter the levels of CD200R1, CD200R2 and CD200R3, however, minocycline showed a tendency to increase the transcripts of CD200R2 and CD200R3 at 20 days post infection.

Conclusions:
Our results suggest that minocycline might inhibit microglia activation through its inhibitory effects on CD200R4 expression. CD200 receptors might have different roles during microglia activation and neuroinflamation. Thus, present possible therapeutic targets to control inflammation in the central nervous system.

Key Words: CD200 receptors; Microglia; Minocycline
Funding Agency: This study was supported by grants from Goljes Foundation; and Stiftelsen

Neuroscience
Category: Graduate (MSc: Basic Sciences)

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Enhanced neuronal activity preconditioning through NMDA receptors delayed kainate-induced degeneration of CA 3 hippocampal neurons

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Introduction:
Intraventricular injection of kainate (KA) causes an acute excitotoxic lesion to hippocampal CA3 region. NMDA was shown to protect neurons through synaptic activation against in vitro cell death inducing treatments. We used in vivo approach to study NMDA preconditioning of KA–induced neurodegeneration.

Methods:
NMDA was injected in the lateral ventricle of anesthetized rats and followed by intraventricular KA (0.15 μg). Following perfusion, brains were sectioned on vibratome and sections were stained with thionin for LM or processed for EM examination. C-Fos immunostaining was used to estimate neuronal activation. Quantitative evaluation of c-Fos-labelled cell densities was complemented by ANOVA with post-hoc analysis of significant differences using SPSS.

Results:
NMDA-activated neurons showed a marked c-Fos cell density in all hippocampal regions as compared to saline-treated controls. KA alone induced an increasing c-Fos reaction with the exception of CA3a sub region, where only few neurons expressed c-Fos. Failure to express c-Fos in CA3a was already apparent by one hour post KA injection. It corresponded to cell degeneration with necrotic and apoptotic signs confirmed by EM examination. On the contrary, c-Fos induced by NMDA injection, which preceded KA by one hour, was still elevated in CA3a at 1 and 2 hrs after KA. The onset of neuronal degeneration was delayed in similar way. However, c-Fos and neurons of CA3a deteriorated by 4 hrs to the same level as those seen after KA alone. Involvement of NMDA receptors was confirmed by complete inhibition of NMDA-induced c-Fos expression with NMDA receptor blocker.

Conclusions:
Delayed disappearance of c-Fos labelling and neurodegeneration in CA3a of NMDA preconditioned and KA-treated rats indicated transient in vivo neuroprotection. Enhancing synaptic activity of neurons in the ischemic or injured brain might be the way to rescue neurons suffering from concomitant excitotoxicity.

Key Words: Kainate excitotoxicity; Hippocampal CA3a neurons; NMDA preconditioning
Funding Agency: College of Graduate Studies Grant to S.Mohammadi (MSc Student)

Obstetrics and Gynecology
Category: Undergraduate

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Risk factors for preterm delivery in Kuwait: A case-control study

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Introduction:
Preterm deliveries account for about 10% of all births and result in 75% of neonatal deaths and the vast majority of neonatal intensive care admissions. This study aimed to compare mothers with preterm and term delivery, and to investigate the risk factors for preterm delivery.

Methods:
64 cases (preterm deliveries) and 128 controls (term deliveries) were recruited from the delivery units of all Kuwait public hospitals. A mother with a live-born delivery before 37 completed weeks' gestation was included as a case. The two consecutive mothers with live-born deliveries between 37 and 41 completed weeks' gestation were taken as controls. Data was obtained by interviewing mothers in postnatal wards, using a specially designed questionnaire that covered socio demographic characteristics, reproductive history, medical history, and current pregnancy conditions.

Results:
Statistical analyses were conducted using SPSS v14.0. A history of prior preterm delivery and abortion was reported more frequently in preterm than term deliveries (p=0.001). After adjusting confounding by a binary regression model, polyhydramnios (adjusted OR 5.57, 95% CI 1.70-18.27), antepartum hemorrhage (3.20, 1.06-63), premature rupture of membranes (2.31, 1.04-5.15) and passive smoking (2.66, 1.20-5.86) were shown to be significant risk factors for preterm delivery.

Conclusions:
This study suggests that pregnancies complicated by polyhydramnios, antepartum hemorrhage, and premature rupture of membranes are at risk to culminate into preterm delivery. Passive smoking was also shown to carry a similar risk. In Kuwait, further research is required to address the multifaceted problem of preterm delivery, and to set the grounds for preventive measures.

Key Words: Preterm delivery; Premature birth; Risk factors
Funding Agency: None

Obstetrics and Gynecology
Category: Basic Sciences

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Hyperglycemia alters Maternal-Fetal Transport Kinetics of Some Essential Trace Elements in Human Placenta In Vitro

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Introduction:
Previous reports from our laboratory had shown that maternal-fetal status of some essential trace elements are altered in diabetic pregnancies. Transport behaviour of esential trace elements such as Cu, Se and Zn was studied in hyperglycemic "diabetic model" placental perfusions, with varying glucose loads, to evaluate role of hyperglycemia per se on their transfer.

Methods:
Human placentae, from uncomplicated pregnancies were collected post-partum. Cu, Se and Zn at twice physiologic concentrations along with antipyrine as reference marker were then injected as a single bolus (100ul) into the maternal arterial circulation of perfused placental lobules and perfusate samples collected from maternal and fetal circulations over a period of 5 minutes. National Culture and Tissue Collection medium, diluted with Earle's buffered salt solution was used as the perfusate. 3 separate perfusion series with glucose loads of 1g/L, 2g/L and 5 g/L in maternal perfusate were done to simulate diabetic state. Concentration of trace elements in perfusate samples was assessed using atomic absorption spectrophotometry while antipryine was assessed colorimetrically.

Results:
Differential transport rates of Cu, Se, Zn and antipyrine in 8 perfusions did not differ significantly (Student's t-test ; $p>0.05$) in euglycemic and hyperglycemic perfusions.TR50 indices of Cu, Zn and Se compared to antipyrine averaged 0.96, 0.95 and 0.96 in euglycemic series while in 2gm glucose perfusion series, the indices averaged 1.01, 0.97and 1.03 respectively. In perfusions with 5 gm/L glucose load, the corresponding TR50 indices averaged 1.00, 1.01 and 0.99 respectively. Transport fraction indices and various pharmacokinetic indices of the 3 trace elements compared to antipyrine showed variable differences. Absorption rate: elimination rate indices of Se and Zn differed significantly (Student's t-test ; $p<0.05$) in hyperglycemic perfusions.

Conclusions:
Our studies show for the first time that transport behaviour of essential trace elements could be altered in hyperglycemic states, with potential harmful effects on fetuses or infants of diabetic mothers.

Funding Agency: None

Obstetrics and Gynecology
Category: Clinical

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Is Vaginal Delivery Becoming Obsolete in Breech Presentation?

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Introduction:
Emerging evidence indicates that increasing caesarean section rate in breech presentation will reduce perinatal mortality and morbidity. The objective of our study was to evaluate the mode of delivery and perinatal outcome in breech presentation.

Methods:
A 6 months pilot study of all patients with singleton breech presentation in labour at Maternity Hospital, Kuwait was undertaken. The past obstetric history was extracted from the obstetric records and the age, parity, gestational age at delivery, antenatal and intrapartum courses of the index pregnancy and the perinatal and maternal outcome were documented. The performance of nulliparous and multiparous patients and preterm and term breech presentation were compared. All the data were analyzed using Fisher exact test/Welch test.

Results:
During the study period, a total of 5, 755 deliveries were recorded at Maternity Hospital and 221 of these were singleton breech presentations, an incidence of 3.84%. 80(36.2%) of the patients were nulliparous and 63.8(141) were multiparous, 53(24%) of these patients were delivered preterm („T36 weeks) and 168 (76%) delivered at term. 73.8% of all the patients were delivered by caesarean section, an incidence which is about three times the mean caesarean section for the Department. The incidence of caesarean section in the nulliparo, (86.2%) was significantly higher than the 66.7% in the multipara, P=0.0014, C.I 1.517-6.485. However, there was no significant difference in the incidence of caesarean section in preterm and term breech presentation, 67.9% vs 76.2%, P=0.2798, C.I 0.336-1.1.303. The Apgar scores at 1/5 min were significantly higher for the term breeches P<0.0001. The perinatal mortality/morbidity was quite low.

Conclusions:
The incidence of breech presentation was 3.84% and the incidence of caesarean section in breech presentation is quite high indicating virtual elimination of vaginal delivery in breech presentation.

Key Words: Breech; Caesarean; Perinatal
Funding Agency: None

Oncology
Category: Clinical

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Nuclear matrix protein 22 (NMP 22) improves the performance characteristics of atypical cytological examination in patients with bladder cancer.

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Introduction:
This prospective study was undertaken to evaluate the diagnostic efficacy of nuclear matrix protein (NMP22) compared to urine cytology in the detection of bladder cancer and also to determine whether indexing atypical cytology to NMP22 could enhance the clinical utility of atypical cytology.

Methods:
In 80 of the 197 patients examined, a urine sample for cytology was available prior to cystoscopy and resectional biopsy. Diagnosis of bladder cancer was confirmed histologically. In 46 of these patients NMP22 was assayed. Cytological detection of bladder cancer was compared with NMP22 detection and correlated with tissue diagnosis.

Results:
In 30 (77%) of the 39 patients with a histologically proven cancer the cytology was positive in 12 and atypical/highly suspicious in 18. In 30 of 41 patients with a benign histology the cytology was normal while the remaining 11 patients (26.8%) had a suspicious (8 cases) or a positive (3 cases) report rendering a sensitivity of 57% and specificity of 91%. NMP22 assay had sensitivity of 78% and specificity of 43%. In 13 of the 16 patients with atypical cytology the NMP22 was positive and correlated with the tissue positivity in 11 cases. Combined NMP22 and cytology had a sensitivity of 80% and specificity of 41%. For those with atypical cytology addition of NMP22 improved the sensitivity from 66% to 84% but specificity declined from 77% to 33%.

Conclusions:
Cytologic examination is useful for screening of patients with bladder cancer. In patients with atypical cytology addition of NMP22 significantly improves sensitivity.

Key Words: Bladder cancer; Urine cytology; NMP22 assay
Funding Agency: This research was supported by Kuwait University Research Grant # MS02/03

Oncology
Category: Clinical

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Bowel complications after Radical Radiotherapy in Cancer Cervix Uteri.

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Introduction:
The aim of this study is to analyze the acute and late bowel complications after treatment with radical radiotherapy.

Methods:
This study is a retrospective analysis of forty-six newly diagnosed patients of invasive cancer uterine cervix treated with radical radiotherapy (conformal external beam radiotherapy + intra-cavitary brachytherapy) between 1995 and 1999. Complications were graded from grade 1 to 4 according to RTOG acute and late radiation morbidity scoring criteria.

Results:
During treatment, 3 patients (6.52%) developed nausea and vomiting. Diarrhoea grade 1 occurred in 11 (23.91%), grade 2 and 3 in 8 patients (17.38%) and rectal bleeding in 1 (2.17%) of the patients. Nine patients (19.56%) developed late bowel toxicity with severe complications occurring in 5 (10.86%). One of these patients (2.17%) developed recto-vaginal fistula and 4 (8.69%) developed intestinal obstruction requiring surgery. Factors such as previous history of abdominal surgery, external radiotherapy dose, total dose to ICRU point A (combined external and intra-cavitary), total point B dose or dose to ICRU rectal reference point did not show significant association with bowel complications. (Dose to ICRU rectal reference point was available in 33/46 i.e. 71.74% of our patients).

Conclusions:
The incidence of acute and late radiation morbidity to the bowel in our study is within acceptable limits when considering conventional treatment modalities. As None of the present calculated dose points correlated with the bowel complications, it is recommended to take into consideration other areas of the bowel in future calculations e.g. parts of the rectum and recto-sigmoid nearest to the radiation sources in brachytherapy. 3D CT assisted planning for intra-cavitary brachytherapy applications and IMRT need to be introduced in the near future.

Key Words: Cancer uterine cervix; Radical radiotherapy; Bowel complication
Funding Agency: None

Oncology
Category: Clinical

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Prognostic factors in cervical carcinoma treated with radiotherapy

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Introduction:
In carcinoma cervix treated with radiotherapy, certain patient characteristics and tumour characteristics affect the course of the disease and survival. The aim of this study is to study these factors and their implication on treatment failure and survival.

Methods:
This study is a retrospective analysis of forty-six newly diagnosed patients of invasive cancer uterine cervix treated with radical radiotherapy between 1995 and 1999. Pre-treatment prognostic factors e.g. age of the patient, nationality, size of the primary cervical tumour, type of the tumour (exophytic, ulcerative or infiltrative), histology and grade of the tumour were studied to look for their effect on local tumour control and survival.

Results:
In our series, only the size of the primary cervical tumour emerged as the single most important factor to influence local tumour control and disease free survival. Twenty-nine patients (63%) had tumour size <4 cm and only 2(6.9%) of them developed local relapse, whereas 14 patients (30.43%) presented with tumours >4cm and 7 (50%) of them relapsed locally, the difference was significant with p value <0.01. The disease free survival in this group was 33.3% as compared to 54.6% in patients with lesions less than 4 cm with a significant difference at p<0.01. Three patients (6.5%) had barrel shaped tumours and showed no local relapse.

Conclusions:
As fifty percent of the cases with bulky lesion (>4cm) relapsed locally and showed poor disease free survival, the way forward is to consider increasing the brachytherapy dosage on CT assisted plan and / or combining with surgery in suitable cases. Extended field radiotherapy can also be explored to improve survival.

Key Words: Cervical carcinoma; Radiotherapy; Prognostic factors
Funding Agency: None

Oncology
Category: Clinical

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The Process of Making a Diagnosis of Papillary Thyroid Carcinoma (PTC) in Fine Needle Aspiration (FNA) Smears: Correlation with Clinical Features and Imaging Findings.

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Introduction:
Papillary thyroid carcinoma (PTC) has well defined cytomorphologic features. However, while making a diagnosis of PTC in fine needle aspiration (FNA) smears, a large number of cases have diagnostic labels such as suspicious/suggestive (S/O) of PTC, and PTC needs to be ruled out, etc. The objective of this study was to find out the difference in clinical features and imaging findings, if any, between cases diagnosed as PTC or S/O PTC and the rest of the lesions.

Methods:
78 cases, diagnosed over one year period, were divided into two groups. Group A included 38 cases diagnosed as PTC and S/O PTC. Group B included 40 cases diagnosed as rule out (R/O) PTC, and S/O neoplasm, R/O neoplasm or a nonneoplastic lesion, with one or more features of PTC. These two groups were compared using Students t-test and Fisher's Exact Test.

Results:
A significant difference was observed in respect of mean age between group A (35.5±8.91years) and group B (43.2±11.12, $p< 0.001$). The number of cases above the age of 45 years were significantly lower in group A (10.8%) as compared to group B (40.0%, $p=0.004$). No significant difference was observed between the two groups in male: female ratio (4:34 vs. 7:33, $p=0.519$). There was also no significant difference in respect of frequency of solitary nodule (78.9% in group A vs. 65.0% in group B, $p=0.212$) but significantly higher number of SN were located in the left lobe in group A (46.7%) than in group B (19.2%, $p=0.047$). There was also highly significant difference between the two groups in respect of association of nonneoplastic lesions ($p< 0.0001$).

Conclusions:
Patients diagnosed as PTC or S/O of PTC in FNA cytology are significantly younger, have a higher frequency of solitary nodules in the left lobe, and are less frequently associated with nonneoplastic lesions than cases having other diagnostic labels such as R/O PTC, and S/O or R/O neoplasm, etc., with one or more cytologic features of PTC.

Key Words: Papillary thyroid carcinoma; Fine needle aspiration cytology; Age and imaging
Funding Agency: None

Ophthalmology
Category: Clinical

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Atropine may be a Good Alternative to Patching for the noncompliant Child with amblyopia

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Introduction:
Amblyopia is a substandard corrected visual acuity (VA) without evidence of organic eye disease. The mainstay of treatment has been occlusion of the better eye by an opaque patch. The success of occlusion depends heavily on compliance. Pharmacological penalization is an alternative therapy for noncompliant child. The aim of this study is to investigate the effects of atropine penalization in amblyopic patients who are noncompliant with conventional occlusion.

Methods:
This was a retrospective study of 114 children aged 24 to 78 months with unilateral Ambyliopia diagnosed during the time period December 1997 to august 2003 and fulfilling the inclusion criteria. The mean follow up time after starting amblyopia treatment was 38.4, SD of 27.12 months. Children who had refractive errors were instructed to wear the prescribed spectacles full time for 8 weeks, those who were still amblyopic were prescribed 6 hours occlusion per day. Children with no refractive errors were prescribed 6 hours occlusion per day. Children who were non compliant with occlusion were instructed to instil one drop of atropine 1% into the nonambyliopic eye once per day. The child was considered to be cured if the acuity in the ambyliopic eye reached equal vision to the nonambyliopic eye or if there was one line difference
between them.

Results:
A total of 114 patients participated in the study 72 (63.16%) patients were compliant with occlusion, 64 of them (88.9%) patients reached cure within mean time of 23.23, SD of 16.89 months. The remaining 42(36.84%) patients who are not compliant with occlusion were instructed to use atropine 1% eye drops once per day. 38 of them (90.5%) patients were compliant with penalization and all of them reached cure with a mean time 12.9, SD of 9.7 months.

Conclusions:
The result of this study suggests that atropine penalization should be considered as an alternative therapy in those who are noncompliant with occlusion in treatment of amblyopia.

Key Words: Amblyopia; Occlusion; Penalization
Funding Agency: None

Ophthalmology
Category: Clinical

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Diabetic Retinopathy: Use of Automated Detection to Determine The Need For Formal Retinal Evaluation

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Introduction:
To evaluate the ability of an automated reading software (Retinalyze system) for automated pre-screening for diabetic retinopathy.

Methods:
Four hundred fundus photographs were obtained in 200 eyes of 100 patients with diabetes who were randomly selected from the Bro Taf diabetic retinopathy screening program in Wales. A gold standard reference was defined by classifying each patient as having or not having diabetic retinopathy based on overall visual grading of the digitized images using the Bro Taf reading protocal. Automated grading was done using automated red or bright lesion detection adjusted for quality and visibility thresholds.

Results:
Automated red and bright lesion detection was able to exclude retinopathy in 78% of patients without retinopathy given good image quality and an optimum visual threshold. Only 1 of 14 patients was false negative, that too with mild grade 2a DR or minimal diabetic retinopathy.

Conclusions:
Pre-screening for diabetic retinopathy by automated detection of single fundus lesions can be achieved with minimal false negativity and can help to decrease the burden of manual diabetic retinopathy screening.

Key Words: Automated Screening; Diabetic retinopathy; Digital fundus images
Funding Agency: None

Ophthalmology
Category: Clinical

166

Clinical Application of Endoscopy in Cataract and Anterior Segment Surgery

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Introduction:
Ophthalmic microendoscope has been used mainly for posterior segment procedures and vitreo retinal surgery. Recently endoscope assisted phacoemulsification, in eyes with opaque cornea, has been reported. The aim of the present study is to evaluate the use of endoscope in phacoemulsification and anterior segment maneuvers like synechotomy in eyes with opaque cornea.

Methods:
It is a prospective study done in Al-Bahar eye center. A consecutive series of 8 patients who underwent endoscope assisted anterior segment surgery are being reported in which conventional surgery through microscope was not possible. Five eyes of 5 patients underwent endoscopic assisted phacoemulsification. In one patient endoscope was used to segment iridocorneal synechae. In one patient of intractable glaucoma endoscope was used to identify the position of haptics and for cyclophotocoagulation of ciliary processes. In one patient it was used to identify the haptics of intraocular lens (IOL) in a semidilated pupil.

Results:
Vision improvement was seen in 5 out of 5 cases of endoscopic phacoemulsification. No complication or adverse event occurred. In the case of irido-corneal adhesion dissection, the procedure was completed with the help of endoscope, with minimal endothelial loss. In the case of glaucoma, intraocular pressure decreased to normal levels after endoscopic cyclophotocoagulation. In one patient the inferior haptic of the IOL was seen to be in sulcus through endoscope. It was reposited back in position, into the capsular bag.

Conclusions:
Endoscopy is useful in phacoemulsification in eyes with hazy cornea. It can be used to examine the angle, to cut irido-corneal adhesions and to cyclophotoablate the cilliary processes. We believe that mastering this technique and modifying the endoscope to meet the manipulative constraints will yield promising results in what we now classify as difficult anterior segment surgeries.

Key Words: Ophthalmic microendoscope; Vitreoretinal surgeries; Synechotomy
Funding Agency: None

Orthodontics
Category: Clinical

167

Occlusion and Orthodontics vs. TMD: Are there any associations?

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Introduction:
Clinical findings on occlusal traits as risk factors for temporomandibular disorders (TMD) are inconsistent. Likely reasons are variations in sample representativity and age, and lack of appropriate control groups. Our aim was to test the difference in signs and symptoms of TMD between representative groups of young adolescents with malocclusions that are thought to predispose to TMD due to occlusal instability, reduced muscle resistance, and abnormal head posture and/or abnormal condylar position, and a representative group of young adolescents with almost ideal occlusion.

Methods:
A population-based sample of about 1600 13-14-year-old school children in Kuwait was examined in a well-lit classroom according to standardized procedures. Occlusal scores included overjet (OJ), overbite (OB), teeth in anterior (ACB) or posterior (PCB) crossbite, and presence of almost ideal occlusion. Clinical signs of TMD were scored as reduced mouth opening (<35 mm), pain on opening, and presence of joint sounds. Self reported symptoms of TMD included a history of TM joint sounds or a history of pain in the TM joint or muscles. Chi square analyses were used to test the differences in frequency of signs and symptoms of TMD between each of the following five experimental groups: all subjects with OJ≥6.5 mm (N=97); negative OB (N=44); PCB on ≥ 2 teeth (119); neg. OJ or ACB on ≥ 1 tooth (144); and OB>2/3 and pos. ≤ 3.5 mm (N=157); and a control group of all subjects with almost ideal occlusion (N=182).

Results:
Clinical signs of TMD were more frequent ($P<0.05$) and subjective symptoms of TMD marginally more frequent ($P=0.07$) in subjects with neg OJ or ACB than in controls. No other differences were detected.

Conclusions:
Our findings suggest few occlusal risk factors for temporomandibular disorders (TMD), but that subjects with negative overjet (OJ) and anterior crossbite (ACB) may be at increased risk.

Key Words: TMD; Occlusion; Adolescence
Funding Agency: This research was supported by Kuwait University Grant # DD07/00.

Orthodontics
Category: Clinical

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Lateral cephalometric norms for adolescent Kuwaitis: Soft tissue measurements

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Introduction:
A comprehensive cephalometric analysis must include an evaluation of positions, thicknesses and relationships of relevant soft tissue components. The purpose of this study was to establish lateral cephalometric soft tissue norms for adolescent Kuwaitis, and to compare these norms to those of the common analysis systems.

Methods:
Digital lateral cephalograms were made of 82 Kuwaiti boys and 80 Kuwaiti girls of mean age 13.27 and 13.21 yrs (SD 0.42 and 0.43), respectively, with ideal dental occlusion. Anatomic landmarks were identified directly on the digital computer images. Linear and angular measurements were calculated electronically using the Dolhin version 9 software package.

Results:
Merrifield's Z Angle was clinically smaller and Holdaway's H Angle clinically larger than the published norms. The increased ranges of all anteroposterior angular and linear parameters relative to the respective ranges were considered clinically significant. The increased protrusion of labrale superius relative to Ricketts E Plane and Burstones SnPg' line as well as the increased thickness of the upper lip at point A and the increase in upper lip taper as compared to the previously submitted norms approached clinical significance. With the exceptions of the linear dimensions Incision superius-Stomion superius and Stomion inferius-Menton', the ranges of all labial norms were clinically larger than the respective ranges available in the analysis systems. Following Bonferroni correction, a gender difference was only detected in the linear dimension Subnasale-Stomion superius, with the average boy having 1.64 mm longer upper lip.

Conclusions:
Our findings suggest that Kuwaiti adolescents with ideal occlusion have more protrusive lips than Caucasians. This goes in hand with our previous findings regarding the hard tissues. This finding is of direct clinical significance for the orthodontic treatment planning.

Key Words: Cephalometric norms; Soft tissue; Treatment planning
Funding Agency: This research was supported by Kuwait University Grant # DD07/00.

Orthopaedic Surgery
Category: Clinical

169

Complicated Supracondylar fracture of humerus in children: Should it be classified as Gartland type IV?

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Introduction:
Supracondylar fracture in children with associated complications such as absent radial pulse, nerve injury and communition at fracture site resulting in instability in flexion and extension, forms a different group of children whose mode of injury and management may differ than usual Gartland type III fractures. We present our experience in the management of this group.

Methods:
92 children with Gartland Type III fracture were treated and followed up. 18 of these were classified as complicated fracture. 8 children had absent Radial pulse; 3 had punctured wound; 6 had nerve injuries and 7 patients had unstable communuted fracture which was difficult to reduce by usual method of reduction in flexion or extension. All patients were treated by closed reduction and per cutaneous K-wire fixation. In unstable group, separate K wire was used in the distal fragment to manipulate and reduce the fracture. 1 patient required open reduction. In 2 patients brachial artery was repaired. In others post operative oxygen saturation improved to 100% after fixation.

Results:
All fractures healed well without non union, contracture or myositis. 93 % recovered full elbow ROM. One patient developed P.O. ulnar nerve paraesthesias and 2 patients developed mild varus deformity. All nerve injuries recovered without surgery in six months.

Conclusions:
Most type III supracondylar fractures in children can be treated by close reduction and per cutaneous K wire fixation. New method of closed fixation for unstable fracture results in adequate reduction. Management of complicated supracondylar fracture require other than usual appraoch. This group should be added to original gartland classification. It is proposed that unstable fracture be classified as Type IV fracture. Fractures with associated Nerve injury as Type V(a) and fractures associated with Vascular complications as type V(b).

Key Words: Fracture; Humerus; Children
Funding Agency: None

Paediatric general surgery
Category: Graduate (Resident)

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Does the delay in the presentation of appendicitis affect the surgical outcome in children

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Introduction:
Appendicitis is a common and urgent surgical illness with significant morbidity and mortality. No single sign, symptom, or test accurately makes the diagnosis accurately. Therefore, a delay of presentation and diagnosis can lead to serious complications.

Methods:
To obtain the annual prevalence of appendicitis of Kuwaiti children ≤7 years. To assess if a delay of presentation and diagnosis of acute appendicitis would affect the post-operative outcome in children under 12 years. Patients under 12 years old who underwent appendicectomy in Ibn Sina (children hospital) were evaluated retrospectively. They were divided into two groups according to their age. First group were children ≤7 years and the other group were 8 to12 years. The list of patients was obtained from the surgery registry book at the main theatre for a period of one year.

Results:
A total of 103 children were evaluated. 44(42.7%) were ≤7 and 59(57.3%) were 8 to 12 years. There were 69 (67%) male and 34 (33%) were female. The annual prevalence of appendicitis in Kuwaiti children of ≤7 years is approximately 13 per 10, 000. All patients presented with abdominal pain and tenderness in the right iliac fossa. 26 (25.2%) patients had perforated appendix of which 15 (57.7%) had post-op complications. 51 (49.5%) children who had non-perforated appendicitis presented in the 1st day, and only 10 (9.7%) presented on day one with a perforation. 32 children had post-op complications, 20 of whom had fever >38.5c. The mean duration of the presenting complaint and mean delay prior to operation were shorter in patients with non-complicated outcomes by 0.25 days and 00:18 hours correspondingly.

Conclusions:
Appendicitis is a common surgical illness in children <7 years. Delay in presentation can lead to serious complications such perforation of the appendix. In addition there was no increase in post-op complication with increasing time from initial symptoms after the second day of presentation.

Key Words: Appendicitis; Children; Appendectomy
Funding Agency: None

Pathology
Category: Graduate (Resident)

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Evaluation of Prostate Specific Antigen (PSA) Assays on the Beckman Access Analyzer

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Introduction:
Prostatic carcinoma (PCa) is a common cancer in men. Prostate specific antigen (PSA) is the gold standard biomarker available for PCa diagnosis, follow up, and management. To introduce a new assay for PSA in Mubarak Hospital, this study evaluates the measurement of serum PSA using chemiluminesent immunoassay on the Beckman ACCESS 2 used in Mubarak Hospital against the Abbott ELECSYS 2010 used in Kuwait Cancer Control Center (KCCC) Tumor Biology Laboratory.

Methods:
Venous blood samples were obtained from 101 patients in the wards and outpatient clinics. Serum level of total PSA was determined by ACCESS 2 and an aliquot of each sample was sent to the KCCC Tumor Biology Laboratory to be analyzed by ELECSYS 2010. Four patients' samples with different PSA levels were used for the evaluation of the performance characteristics of the assays. Results were compared by the linear regression analysis and the Bland-Altman analysis was used to evaluate the degree of differences in the assays.

Results:
The mean (range) of PSA values obtained in ACCESS 2 and ELECSYS 2010 were 3.88 (0 - 46.82) ng/ml and 3.43 (0 - 38.76) ng/ml, respectively, ($p<0.0001$). The ACCESS 2 analyzer appeared to significantly over-estimate PSA values in comparison to ELECSYS 2010. However, the correlation coefficient for values obtained by either analyzer was excellent ($r=0.999$). These observations were comparable to those obtained in a subgroup analysis (n=31) of patient samples with PSA values 3.1-10 ng/ml. The intra-assay precision (CV %) was $\leq$3.3% and $\leq$3.9% for total and free PSA assays respectively at the levels evaluated. The inter-assay CV% was $\leq$7.2% and $\leq$8.7% for total and free PSA assays respectively (n=4).

Conclusions:
The results demonstrate that PSA measurement on ACCESS 2 in this study is reproducible, precise and accurate, and can therefore be employed in routine patient care testing.

Key Words: Prostatic carcinoma; Prostate specific antigen; Assay techniques
Funding Agency: Departmental resources

Pathology
Category: Clinical

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Effect of Smoking on Adipokines, Insulin Resistance and markers of inflammation in men with Type 2 Diabetes.

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Introduction:
Obesity and smoking induce several cytokines and inflammatory markers that might contribute to insulin resistance (IR) and metabolic abnormalities that increase the coronary heart disease (CHD) risk in Type 2 Diabetes (T2DM). Studies have tried to show a relationship between smoking, low-grade inflammation, adipokines, insulin resistance, and T2DM but reports have been inconsistent. This study evaluates whether associated metabolic derangements differ between T2DM patients with different smoking habits and if the degree of obesity modifies smoking-related effects.

Methods:
Fasting adipokines (leptin, adiponectin, resistin), insulin, glucose, HOMA index for insulin resistance, HbA1c, lipid profile and high-sensitivity CRP (hs-CRP) were determined in 106 male patients with T2DM in whom the waist circumference (WC) and body mass index (BMI) were also measured. Patients were categorized by BMI, degree of IR and smoking status (never (nonsmokers) (n=47), ex- (n=28), and current (n=31).

Results:
WC and BMI were not significantly different between smokers, ex-smokers and nonsmokers. Independent associations with smoking include IR (HOMA > 2 in 57%), poor glycemic control (HbA1c > 8% in 77%), low HDL cholesterol (44%), microalbuminuria (62%) and CHD (42%). Smokers had significantly ($p < 0.05$) higher glucose (11$\pm$4 vs 10$\pm$4 mmol/L); total cholesterol (6$\pm$1 vs 5$\pm$0.9 mmol/L) and triglycerides (2.4$\pm$1.5 vs 1.5$\pm$0.9 mmol/L) and differences remained after correction for BMI. hs-CRP and all adipokines were significantly correlated with indices of obesity but only leptin was significantly lower when smokers (17$\pm$14 ng/ml) were compared with non-smokers (32$\pm$22 ng/ml).

Conclusions:
We conclude that smoking modulates leptin levels and is associated with metabolic profile that increases CHD risk but the degree of obesity is the main determinant of low-grade inflammation and adipokines in male T2DM subjects.

Key Words: Smoking; Adipokines; Type 2 Diabetes
Funding Agency: None

Pathology
Category: Clinical

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Management of low HDL levels in a Lipid Clinic - How successful are we?

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Introduction:
The serum HDL level consistently inversely correlates with coronary heart disease (CHD) risk. This study reviews, over 5-years, the prevalence and response to treatment of low HDL in patients attending a Lipid Clinic in Kuwait.

Methods:
Of 1117 patients currently attending the Lipid clinic in Mubarak Al-Kabeer Hospital, 54 (30M, 24F) met the the criteria for low HDL-C (M <0.9 mM, F< 1.29 mM) with 5yr follow-up data, and additionally had features of the metabolic syndrome. 53% of male patients and 75% of female patients were diabetic. Patients were treated with advice on lifestyle modification (all), statins (28), fibrate (25) and statin + fibrate[1], and medications for diabetes and/or hypertension as appropriate. Changes in anthropometric indices, lipid profile and BP were assessed.

Results:
Over the 5-year follow-up period, there were significant ($p<0.05$) changes in weight and lipid profile irrespective of the modality of treatment and diabetes status. 33% of males lost mean (+ SD) 3 ($\pm$2) kg weight but 67 % gained 6.3 ($\pm$5.3) kg. 25 % women lost 3.8 (+ 3.6) kg and 75% gained 4.4 ($\pm$4.2) kg. HDL-C increased by 0.16 ($\pm$0.06) mM ($p <0.0001$) in 57 % of males and by 0.15 ($\pm$0.07) mmol/L 54 % of females ($p < 0.0001$). There was significant correlation between weight and HDL-C before treatment ($r=0.458$, $p=0.017$) but no correlation after treatment in women. There was also no correlation between change in weight and change in HDL. The change in HDL-C with statin is significantly higher than the change with fibrate ($p=0.007$). The change over time in HDL-C level was more significant ($p< 0.05$) in non-diabetic patients

Conclusions:
There were significant changes in HDL-C and other lipid parameters during the follow-up period but there was no correlation between change in weight and change in HDL-C. This study shows that the change in HDL-C with statin is significantly higher than with fibrate contrary to current thought.

Key Words: HDL; Coronary heart disease; Management
Funding Agency: None

Pathology
Category: Undergraduate

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Serum Adiponectin Level Among Healthy Subjects: Relationship To Glucose And Family History of Diabetes Mellitus

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Introduction:
Adiponectin is a recently discovered adipocyte-derived hormone that has been proposed to play a significant role in the co-morbidities associated with obesity. The aim of our study was to explore the relationship between serum adiponectin level and anthropometric and metabolic parameters in apparently healthy subjects.

Methods:
Fifty-eight healthy male subjects with mean (95% confidence interval, CI) body mass index (BMI) of 25 (22.98 to 27.49) Kg/m^2 and 53 patients with Type 2 diabetes mellitus (T2DM) and mean (95% CI) of 26.38 (22.23 to 30.52) were recruited into this study. Anthropometric measurements (height, weight, body mass index, waist circumference), blood pressure and family history of diabetes in parents, siblings and relatives were recorded. Fasting serum adiponectin, insulin and plasma glucose, lipid profiles, and uric acid levels were measured.

Results:
The results revealed that adiponectin showed significant inverse correlations with indices of obesity in patients with T2DM but not in the healthy subjects. Adiponectin also showed significant negative correlation ($r=-0.28$; $p=0.03$) with glucose in the healthy subjects. In healthy subjects, the mean (95% CI) adiponectin in those without family history of diabetes (20.32 (16.73 to 23.90) mg/ml) was significantly higher than in healthy subjects with family history of diabetes (16.33 (14.26 to 18.40) ng/ml) and patients with T2DM (15.80 (14.25 to 17.36) mg/ml) ($p<0.05$). When patients were grouped according to family history of diabetes, the lowest adiponectin was found in patients with history of T2DM in both parents (father and mother).

Conclusions:
This study shows that adiponectin is inversely related to fasting glucose in healthy subjects. Our results also suggest that plasma adiponectin concentration may be a convenient marker for identifying healthy subjects who may be at risk of developing T2DM. Longitudinal studies are required to confirm this potential application of adiponectin.

Key Words: Adiponectin; Obesity; Anthropometric
Funding Agency: None

Pathology
Category: Clinical

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Effect of some hemoglobin variants on HbA1C assay on Tosoh G7 and Cobas Integra 400 systems

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Introduction:
HbA1C assay has become the gold standard for the long-term glycemic control and is directly related to the risk for the development of chronic complications related to diabetes. Hb variants can profoundly affect the accuracy of its measurement. The effects vary depending on the specific Hb variant and the method used. The aim of this work was to study the effect of some Hb.variants on the level of HbA1c assay by Tosoh G7 and Cobas integra 400 systems.

Methods:
141 EDTA samples run on Tosoh G7 HPLC system in which Hb variants were identified were run by immunoassay on Cobas integra 400.The presence of Hb variants was identified by inspection of chromatograms obtained by Tosoh G7 HPLC system. In 122 samples the variant hemoglobin was identified by Tosoh G7 as V1 and in 8 samples it was identified as V0.11 hemoglobin variant cases were identified as both V0 and V1 variants. 23 of the141 samples were run for Hemoglobin electrophoresis which identified cases with V1 as HbS variant, and cases with V0 as Hb D or G trait.119 out of the 122 (97.5%) V1 variant samples were heterozygous (AS), three samples were HbS with high HbF.

Results:
HbA1c results obtained by both machines were significantly correlated ($P < 0.001$, $r=0.91$) for all samples studied as well as for V1 variant samples ($P<0.001$, $r =0.95$).The results of paired t-test to examine the difference between HbA1c results obtained by Tosoh versus that obtained by Cobas 400 for the variants studied showed a highly significant difference both in all cases ($p<0.001$) and V1 cases ($P<0.001$) studied where HbA1c results obtained by Cobas 400 were higher than that obtained by Tosoh G7(mean diff. =2.6%) (Bland Altman Bias Plot).The difference was not significant in case of V0 samples.

Conclusions:
We can conclude that the presence of HbS trait has positive interference with HbA1c level obtained by Cobas Integra400 system used in most of MOH laboratories in Kuwait compared to Tosoh G7 HPLC system.

Key Words: HbA1C; Tosoh G7; Cobas Integra 400
Funding Agency: None

Pathology
Category: Clinical

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Significance of cytologic atypia in fibroadenomas.

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Introduction:
The cytologic features of fibroadenomas (FA) are well characterized and the lesion readily identified. However cellular atypia, dispersal of single cells and increased cellularity may at times cause concern. Our study was conducted to determine the outcome of FA with atypia and identify the sources of diagnostic difficulty.

Methods:
Over a three year period (2004-2006), 595 cases of FA were diagnosed on fine needle aspirates (FNA). A cytohistologic correlation was available in 21 cases of FA with atypia and these cases were reviewed.

Results:
The mean age was 34 years (range 15 to 53 years). The masses were palpable and located in the right (38%) and left (62%) breast.The cytologic smears had mild to moderate nuclear atypia (11 cases), dyscohesive clusters (3 cases), dyscohesive clusters with nuclear atypia (5 cases) and dyscohesive clusters with dissociated single cells (2 cases). Tissue diagnosis was fibroadenoma (16 cases), phyllodes tumour (2 cases), ductal carcinoma (2 cases) and one case of fibrocystic change with papillomatosis. One and three cases of fibroadenoma had associated lobular and ductal hyperplasia respectively.

Conclusions:
Only 3.5% of FA were called atypical on FNA with a recommendation for excision. Majority (97.5%) of these were benign on histology while two cases (9.5%) were detected to have a carcinoma. Both lesions were removed based on the atypical cytology and no adverse outcome was seen.

Key Words: Fine needle aspiration; Fibroadenoma; Cytologic atypia
Funding Agency: None

Pathology
Category: Basic Sciences

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RET oncogenic activation and Nuclear Factor Kappa-B inhibition contribute to the pathogenesis of papillary thyroid cancer

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Introduction:
Thyroid cancer is the second most common cancer in Kuwaiti women and among the most frequent in Kuwaiti men. It is often associated with thyroiditis but the molecular mechanisms underlying this association and thyroid carcinogenesis here are not identified. RET proto-oncogene activation by somatic rearrangement has been implicated in the pathogenesis of papillary thyroid cancer (PTC) with marked variations between different countries. Actived RET has been shown to activate the transcription factor NFKB which is a hallmark of inflammatory responses and a tumor promoter in inflammation-associated cancers. The aim of this study is to provide insight into the molecular etiopathology of thyroid cancer in Kuwait by determining the involvement of RET and NFKB.

Methods:
We have studied 103 thyroid samples which included 71 PTCs and 32 various non-malignant thyroid lesions classified according to WHO histological criteria. RET expression and rearrangement were studied by RT-PCR. Results were confirmed by Southern blot using specific probes. NFKB expression were studied by immunohistochemistry.

Results:
60% of PTC samples showed expression of the RET oncogene while 30% of other thyroid conditions were positive for RET (70% of these positive cases were Hashimoto's thyroiditis (HT)). No chromosomal rearrangement has been identified so far in any of the samples. Intense cytoplasmic staining of NFKB was seen in all samples with no nuclear staining which denote lack or inhibition of NFKB activity. Normal thyroid follicles were negative for RET and NFKB.

Conclusions:
Our results suggest that RET oncogene activation is involved in the pathogenesis of at least half of PTC cases in Kuwait. Activation of RET and inhibition of NFKB may constitute molecular links between thyroiditis and PTC. Further investigations may clarify this.

Key Words: Papillary thyroid cancer; RET oncogene; Nuclear factor kappa-B
Funding Agency: # MG 02/05

Pathology
Category: Clinical

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Evaluation of Renal Biopsies in Mubarak Hospital

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Introduction:
The renal biopsy is invaluable method in the evaluation of patients with renal diseases including transplants. Apart from the accurate histological diagnosis, it provides important information about evolution and prognosis of the disease process and guides the development of a rational approach to the treatment of renal disease.

Methods:
We analysed the frequency of various biopsy proven renal disorders prevalent in Kuwait by reviewing all biopsies in our surgical pathology files for 2005 and 2006.

Results:
Nine hundred and twentysix (926) renal biopsies constituted approximately 9.5% of 9788 biopsies. Five hundred and seventy four (62%) were allograft and three hundred and fifty two (38%) were native. Of the allograft biopsies, 35% were baseline biopsies. Acute transplant rejection was the most common abnormality seen in the remaining allograft biopsies followed by chronic allograft nephropathy. In the native kidney disease, lupus nephritis, minimal change disease, FSGS, mesangeal glomerulonephritis and membranous GN were most commonly seen lesions in the descending order. Minimal change disease (MCD) was more common in adults in contrary to other studies which is probably due to typical population structure in Kuwait.

Conclusions:
Renal biopsies contribute a substantial portion of surgical pathology load in Mubarak Hospital largely due to an active renal transplant programme. MCD shows an unusual age distribution in our material.

Key Words: Allograft; Native; Renal Biopsy
Funding Agency: None

Pathology
Category: Clinical

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APOE genetic polymorphism in relation to blood levels of homocysteine and C-Reactive Protein in Arab schizophrenic patients

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Introduction:
Schizophrenia (SZ), a complex genetic disorder, is an important cause of psychiatric morbidity and handicap in the Arabian Gulf Region. There is some evidence that APOE polymorphism may play a role in the pathogenesis of SZ and its clinical phenotype. This study extends our previous observations on APOE allelic frequencies in SZ and investigates the influence of APOE polymorphism on blood markers of oxidative damage (homocysteine, tHcys) and persisting inflammation (high sensitivity C-reactive protein, hsCRP) in Arab patients with SZ.

Methods:
2 groups of age-, BMI and WHR-matched subjects were studied: 1 A: 207 SZ patients, on follow up at the Psychiatric Hospital; 2 B: n=165 apparently healthy control (HC) subjects recruited from the Central Blood Bank. Fasting Blood samples were collected from each subject and analysed for serum tHcys and hsCRP by automated ELISA (IMMULITE® 1000 Analyzer). APOE genotyping was done for all the subjects by validated PCR/restriction enzyme digestion methods.

Results:
APOE genotype E3E2 and allele E2 were more frequent in HC than in SZ, $p<0.01$. Similarly blood tHcys and hsCRP levels were higher in SZ than in HC, as expected, and in both groups were weakly correlated with each other (r 0.10, p 0.08). In both SZ and HC groups, the APOE allelic pattern had no influence on tHcys levels. However, in the SZ group but not the controls, CRP levels were highest with E2 ($p<0.01$) and also differed between E3 and E4, being higher with E4 (p 0.l05).

Conclusions:
(i) APOE allele E2 seems protective from SZ, being significantly commoner in healthy controls than in patients with SZ; (ii) persisting inflammation in SZ as indicated from hsCRP levels, appears more pronounced with E2 and lowest in E4, although tHcys, as index of oxidative damage, did not appear to be influenced by the APOE polymorphism. These observations require further evaluation in a clinical context.

Key Words: APOE Genotyping; Homocysteine; Schizophrenia
Funding Agency: Kuwait University Research Administration Grant # MG 02/02

Pathology
Category: Clinical

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Plasma Homocysteine and C - Reactive Protein levels in relation to disease progression in Multiple Sclerosis

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Introduction:
In multiple sclerosis (MS), progressive demyelinating damage occurs in the CNS in relation to persisting chronic inflammation, oxidative stress and apoptosis. There have been a few reports that the oxidative damage in MS may be mediated by high levels of homocysteine (tHcys). It is however unknown if homocysteine has any effect on the risk of disability/ progression of MS. This study therefore evaluated (i) plasma tHcys levels in MS in comparison to an age and BMI-matched healthy control population; (ii) blood levels of vitamin B_{12} and folate as putative determinants of tHcys levels and (iii) possible associations, in MS, between tHcys and high sensitivity C-reactive protein (hsCRP), a marker of continuing inflammation.

Methods:
2 groups of age-matched subjects were studied: 1 A: n=53 patients, diagnosed with MS, and on follow up at Mubarak Hospital; 2 B: n=65 apparently healthy control subjects recruited from the Central Blood Bank. Fasting Blood samples were collected from each subject and analysed for serum tHcys, vitamin B_{12}, folate and hsCRP by automated ELISA using validated kits on an IMMULITE® 1000 Analyzer. For each MS patient an Expanded disability Scale (EDSS) score was noted, and subsequent categorization was as benign disease (EDSS $\leq$3) and severe disease (EDSS >3).

Results:
Patients with MS had median plasma tHcy levels significantly higher than controls [8.5 (range 3.8 – 23.8) vs. 5.6 (2.3 – 17.9) µmol/L, $p < 0.01$]. There was no difference in tHcys levels based on EDSS score. Serum concentrations of vitamin B_{12} and folate were not different between patients and controls suggesting that the difference in tHcys was not related to vitamin deficiency. hsCRP levels were lower in patients with MS and appear to be influenced by EDSS score ($r=0.85$, $p<0.01$) and tHcys levels ($r=0.62$, $p=0.07$) after correction for the BMI.

Conclusions:
(i) Levels of tHcy are increased in MS and this change is not due to vitamin B_{12} and folate deficiency; (ii) The disease severity and progression of MS, as evident from EDSS scores, did not appear associated with tHcy levels; (iii) CRP levels were positively associated with tHcys and EDSS levels after correction for BMI, indicating a possible role in assessing disease severity in MS.

Key Words: Homocysteine; C-Reactive Protein; Multiple Sclerosis
Funding Agency: Kuwait University Research Administration Grant# MG 02/02

Pathology
Category: Undergraduate

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The use of the albumin:creatinine ratio (ACR) may result in significant missclassification of male and female patients if the same cut-off values are used.

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Introduction:
Among diabetics, Microalbuminuria (MA) has been shown in epidemilogic studies to be a predictor of increased risk of renal and cardiovascular disease. Guidelines recommend determination of MA by random early morning urine albumin (μg)/creatinine (mg) ratio (ACR). The American Diabetes Association (ADA) uses the same cut-off values in both men and women for definition of normo-, micro- and macro-albuminuria, without accounting for gender differences in creatinine or albumin excretion. We hypothesise that the use of ADA-ACR may result in significant missclassification of male and female patients if the same cut-off values are used.

Methods:
We analysed the results of 379 consecutive patients referred to the Mubarak Al Kabeer Hospital for the determination of ACR. Patients were classified apriori according to the ADA – ACR guidelines as normo-, micro- and macro-albuminuric. Patients were then reclassified aposteriori using gender - adjusted ACR as normo-, micro-, macro-albuminuric.

Results:
Urine creatinine was significantly correlated with MA in females ($r=0.24$, $p=0.002$) but not males ($r=0.11$, $p=0.12$). The average creatinine for the females was 9.5 ± 5.6 and for the males was 12.3 ± 7.2. The ACR-based classifications of normo-, micro-, macroalbuminuria for men were 89.6%, 9.9%, and 0.5%, respectively. However, when the corrections were made for gender differences in urine creatinine excetions using the gender-adjusted ACR formula, the men were reclassified as 84.2%, 14.9%, 1%, respectively ($p<0.05$). On the other hand, for the women there was no significant change in the MA classifications before and after gender correction.

Conclusions:
There is significant misclassification of MA in men when following the ADA guidelines using unadjusted-gender ACR. This suggests that it is critical that the current guidelines be reviewed to prevent misclassification of patients who may require therapy to prevent development and progression of renal or cardiovascular disease.

Key Words: ACR; Creatinine; Gender differences
Funding Agency: None

Pathology
Category: Clinical

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Obesity is an independent risk factor for plasma lipid peroxidation and depletion of erythrocyte cytoprotectic enzymes in humans.

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Introduction:
Obesity, defined as a body mass index (BMI) greater than 30kg/m^2, is now recognised as a risk factor for diabetes mellitus, hyperlipidaemia, colon cancer, sudden death and other cardiovascular diseases. In this study, it is hypothesized that obesity is an independent risk factor for lipid peroxidation and decreased activities of cytoprotective enzymes in humans.

Methods:
Fifty normal healthy subjects with healthy BMI(19–25kg/m^2) and 250 subjects with different grades of obesity (30-50kg/m^2) with no history of smoking or biochemical evidence of diabetes mellitus, hypertension, hyperlipidaemia, renal or liver disease or cancer were investigated. To test this hypothesis, we assessed lipid peroxidation and cytoprotection by measuring the concentrations of plasma malondialdehyde (P-MDA) and the activities of erythrocyte copper zinc-superoxide dismutase (CuZn -SOD) and glutathione peroxidase (GPX).

Results:
The concentration of P-MDA was significantly lower ($P<0.001$) in subjects with healthy BMI(2.53±0.04μmol/l) than in those with BMI above 40kg/m^2 (4.75±0.05μmol/l). Furthermore, there was a significantly positive association ($r=0.342$, $P=0.013$) between BMI and P-MDA. On the other hand, subjects with healthy BMI had significantly higher ($P<0.001$) erythrocyte CuZn-SOD (1464±23 units/g Hb) and GPX (98.4±3.3units/g Hb) than those with BMI above 40kg/m^2(1005±26units/g Hb) and 84.3±6.7units/g Hb) respectively. Furthermore, erythrocyte CuZn-SOD and GPX activites were negatively associated with BMI ($r=0.566$, $P=0.005$) and $r=-0.436$, $P=0.018$) respectively.

Conclusions:
It is concluded from these results that obesity in the absence of smoking, diabetes, melltius, hyperlipidaemia, renal or liver disease causes lipid peroxidation and decreased activities of cytoprotective enzymes, and should therefore receive the same attention as obesity with complications.

Key Words: Obesity; Free radicals; Antioxidant
Funding Agency: None

Pathology
Category: Clinical

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Is Raf-Kinase Inhibitor Protein Expression in Patients with Colorectal Cancer related to their Prognosis?

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Introduction:
Background and Purpose: Raf-Kinase inhibitor protein (RKIP) is an endogenous inhibitor which contributes in the inhibition of Raf-MAPK kinase (MEK)-ERK pathway and in the suppression of the Nuclear Factor Kappa B (NFkB) activation. Impressively, the new fashion of RKIP is the suppression of tumor metastatic behavior.Purpose: our study addressed whether the RKIP expression in primary colorectal cancers (CRCs) correlates with the risk of metastasis and overall survival.

Methods:
Two different cohorts of human colorectal cancers (retrospective studies of 268 CRC patients and 65 early-stage CRCs) were tested immunohistochemically for the expression of RKIP and overall and metastasis-free survival rates were measured.

Results:
Immunohistochemical staining of RKIP was reduced in metastatic tumors although the normal epithelia expressed it. In primary CRC, RKIP expression was independent prognostic marker for survival using multivariate Cox regression analysis (hazard ratio, 2.81; 95% CI, 1.58 to 4.96; P=0.0002) and independent of Duke's C stage. Patients with Duke's C RKIP positive tumors had similar 5-years survival rates as early-stage patients if tumors had equivalent RKIP expression levels. An independent study of early stage CRCs confirmed that reduced RKIP expression predicted metastatic recurrence and reduced disease-free survival (hazard ratio, 4.5; 95% CI, 1.7 to 12.3; P=0.003). RKIP expression was not correlate with sex, age, mitotic index, lymphatic and vascular invasion, Departmenth of invasion and tumor site. However, a significant correlation was found for apoptotic index (P=0.024).

Conclusions:
RKIP expression can be beneficial for identifying early-stage CRC patients at risk of relapse.

Key Words: Colorectal cancer; RKIP; Immunohistochemistry (IHC)
Funding Agency: KFAS, GRANT#99-0707 and Terry Fox Foundation, Grant # TTF/04/05

Pediatrics
Category: Clinical

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Ten-year (1995-2004) review of hospitalization of children with sickle cell disease in Mubarak Al-Kabeer Hospital, Kuwait

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Introduction:
Sickle cell disease (SCD) is typically mild among Kuwaiti patients because they carry the Arabia/India beta ^{S} -globin haplotype with its associated elevated Hb F levels. However, there is a subset of patients who have frequent crisis and there is a need to document the cause and pattern of hospitalization among these patients.

Methods:
This is a retrospective study of admissions of SCD patients to the pediatric wards of Mubarak Al-Kabeer Hospital from 1995 to 2004. The patients' hospital charts were reviewed and personal data and details of the admissions were extracted.

Results:
Over the 10-year study period, there were 57, 635 admissions to the 3 general pediatric wards of the hospital. Of these, 351 (0.6%) were for sickle cell-related problems. Fifty SCD patients were responsible for these admissions. They were aged between 10 months and 14.8 years with a mean of 8.7$\pm$2.8 years, made up of 30 males and 20 females. There were 18 SS, 28 SBeta-thal and 4 SD. Their Hb F levels ranged from 10 to 41% with a mean of 22.9$\pm$7.7%. The diagnoses on admission were: 222 (63.2%) vaso-occlusive crisis (VOC), 32 (9.1%) acute splenic sequestration crisis (ASS), 31 (8.8%) hemolytic crisis (HC), 23 (6.6%) acute chest syndrome (ACS) and 43 (12.3%) others. The latter included patients admitted for blood transfusion, for investigation of fever, for gastroenteritis, upper respiratory tract infection etc. There was no death of any SCD patient and None required intensive care.

Conclusions:
While SCD is indeed mild in Kuwaiti patients, there is still frequent admission, especially for vaso-occlusive crisis, in a group of patients. The factors that characterize this group need to be investigated.

Key Words: Sickle cell disease; Children; Hospitalization
Funding Agency: None

Pediatrics
Category: Clinical

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Surgical results in patients with complete atrioventricular septal defect and a functional single ventricle

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Introduction:
Overall mortality of patients with single ventricle (SV) is still high; though good mid- and long-term results of staged procedures have been reported. This study assessed retrospectively risk factors and long-term survival analysis that affect the surgical outcomes in the bidirectional cavopulmonary shunt (BCPS) and total cavopulmonary connection (TCPC) in complete atrioventricular septal defect (CAVSD) and SV.

Methods:
Between 1992 and 20005, 63 patients with CAVSD and SV underwent surgical interventions. The median follow-up period was 36 months (range 6-108) and 98.4% were followed up completely. The median age was 1 months at time of BT shunt or pulmonary artery banding and/ or coarctation of aorta (COA) repair, 16.2 months at BCPS, and 27 months at TCPC. Variables of anatomical lesions with SV (e.g. Situs type, hypoplastic ventricle), age at operation, and surgical procedures were analyzed. Overall survival with or without surgical intervention was 76.3% at 14 years. Of all 18 deaths, 3 (17%) died pre surgical intervention, 11 (61%) post palliation, 3 operative death (2 post BCPS and 1 post TCPC) and 1 late death (None cardiac).

Results:
In univariate analysis, presentation with congestive heart failure, pulmonary artery banding, and COA repair were signficant risk factors against long-term survival, while pulmonary atresia with BT shunt, was proved to be favorable prognostic factor. In multivariate analysis only COA repair continues to be statistically significant ($P<0.001$, Hazard ratio=3.5). 14-year survival rates of patients post palliation was 63.3%, post BCPS was 90.1% and post TCPC was 71.4% (Log rank $P=0.048$).

Conclusions:
This study revealed that overall survival was disappointing especially when SV associated with COA and heart failure in the pre-BCPS stage. Palliative procedures such as banding pulmonary artery and COA repair contributed to shorter survival pre-BCPS, however BCPS offered higher probability to proceed to TCPC procedure successfully.

Key Words: Congenital Heart Disease; Complete Atrioventricular; Cavopulmonary
Funding Agency: None

Pediatrics
Category: Clinical

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Audit of retinal screening for children and adolescence with type 1 diabetes

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Introduction:
Diabetic retinopathy is a highly specific vascular complication of type 1 diabetes, The recommendations for initial and subsequent ophthalmologic evaluation of patients with diabetes are accepted world widely, This study evaluates the efficacy of the current retinal screening protocol (ISPAD guidelines) for children and adolescents with type1 diabetes attending the Paediatric Department in Ahmadi Hospital

Methods:
We reviewed the records of 47 children and adolescents with type 1 diabetes in order to asses their ophthalmologic status by evaluating their initial, subsequent visits and their type of screening by using dilated fundoscopy as screening programme.

Results:
There was no detected abnormality by using the dilated fundoscopy as screening programme, There was delay in screening patients around time of diagnosis, They were seen more frequently in their subsequent visits

Conclusions:
Retinal screening is important for early detection, The audit of attendance is useful tool to measure our resources.

Funding Agency: None

Pediatrics
Category: Clinical

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Nitric oxide-mediated Activation of NADPH oxidase by Salbutamol during Acute Asthma in Children

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Introduction:
Asthma is an inflammatory disease characterized by a combination of bronchoconstriction and inflammatory changes, and oxidative stress is believed to be one of the molecular mechanisms of its pathogenesis. The objective of this study was to evaluate the status of NADPH oxidase (NOX), a major source of superoxide anion production, in asthma patients in relation to salbutamol treatment.

Methods:
Peripheral blood lymphocytes (PBL) were cultured from blood samples of asthma patients and healthy controls. Enzyme activities of NADPH oxidase and catalase, nitric oxide (NO) levels and lipid peroxidation were measured in PBL before and after salbutamol treatment.

Results:
PBL from asthmatic patients were found to have a significantly increased ($p<0.01$) enzymic activity of NOX. Plasma levels of malondialdehyde (MDA), an index of lipid peroxidation, and NO were also markedly elevated in asthma patients as compared to control samples. A significantly decreased ($p<0.05$) catalase activity observed in PBL from asthma patients underscored the severity of oxidative stress during asthma. Treatment of PBL with salbutamol (10μg/ml), prevented the attenuation of catalase activity but significantly increased the levels of NO and NOX activity. Levels of NOX-1 mRNA were significantly ($p<0.001$) increased in PBL following treatment with NO donor (500μM), S-nitroso-N-acetyl penicillamine (SNAP). Western blot analysis revealed that gp91phox protein was also significantly (2 to 3-folds) increased following treatment with SNAP. The observed transcriptional regulation of NOX-1 and gp91phox by NO was observed to result in an increased NOX activity as well.

Conclusions:
This study concludes that salbutamol treatment, though enhances superoxide anion production through NO-mediated mechanisms, has beneficial antioxidant effects through activation of catalase and attenuation of lipid peroxidation.

Key Words: Asthma; Oxidative stress; Salbutamol
Funding Agency: None

Pediatrics
Category: Clinical

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Role of Computed Tomography (CT) in pediatric respiratory diseases

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Introduction:
Respiratory illness is one of the major causes of morbidity and mortality in children. Chest radiograph (C x ray) combined with the clinical history remain the corner stone in the diagnoses of most pediatric respiratory diseases. Recently, CT lung is being increasingly requested by pediatrician. This study was carried to:

1. Determine the value of performing lung CT in the management of children with respiratory diseases.
2. Summarize the main indications for ordering pulmonary CT in Pediatrics.

Methods:
A hospital based, retrospective case-review study was carried out. The files of all patients less than 12 year age, and for whom CT lung was performed during the last five years were reviewed.

Results:
In this study, we reviewed thirty patients for whom CT lung was performed. Age ranged from 6 days to 10 years. 66% of the CT scans were requested by the pediatric pulmonologist, 50% of which were requested from outpatient clinic. The main indication for requesting chest CT was persistent abnormal CX-ray findings (90%) in a patient with uncontrolled wheeze and/or recurrent pneumonia. Findings of chest CT was the same as CX-ray findings (80%) and more specific $\pm$ new diagnosis (20%). Results of chest CT influenced medical treatment only in seven of the cases (23%) and led to surgical intervention in two patients (0.06%), (hernia, cystic adenomatoidmalformation).

Conclusions:
CT lung can accurately detect and localize pulmonary disease in children who have fever and/or respiratory symptoms even when chest x-ray is normal or nonspecific. Nevertheless, the technique should be used less often due to concerns regarding radiation doses. Our data demonstrate that the result of CT lung in children doesn't alter clinical decision and management of most of the cases (80%). Therefore CT lung should be requested mainly for the high risk patients (premature, cystic fibrosis, bronchiactasis immune compromised, congenital heart disease and congenital anomalies), preferably by a pulmonologist and after discussing the chest x-ray findings with a radiologist.

Key Words: High-resolution computed tomography; Imaging; Pediatric lung disease
Funding Agency: None

Pediatrics
Category: Clinical

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Lovastatin prevents Galactose-induced inhibition of NADPH oxidase in human neonate skin fibroblasts

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Introduction:
Galactosemia is an autosomal recessive metabolic disorder with severe effects on liver functions, ocular lens and central nervous system. Cellular mechanisms associated with high galactose-induced pathology during galactosemia remain unexplored. We have investigated the effect of high galactose on NADPH oxidase (NOX), a major superoxide anion producing enzyme system, which regulates important cellular functions such as vascular tone, antimicrobial defense and intracellular signal transduction.

Methods:
Foreskin samples were collected following circumcision (according to the protocols set by the ethical committee on use of human tissues) of 2-5 day old babies and dermal fibroblasts were grown from skin explants in growth medium. Cell cultures were treated with varying concentrations of galactose (10–20μM) and/or lovastatin (250-500μM). NOX activity was measured in cell homogenates. Total RNA was extracted for reverse-transcriptase-polymerase chain reaction (RT-PCR) analysis of NOX components and GAPDH. Cell homogenates were used for western blot analysis.

Results:
Treatment of fibroblast cultures with galactose resulted in a significant ($p<0.001$) inhibition in the NOX activity. Co-treatment with lovastatin marked prevented galactose- induced inhibition of NOX. Western blot and RT-PCR analysis however did not reveal any marked effect of galactose on gene expression of NOX. Lovastatin did not influence the expression of NOX either. Lovastatin was however observed to significantly (2-folds) increase the expression of PPAR-γ in the presence or absence of galactose.

Conclusions:
Our results establish for the first time that high galactose levels in conditions like galctosemia can compromise the function of NOX, an important enzyme system for several physiological functions through superoxide anion production. Our study further indicates that Lovastatin might be useful in restoring some of the cellular functions in galactosemic conditions.

Key Words: Galactosemia; Lovastatin; NADPH oxidase
Funding Agency: None

Pediatrics
Category: Clinical

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Parents' attitudes towards performance of lumbar puncture (LP) in Kuwait

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Introduction:
Lumbar puncture (LP) is an important tool for the diagnosis of meningitis. Recently, we observed frequent refusal of parents to allow LP in children with suspected meningitis. The objective of this study was to assess the knowledge, understanding and acceptance of LP by parents.

Methods:
A survey was conducted in the Departments of Pediatrics in three hospitals in Kuwait. A self-administered questionnaire was given to parents of children admitted with various diagnoses. The questionnaire contained questions about understanding, acceptance, and reasons for refusal of LP.

Results:
A total of 358 parents (77.0% mothers and 23.0% fathers) answered the questionnaire. The majority of the parents (75.6%) were Kuwaiti. The mean age±SD of the respondents was 31.0±7.0 years, and 54.0% had post-high school education. Of the surveyed parents, only 15.3% agreed for LP, 42.5% did not agree and 42.2% preferred taking a second opinion. There was no significant association between LP acceptance and age, education, nationality or residence. Fifty seven percent answered that LP is done for diagnosis while 22% did not know the reason for doing the procedure. Only 15.5% answered that there is no other alternative for the diagnosis of meningitis. The majority (79.0%) felt that LP is unsafe because it might cause complications like paralysis (68.0%), pain (44.0%), infertility (41.3%), and deterioration of child's health (30.2%). Seventy percent knew about these complications from a relative or a friend. From those who did not agree on LP, 67.0% felt that they will change their decision if the procedure was fully explained by a doctor with the use of a diagram. Another group (66.0%) felt that the media would help to increase the acceptance of LP among parents.

Conclusions:
The general population needs to be educated about the LP role in diagnosis of meningitis and the safety of the procedure. Both doctor and media would play a major role in educating parents

Key Words: LP; Questionnaire; Kuwait
Funding Agency: None

Pediatrics
Category: Basic Sciences

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Nitric oxide-induced activation of NOX in human dermal fibroblasts is attenuated by Insulin-transferrin-selenium

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Introduction:
Nitric oxide (NO) has significance in all the fields of biology and medicine including diseases of children, and several cellular functions are regulated by NO through its actions as an intracellular signaling molecule. NO is also known to regulate the levels of superoxide anion, either through direct interactions or via its effect on NADPH oxidase (NOX). We have investigated the antioxidant effects of insulin-transferrin-selenium (ITS), a unique metallo-protein complex on NO-mediated activation of NOX in human dermal fibroblasts.

Methods:
Human dermal fibroblasts grown from skin explants were cultured in growth medium. Cell cultures were treated with S-nitroso-N-acetylpenicillamine (SNAP, a NO donor 100-500μM), Apocynin (APO, a NOX inhibitor, 1mM) and/or ITS (10 units/100ml medium). NOX activity was measured in cell homogenates. Total RNA was extracted for RT-PCR analysis of NOX -1, PPAR- γ, IGF-1 and GAPDH.

Results:
Treatment of cell cultures with SNAP significantly ($p<0.01$) increased the NOX activity. SNAP-induced NOX enzyme activity was significantly ($p<0.05$) reduced by both ITS and APO. Gene expression of NOX-1 and IGF-1 was markedly (2 to 3-folds) elevated by SNAP whereas ITS significantly down-regulated the mRNA levels of both NOX-1 and IGF-1. ITS however failed to block the SNAP-induced increase in mRNA levels of IGF-1. APO was also observed to markedly downregulate the SNAP-induced enhancement of NOX-1 and IGF-1 mRNA levels. SNAP was found to markedly elevate gene expression of PPAR- γ irrespective of the presence of APO. Though, ITS did not alter mRNA levels of PPAR- γ, it however significantly reduced SNAP-induced activation.

Conclusions:
We report for the first time a NO-induced activation of IGF-1 which, at least in part, is NOX-mediated, and inhibitory effect of ITS on NO-mediated activation of NOX leads us to a conclusion that ITS complex is an antioxidant which might be useful in blocking NOX-mediated cellular oxidative stress.

Key Words: Nitric oxide; Insulin-transferrin-selenium; NADPH oxidase
Funding Agency: None

Pediatrics
Category: Clinical

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Inflammatory Bowel Disease in Children: An Evolving Disease Entity in Kuwait

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Introduction:
Inflammatory bowel disease (IBD), a chronic disease of unknown etiology is believed to be a rare disorder among the Kuwait pediatric population, since most of the cases of diarrhea were attributed to infective causes. Our aim was to study the epidemiology of IBD among children in Kuwait and compare the disease features with reports from rest of the world.

Methods:
All IBD patients (1-15 yrs in age) referred to the pediatric gastroenterology (GI) unit in Al-Amiri Hospital, Kuwait during the period from February 1998-December 2004 were reviewed.

Results:
Among the 91 IBD patients in this study, seventy four percent were Kuwaiti nationals and twenty three percent of which had a family history of IBD. Sixty five percent of the patients had Crohn's disease (CD), 32% manifested ulcerative colitis (UC) and 3% were diagnosed with indeterminate colitis (IC). The most common presenting symptoms in our patients were abdominal pain (86%), diarrhea (85%) and weight loss (65%) with failure to thrive in 40%. Perianal disease was seen in 19% of CD patients. Ileocolonic region was the commonest site affected in CD patients (46%) followed by isolated ileal disease (25%) and isolated colonic disease (20%). Pancolitis was the commonest (59%) lesion in UC followed by left sided colitis (38%) and proctitis (3%). Steroids were the main medications that induced remission. Twenty one percent of the patients were maintained on Azathioprine or 6-MP. The complications encountered by CD patients involved gut perforation in 7%, intra-abdominal abscess in 5% and bowel stricture in 3% of the patients.

Conclusions:
IBD is not a rare disease in our native pediatric population. Though IBD in our patients does not differ in its presentation, characteristics or localization from that reported in the rest of the world, a significant (23%) number of our patients had a family history.

Key Words: IBD; Ulcerative Colitis; Crohn's disease
Funding Agency: None

Pediatrics
Category: Clinical

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Parental worries and concerns among the use of inhaled corticosteoids in the treatment of childhood asthma in Kuwait

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Introduction:
To illustrate parental worries and concerns towards the use of inhaled corticosteroids in the treatment of childhood asthma. Eminent associations were made to study relations between such concerns and variables such as maternal education level, type of clinic attended, parental understanding of inhaled medications and whether or not a child has positive family history of asthma.

Methods:
Subjects were children's parents visiting out-patient general and respiratory paediatric clinics, Mubarak Al-Kabeer Hospital, Kuwait. One-to-one semi-structures interviews were conducted using a set questionnaire.

Results:
Seventy-two parents of asthmatic children participated. Fifty were concerned about the use of inhaled corticosteroids in the treatment of childhood asthma. Mothers who have achieved college graduate level or above express less worries about ICS side effects compared to those who left school from high school level or less. Less worry was demonstrated by patients being followed up in specialized clinics in comparison to others who have been followed up in general paediatric clinics. Considerable parental misconceptions about inhaled medication used in asthma treatment as the role of ICS was exchanged with that of inhaled bronchodilators. Level of parental concern was shown to be higher among those with positive family history of asthma.

Conclusions:
Parental knowledge about inhaled asthma medication is inadequate. Worries and concerns are influenced by several factors, such as maternal educational level, type of clinic attended, parental understanding of inhaled medications and family history of asthma. Although associations were not significantly related, sufficient number of responses were enough to be demonstrated in this study. This is due to the small number of subjects recruited in this study. Findings are suggestive of the need for better parental education about childhood asthma and its management.

Key Words: Childhood Asthma; Inhaled Corticosteroids; Parental worries
Funding Agency: None

Pharmaceutical Analysis
Category: Basic Sciences

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Rapid tandem mass spectrometric method for determination of gabapentin in human plasma

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Introduction:
Gabapentin (GBP) is currently indicated for the management of neuropathic pain in adults and as adjunctive therapy in the treatment of partial seizures with or without secondary generalization. The present study aims at developing a simple, rapid and valid method of determination of GBP in human plasma using tandem mass spectrometric (MS/MS) technique after a single pretreatment step of human plasma sample.

Methods:
The drug and the internal standard (4-phenyl-4-aminobutanoic acid; IS) were analyzed by flow injection without chromatographic separation, using a mobile phase consisting of acetonitrile-water-formic acid (50:50:0.025, v/v/v), at a flow rate of 0.1 ml/min. The procedure involves plasma deproteinization using acetonitrile. The run-cycle time was less than 3 min. Quantitation was achieved using multiple reaction monitoring (MRM) scan at MRM transitions of m/z 172 > 154 and m/z 180 > 117 for GBP and the IS, respectively.

Results:
Calibration curves were linear over a range of 0.1–10 ug/ml ($r > 0.999$) and the limit of quantification of GBP in plasma was 0.1 ug/ml. Stability test shows that GBP is stable in plasma for at least four weeks when stored at -20°C. The utilization of the method for analysis of GBP in plasma samples of patients showed that the method was suitable for analysis of GBP in clinical samples.

Conclusions:
The method described is simple, rapid, accurate and has sufficient sensitivity to measure GBP in plasma samples of patients treated with GBP which indicates that the method is valuable for therapeutic drug monitoring utilizations.

Key Words: Gabapentin; Tandem mass spectrometry detection; Human plasma
Funding Agency: Kuwait University Research Grant (Grant # PT01/02)

Pharmacology and Toxicology
Category: Graduate (MSc: Basic Sciences)

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Insulin Signaling Pathway: A Comparison Between Diabetic and Non-Diabetic Rats

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Introduction:
Insulin resistance is characterized by an excessive hepatic glucose production and a decline in muscle and adipocyte glucose utilization. The mechanisms underlying insulin resistance are still unclear. Animal models of diabetes have reported a defect in insulin receptor (IR), insulin receptor substrate-1 (IRS-1) and phosphatidylinositol 3-kinase (PI3K) expression and activity. Our objective in this study is to shed light on the PI3K/Akt pathway.

Methods:
For glucose and insulin tolerance tests, the rats were given glucose or insulin and blood samples were collected at various time intervals. RNA extraction and RT-PCR were performed to determine the genetic expression of IR. Differential centrifugation was carried out to isolate total and membranes from livers of GK and control rats for IRS-1 subcellular localization. Total basal and insulin-stimulated protein expression of IR, PI3K and Akt were examined by Western blotting.

Results:
GK rats showed an impairment in glucose tolerance and a decrease in an vivo insulin sensitivity. The basal levels of RNA and protein expression of IR of GK rats were significantly higher than that of the control rats. Similarly, basal microsomal IRS-1 of GK rats was higher compared to their corresponding control values. In contrast, the tyrosine phosphorylation of IRS-1 of GK and control rats was similar. In addition, no differences were observed in the expression of PI3K subunits. Although there was no change in the protein expression of basal Akt, we found that insulin-stimulated phosphorylation of Akt in GK rats was dramatically reduced by 80% as compared to the control rats.

Conclusions:
These results indicate that in non-obese type 2 diabetes exemplified by the GK rats is associated with impaired insulin-stimulated Akt activation in hepatic tissue and suggest that attenuated Akt activation may be involved in a number of metabolic derangements seen in diabetics including the decrease in glycogen synthesis and increase in hepatic glucose output.

Funding Agency: KFAS grant # 2002-130206

Pharmacology and Toxicology
Category: Basic Sciences

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Species differences in cefotiam-induced lipid peroxidation and nephrotoxicity

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Introduction:
Cefotiam is a broad spectrum cephalosporin antibiotics having activity on a wide range of gram-negative and gram-positive bacteria. Cefotiam shows excellent effect on gram-negative microorganisms surpassing 3rd generation cephalosporins. The ability of cefotiam, to induce lipid peroxidation (LPO) and renal damage, was compared in three different species: rat, rabbit and pig.

Methods:
LPO was measured in renal cortical slices as generation of malondialdehyde (MDA). Impairment of renal function was measured as the decrease in renal cortical accumulation of the organic cation tetraethylammonium (TEA). Renal cortical slices from naive rats, rabbits or pigs were incubated in the absence (control) or in the presence of cefotiam (2.10¨C16.71 µM) for 60 min at 37^{o}C. At the end of the 60 min incubation, thiobarbituric acid reactive substances (TBARS) were determined in control and cefotiam-incubated renal slices. TEA accumulation in renal cortical slices was measured after a second incubation at 25 degree C for 90 min. TEA accumulation was measured by scintillation counting of 14C-TEA.

Results:
In vitro exposure to cefotiam induced a concentration-dependent increase of MDA production and a concentration-dependent decrease in renal cortical accumulation of TEA in all investigated species.

Conclusions:
Renal cortical slices from rabbits and rats appeared to be the most susceptible to the peroxidative injury.

Key Words: Cefotiam; Lipid Peroxidation ; Tetraethylammonium
Funding Agency: Research Administration, Kuwait University

Pharmacology and Toxicology
Category: Basic Sciences

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Are anticonvulsant enamiNones adrenergic agonists?

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Introduction:
Recent evidence indicate that enamiNones produce anti-seizure effects by enhancing extracellular GABA levels.We investigated how they may accomplish this in the CNS by comparing the actions of E139, a potent Class I anticonvulsant enamiNone with those of norepinephrine(NE)which is known to enhance GABA release.

Methods:
400uM slices containing the nucleus accumbens were generated from male Sprague-Dawley rats. Evoked excitatory postsynaptic currents (EPSCs) were isolated pharmacologically and biophysically using voltage clamp recording techniques.

Results:
E139(10uM) depressed evoked glutamate-mediated EPSCs by -27.0±2.9% (n=4). NE(100uM) produced a similar EPSC depression of -22.7±3.1% (n=5). Dopamine(DA, 50uM) another catecholamine also depressed EPSCs by -29.4±6.4% (n=7). At peak E139 effect, NE could not produce additional depression (-3.1±3.1%, n=6, $p>0.05$). Similar occlusion was observed when E139 was applied at peak NE effect (8.8±1.8%, n=5, $p>0.05$). The occlusion of E139 effect by NE was mimicked by UK14304, an alpha2 selective adrenoceptor agonist. Phentolamine, a non-selective beta-adrenoceptor antagonist blocked both NE (0.1±12.1%, n=3, $p>0.05$) and E139 (-1.0±6.3%, n=6, $p>0.05$) effects. Yohimbine, a selective alpha2 adrenoceptor antagonist also blocked (-6.1=/-3.7%, n=6, $p>0.05$) both effects while propranolol (beta-antagonist; -30.2±10.2%, n=5) and prazosin (alpha1-antagonist; -19.4±1.5%, n=7, $p<0.05$) did not affect the E139 effect. Also DA receptor antagonists SCH23390 (-40.4±6.8%, n=6, $p<0.05$) and sulpiride (-21.9±2.6%, n=5, $p>0.05$) did not affect the E139 effect. Finally, CGP55845(1uM) a potent GABAB receptor antagonist blocked both E139(1.7±3.1%, n=5, $p>0.05$) and NE effect (7.0±2.3%, n=5, $p>0.05$).

Conclusions:
These results suggest that E139 and NE produce EPSC depression by a similar mechanism and further suggest that E139 may act as an alpha2-adrenoceptor agonist to trigger the release of GABA.

Key Words: EnamiNones; Norepinephrine; Alpha2 adrenoceptors
Funding Agency: Supported by K U Research Grant # PT02/02 to SBK.

Pharmacology and Toxicology
Category: Basic Sciences

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Anticonvulsant enamiNones suppress in vitro seizures by synaptic and non-synaptic mechanisms.

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Introduction:
Some enamiNones have been reported to possess excellent in vivo anticonvulsant activity with minimal side effects. We examined if these enamiNones produced effects in vitro that may underlie their in vivo actions. We tested the hypothesis that E139, a Class I anticonvulsant enamiNone suppresses in vitro seizures induced in the hippocampus.

Methods:
400um coronal slices of the hippocampus were generated from male Sprague-Dawley rats. Field population spikes(PS) were recorded from the cell body layers of areas CA1 or CA3 of the hippocampus by stimulating appropriate afferents. In vitro seizures were generated chemically and electrically(high frequency stimulation;HFS).

Results:
E139(10uM) depressed field PS amplitude recorded in area CA1 by -28.6$\pm$4.5% (n=5). Picrotoxin(100uM) transformed the single PS into multiple PS(4.5$\pm$0.2, n=5) reflecting seizure activity. E139(10uM) reversibly reduced the number of these multiple PS to 3.5±0.2 (-23.4$\pm$1.8%, n=5, $p<0.05$). Epileptiform activity (3.6$\pm$0.6, n=5) was also recorded in zero Mg2+ perfusate and E139(10uM) depressed the number of PS to 1.6$\pm$0.5 (-54.8$\pm$9.7%, n=5, $p<0.05$). In zero Mg2+, spontaneous bursts (SBs) were recorded and their frequency was suppressed by -64.3$\pm$12.3% (n=10, $p<0.05$) with E139(10uM). CGP55845(1uM), a GABAB receptor antagonist partially blocked the E139-induced suppression(-24.3$\pm$17.8%, n=6, $p<0.05$, unpaired t-test). In the stimulus train-induced bursts (STIBS) model, seizure activity was generated in area CA3 by applying several HFS (100Hz) to mossy fibers. Afterdischarges(ADs) and SBs were recorded and E139(10uM) inhibited their frequencies by -48.6±14.3% and -66.7$\pm$6.7% respectively (n=5, $p<0.05$). These E139 effects on ADs and SBs were partially blocked by CGP55845(1uM; -27.5$\pm$5.7% and -44.4$\pm$9.7% respectively, n=7, $p<0.05$; unpaired t-test).

Conclusions:
E139 suppresses in vitro epileptiform activity in the hippocampus by synaptic and non-synaptic mechanisms.

Key Words: Spontaneous bursts; Epileptiform activity; Hippocampus
Funding Agency: Supported by KU Research Grant # PT02/02 to SBK.

Pharmacology and Toxicology
Category: Basic Sciences

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Effect of Apocynin and FPTIII on NADPH oxidase system in kidneys of STZ-treated spontaneously hypertensive rats.

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Introduction:
NADPH oxidase system (NOX) is known to participate in pathogenic events of inflammatory and cardiovascular disorders. Activation of NOX and its role in hypertension is well reported, however its regulatory intracellular signaling pathways particularly in diabetics, are not known. The main aim of this study is to investigate the role of Ras-GTPase in regulation of renal NOX during hypertension and/or diabetes.

Methods:
Diabetes was induced in male WKY and spontaneously hypertensive (SHR) rats by a single injection (55mg/kg/i.p.) of streptozotocin (STZ). WKY and SHR rats with or without diabetes were treated with FPT-III (an inhibitor of Ras-GTPase pathway, 1.5 mg/kg/ alt diem) or apocynin (an inhibitor of NOX, 5mg/kg / i.p, daily) for four weeks starting from day one of diabetes induction. Enzymic activity of NOX was measured using lucigenin and gene expression of NOX-4, p22phox and GAPDH was measured by reverse-transcriptase polymerase chain reaction (RT-PCR).

Results:
We observed that STZ-injection caused a marked increase in renal NOX activity of both normotensive (WKY) and hypertensive rats, however the effect was more significant ($p<0.01$) in SHR. Both FPTIII and apocynin prevented activation of NOX activity in kidneys of diabetic hypertensive rats, without any significant effect in non-diabetic normotensive or hypertensive rats. FPTIII did not affect mRNA levels of NOX-4 or gp22phox as analyzed by RT-PCR. Interestingly, apocynin was observed to significantly (2 to 3-folds) enhance the expression of both NOX-4 and gp22phox in normotensive diabetic rats only. Both FPTIII and apocynin also prevented the diabetes and / hypertension-induced increase in urinary excretion of protein.

Conclusions:
Our study concludes that Ras-GTPase is an important regulator of NOX activity in kidneys. FPTIII and apocynin propose a novel class of therapeutic agents to control NOX-mediated inflammatory events in diabetes and hypertension, and prevent renal dysfunction.

Key Words: Hypertension; Ras-GTPase; NADPH oxidase
Funding Agency: None

Pharmacology and Toxicology
Category: Basic Sciences

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Angiotensin-(1-7) prevents diabetes-induced cardiovascular dysfunction

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Introduction:
We were the first to show that angiotensin-(1-7) [Ang-(1-7)] can produce vasodilation by acting through a unique (non-AT1/AT2) receptor and release of prostaglandins. We also showed that Ang-(1-7) has anti-hypertensive properties. The aim of this study was to test the hypothesis that treatment with Ang-(1-7) or Ang-(1-7) non-peptide analogue AVE0991 can produce protection against diabetes-induced cardiovascular dysfunction.

Methods:
We examined the influence of chronic treatment (four weeks) with Ang-(1-7) (24£gg/kg/hr ip) or AVE0991 (24£gg/kg/hr ip) on proteinuria, vascular responsiveness of isolated carotid and renal artery ring segments and mesenteric bed to vasoactive agonists, and cardiac recovery from ischemia-reperfusion in streptozotocin-treated rats (diabetes). Animals were sacrificed four weeks after induction of diabetes and/or treatment with Ang-(1-7) or AVE0991.

Results:
There was a significant increase in urine protein (231, b 2 mg/24hrs) in diabetic animals compared to controls (88, b 6 mg/24hrs). Treatment of diabetic animals with Ang-(1-7) or AVE0991 resulted in a significant reduction in urine protein compared to vehicle-treated diabetic animals (183, b 16 and 149, b 15 mg/24hrs, respectively). Treatment with Ang-(1-7) or AVE0991 also prevented the diabetes-induced abnormal vascular responsiveness to norepinephrine, endothelin-1, carbachol and histamine in the perfused mesenteric bed and isolated carotid and renal arteries. In isolated perfused hearts, recovery of left ventricular function from 40 minutes of global ischemia was significantly better in Ang-(1-7)- or AVE0991-treated animals.

Conclusions:
This is the first study to show that Ang-(1-7) is protective in diabetes and suggest that activation of Ang-(1-7)-mediated signal transduction could be an important therapeutic strategy to reduce cardiovascular events in diabetic patients.

Key Words: Heart; Kidney; Vascular dysfunction
Funding Agency: This work was supported by a grant from Kuwait University Research

Pharmacology and Toxicology
Category: Basic Sciences

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The non-selective adenosine receptor agonist 5 -N-ethylcarboxamidoadenosine (NECA) induces both pro-inflammatory and anti-inflammatory effects in mice

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Introduction:
The role of adenosine in asthma is inconclusive. Whilst some studies have shown that adenosine is a bronchonstrictor and pro-inflammatory mediator, others have suggested that adenosine has anti-inflammatory actions.

Methods:
In this study, we have investigated, 1) the effects of NECA on airway cellular influx in intraperitoneally ovalbumin (OVA) immunized mice and, 2) its effects on intranasal (i.n.) OVA-induced cell influx in immunized mice. All mice were immunized with OVA in alum on day 0. To assess the effects of NECA on immunized mice, animals were treated with NECA (0.1 mM - 1mM) or vehicle (n=6-7 per group) on days 10 and 11 and bronchoalveolar lavage (BAL) was performed on day 13. To assess the effects of NECA on OVA-induced inflammation, mice were challenged with OVA or PBS (i.n.), and then treated with NECA (0.3 mM; i.n.) 5-10 min later, on days 10, 11, 12 and 13 (n=10-12). BAL was performed on day 15.

Results:
In immunized mice, NECA administration caused a pronounced neutrophilia at 1 mM compared to vehicle ($4.1 \times 10^4 \pm 1.7 \times 10^4$ cells/ml vs $0.6 \times 10^4 \pm 0.3 \times 10^4$ cells/ml; $P<0.05$). Intranasal OVA challenge induced a significant increase in both neutrophil ($32.2 \times 10^4 + 9.4 \times 10^4$ cells/ml vs $0.7 \times 10^4 \pm 0.4 \times 10^4$ cells/ml; $P<0.05$) and eosinophil ($44.7 \times 10^4 + 10.9 \times 104$ cells/ml vs $0.03 \times 10^4 + 0.03 \times 10^4$ cells/ml; $P<0.05$) counts. Treatment with NECA significantly reduced both OVA-induced neutrophil ($6.4 \times 10^4 \pm 2.2 \times 10^4$ cells/ml vs $32.2 \times 10^4 + 9.4 \times 10^4$ cells/ml; $P<0.05$) and eosinophil ($11.1 \times 10^4 + 4.0 \times 10^4$ cells/ml vs $44.7 \times 10^4 + 10.9 \times 10^4$ cells/ml; $P<0.05$) influx.

Conclusions:
These results show that, in immunized but not challenged mice, NECA can induce a mild neutrophilic inflammation. However, when given together with a strong inflammatory stimulus, NECA can induce significant anti-inflammatory effects.

Key Words: Asthma; Adenosine; Mice
Funding Agency: None

Pharmacology and Toxicology
Category: Basic Sciences

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Reversible spermato-toxic effects of a purine nucleoside analogue-Acyclovir [9-(2-hydroxyethoxymethyl)-9H–guanine] are associated with elevated lactate dehydrogenase activity in the testis

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Introduction:
Acyclovir [9-(2-hydroxyethoxymethyl)-9H–guanine] is a synthetic nucleoside analogue, widely used as an antiviral drug to treat Herpes simplex virus and Varicella zoster virus infections. The present study was designed to investigate its spermato-toxic effects and correlate the same with its effects on lactate dehydrogenase (LDH) activity in the testis.

Methods:
Swiss albino male mice (N=6/group/dose/sample time) were treated (i. p.) every day with 4, 16, 32, and 48 mg/kg body weight of Acyclovir for 15d. The sperm count, sperm motility and sperm morphology assay in sperm samples from the caudae epididymes and LDH concentration (Optimized Standard Kit; Roche/Hitachi) in the testes were estimated on 7, 14, 21, 28, 35, and 70d following the last exposure.

Results:
Acyclovir decreased the sperm count from 7-35d ($P<0.001$) with a recovery observed on 70d except at 48 mg/kg dose-level ($P<0.05$; One way Analysis of Variance (ANOVA) followed by Bonferroni's post hoc test). Acyclovir also inhibited the sperm motility ($P<0.001$) from 7 - 35d with maximum effect on 28 and 35d, but without any effect on 70d. On the other hand, sperm abnormalities increased on 21, 28 and 35d only at 16-48 mg/kg, 32-48 mg/kg, and 32 mg/kg dose-levels respectively ($P<0.05$). The LDH activity was increased ($P<0.05$-0.001) from 7d (except at 4 mg/kg) to 35d. Only 48 mg/kg dose group showed increase in LDH concentration on 70d. Decreased sperm count and motility showed negative correlation (Pearson product moment correlation) and elevated sperm abnormalities showed positive correlation with increased intra-testicular LDH activity.

Conclusions:
Acyclovir is cytotoxic to germ cells, but only moderately alters the sperm morphology and these changes take place in a direct relation with the LDH concentration in the testis

Key Words: Gonadotoxicity; Cytotoxicity; Intra-testicular enzymes
Funding Agency: None

Pharmacology and Toxicology
Category: Basic Sciences

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The effect of cardiac ischemic preconditioning on rat left ventricular gene expression profile: A microarray-based genomic approach

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Introduction:
Cardiovascular disease is the leading cause of death in the world and is responsible for about 40% of deaths in Kuwait. Ischemic preconditioning (IPC) is a phenomenon where heart is rendered more resistant to subsequent ischemia-reperfusion (I-R)-induced injury by one or more brief episodes of I-R. The mechanisms responsible for cardio-protective effects of IPC are not well characterized. The objective of the study was to characterize gene expression profiles in the left ventricles of male Wistar rat hearts exposed to I-R or IPC followed by I-R.

Methods:
Group 1 was hearts that were perfused for 30 min. Group 2 was perfused hearts that subjected to 40 min I and 30 min R. Group 3 was perfused hearts that were subjected to IPC (5 min I + 10 min R + 5 min I + 10 min R) followed by I-R. Total RNAs were isolated from left ventricular tissues. Codelink gene expression system (GE Healthcare) was used for cRNA target preparation, hybridization of microarrays (Rat UniSet 10K CodeLink bioarrays) and detection. Microarrays were scanned with Affymetrix 428 Array Scanner. Data analyses were carried out with GeneSifter microarray data analysis software.

Results:
Expression of 140 transcripts were changed (44 up-regulated, 96 down-regulated) due to I-R (Group 2) compared to only perfused hearts (Group 1). 23 transcripts, that were down-regulated due to I-R, were up-regulated by IPC. IPC down-regulated expression of seven transcripts which were up-regulated by I-R.

Conclusions:
Evaluation of global gene expression profiling via microarray-based technologies provides a molecular portrait of IPC on left ventricle and it may result in insights into the mechanism(s) of cardio-protective effect of IPC. Intriguing genes and pathways for further study are identified. Information gathered from these studies particularly will be useful when cardio-protective mimetic drugs such as FPTIII, a specific inhibitor of Ras farnesyltransferase, are used against I-R injury.

Key Words: Gene expression profiling; Cardiac ischemic preconditioning; Ischemia reperfusion
Funding Agency: This work was supported by Kuwait University, Research

Pharmacy
Category: Basic Sciences

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Formulation of Sustained Release Ketorolac Tromethamine

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Introduction:
Ketorolac tromethamine (KT) is a non-steroidal anti-inflammatory drug with short duration of action. The aim of this study is to prepare sustained-release pellets with less side effects and better patients' compliance.

Methods:
Non-pariel seeds were initially coated with Eudragit®-RS (RS). KT was subsequently applied onto the non pariel using different proportions of Eudragit RL (RL)/RS to achieve the targeted release pattern. Drug content, stability and release were determined before and after storage at different conditions.

Results:
Drug release followed the order: RS <RL:RS (1:3) < RL: RS (1:2) < RL. Formula III (RL: RS of 1:3) showed complete and extended release over 12 h. KT release followed Higuchi diffusion controlled model. Storage of the selected formulation at 40^{o}C/75%-RH resulted in discolouration after three months. Flow of such pellets was diminished, which could be attributed to the elevation of moisture content from 2.29% to 2.99% after two months. The storage at 25^{o}C/60%-RH maintained the physical parameters, while under 40^{o}C/75%-RH, resulted in acceleration of drug release, which is attributed to the elevated moisture content of the pellets. Storage of pellets at 30^{o}C/70%-RH did not appreciably change dissolution characteristics. Storage of the pellets under the three conditions didn't affect the chemical stability of the drug.

Conclusions:
The proposed formulation provided sustained KT-release over 12 hours and characterized by good physical and chemical stability.

Key Words: Ketorolac ; Sustained release; Eudragit RL/RS
Funding Agency: None

Pharmacy
Category: Undergraduate

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Comparison of drug-drug interactions using two different databases

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Introduction:
Drug-drug interaction is common clinical problem that can result in serious consequences to the patients' health. Computerized drug interaction databases are used to detect interactions before prescriptions are dispensed. MicroMedex's Drugdex and Gold Standard Clinical Pharmacology provide the level of interaction, severity, documentation and the mechanism of action of each drug-drug interaction that may exist in any prescription. This study set out to compare the level of drug-drug interaction information provided by MicroMedex and Clinical Pharmacology. The databases were assessed for ease of information accessibility, reliability, and number of drug names that can be used for searching.

Methods:
Drug-drug interactions were checked by analyzing 50 outpatient prescriptions from the armed forces hospital using MicroMedex Drugdex and Gold Standard Clinical Pharmacology databases.

Results:
Both databases showed that there were drug-drug interactions in 39 prescriptions. Most of the interactions were of moderate severity with a score of 2 (69.67% MicroMedex, 56.67% Clinical Pharmacology). Moreover, comparing the databases for some specific drug interactions showed a 43.33% difference in the grading level between the two databases.

Conclusions:
MicroMedex's Drugdex provides a more practical database that can be used in hospitals with easy accessibility and saves time when checking the drug-drug interaction by its multiple drug entry search key word. However, for the comprehensive explanatory of the mechanism of action of each interaction the Gold Standard Clinical Pharmacology can be used.

Key Words: Drug interactions; Computer databases; Prescription
Funding Agency: None

Pharmacy
Category: Undergraduate

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Pharmacy Students' Evaluation of the Kuwait University Pharmacy Curriculum

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Introduction:
To evaluate pharmacy students' perceptions of the undergraduate pharmacy curriculum at Kuwait University

Methods:
The International Pharmacy Students Federation's (IPSF) self-administered curriculum evaluation questionnaire was distributed among pharmacy students in professional years of study. The questionnaire elicited background information, in addition to questions about the students' point of view of the teaching staff, required and acquired skills, and their expectations and feelings toward the program itself. A 5-point Likert scale (strongly agree to strongly disagree) was used to evaluate their agreement with each statement of the questionnaire.

Results:
108 (66 %) students completed questionnaires. Although 42 % of the students desired to do postgraduate study in pharmacy, only 32 % had always wanted to study pharmacy. Students would prefer working in a hospital rather than community, industry or academia. Generally, most students considered that the current curriculum had a positive impact on their analytical thinking, written communication, planning and team-work skills. However, 71% responded that a good memory is all that is needed to do well on the course. Some also felt that the aims and objectives of the program are vague (34%) with students restricted on how and what they study and dissatisfied with the parameters used to assess their performance (62%). There was strong agreement on students having too much material to cover (90%) with too little time (83%) resulting in difficulties in comprehending the whole material (60%). About one third of students reported that their teachers explained work well and provided valuable feedback. Overall, 27% of the students were satisfied with the quality of the course.

Conclusions:
Students have mixed viewpoints about the current pharmacy curriculum. Although the program improves their skills, students would like more freedom in choosing their subjects and improved assessment and feedback. Students' opinions should be considered to help improve the quality of the curriculum.

Key Words: Pharmacy education; Student aspirations; Curriculum development
Funding Agency: None

Pharmacy
Category: Clinical

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Pharmaceutical Care in the Community Pharmacies of Kuwait

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Introduction:
Pharmaceutical care is defined as "the process through which a pharmacist cooperates with the patient and other professionals in designing, implementing, and monitoring a therapeutic plan that will produce specific therapeutic outcomes"1. This study was conducted to i] describe the current pharmacy practice in community pharmacies based on self-reported practice by pharmacists, ii] to explore the awareness of the pharmacists of the pharmaceutical care concept, iii] identify their willingness to its implementation, and iv] identify the barriers that may limit its implementation.

Methods:
A developed and pre-tested questionnaire was used to collect data via face-to-face structured interview of 70 community pharmacists selected from private-retail community pharmacies using stratified and systematic random sampling.

Results:
The response rate was 85.7%. Forty two (73.7%; 95% CI: 60.1-84.1%) of the respondents had always performed interventions on the prescriptions through interacting with physicians. Thirty nine (65%; 51.5-76.6%) had always labeled the dispensed drugs. Forty six (76.7%; 63.7-86.2%) had always provided patient's counselling. Nineteen (31.7%; 20.6-45.1%) of the respondents claimed that they were aware of the pharmaceutical care concept. Eleven (57.9%) and 47.4% of those claiming to be aware of the pharmaceutical care concept indicated that its main focus is the patient and the appropriate objectives of the concept, respectively. Fourteen (73.7%; 48.6–89.9%) of them claimed that they had already implemented the pharmaceutical care services in their practice. Thirty three (71.7%; 56.3–83.5%) demonstrated willingness to implement the pharmaceutical care practice in their pharmacies. The main barriers perceived by the participants were lack of time (58.3%), lack of educational programs and training (53.3%) and lack of communication skills (31.7%).

Conclusions:
The current practice of community pharmacists in Kuwait needs further improvement. The awareness of the respondents of pharmaceutical care was low. Their willingness to implement the pharmaceutical care services in their practice was high. Therefore, implementation and promotion of pharmaceutical care by the health authorities and the Pharmaceutical Association of Kuwait can significantly improve patient care.

Key Words: Pharmaceutical Care; Community Pharmacy; Kuwait
Funding Agency: None

Pharmacy
Category: Basic Sciences

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APCI-LC/MS stability studies of novel triazolyl-oxazolidiNone antibacterial agents

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Introduction:
Novel triazolyl-oxazolidiNones 1 active against Gram-positive bacteria were synthesized. The stability of compounds in human plasma is important in achieving effective antibacterial therapeutic plasma levels. We conducted the stability studies of triazolyl-oxazolidiNones (PH-027, PH-038 and PH-041) in human plasma using APCI-LC/MS method.

Methods:
Plasma samples (50 µl) containing known concentrations of the compounds (stored at 22^{o}C and -20^{o}C for 5 weeks) were drawn at appropriate time-intervals and analyzed by a developed LC/MS method using ion-trap MS, operated in full-MS scan using a positive APCI. Stability profiles were established by plotting the logarithmic values of the percentages of remaining analyte concentrations vs. time.

Results:
The full MS profiles show the molecular masses of PH-027, PH-038 and PH-041 at m/z 348, 389 and 451, respectively. Calibration plots using (linezolid m/z 338 as internal standard) were linear (r: 0.99) over the selected concentration ranges. The values of RSD% and DEVs% were <8.8% and ±15.5% indicated good precision and accuracy. Stability studies indicated that the compounds were stable in human plasma at 22^{o}C and -20^{o}C. The kinetic parameter ranges were K_{deg} 0.02-0.08 week-1, $t_{1/2}$ 8.5–44.1 weeks, t_{90} 1.2-6.7 weeks. The results showed no significant differences in the kinetic parameters of the compounds at the experimental temperatures.

Conclusions:
The triazolyl-oxazolidiNones were stable in human plasma at room and freezing temperatures with relatively low degradation rates. The morpholino derivative PH-027 was most stable with longer $t_{1/2}$ and t_{90} and lower K_{deg} values. The method could be useful in determination of this class of compounds from biological matrix.

Key Words: APCI-LC-MS; OxazolidiNones; Stability
Funding Agency: Supported by Research Administration, Kuwait University

Pharmacy
Category: Basic Sciences

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A novel approach to the preparation and scale up production of Pentoxifylline controlled release tablets

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Introduction:
The purpose of this study was to prepare 600 mg pentoxifylline tablet formulation with acceptable controlled release (CR) profile and to scale it up to a pilot level.

Methods:
Tablets were prepared using wet granulation (WG), direct compression (DC) and hot melt (HM) techniques. The prepared formulae were subjected to various physicochemical and physicomechanical testing to determine the most appropriate formulation with an acceptable CR profile. Factors affecting the release profile either related to the formulation (content and type of gum, tablet hardness, granules particle size and tablet surface area/shape) or the production technique (Method of preparation, type of granulating fluid and thermal treatment) were studied. Formulae that showed satisfactory CR profiles were subjected to scale –up production up to 20 kg per batch.

Results:
Seven formulae prepared by WG technique, two prepared by DC technique and one by hot melt technique showed satisfactory CR profiles. Water, as a granulating agent, showed superior CR behavior compared to isopropyl alcohol. Decreasing the granule particle size and the tablet surface area improved the CR behavior. Scaling–up the previous formulae affected the release profiles dramatically. Only three formulae prepared by WG technique gave acceptable profiles.

Conclusions:
Pentoxifylline CR tablets using wet granulation technique and water as a granulating fluid with low granule particle size and either xanthan gum or HPMC E4 as gum type matrix and low tablet surface area gave satisfactory formula with acceptable CR profiles comparable to the innovator product.

Key Words: Controlled Release; Scale Up; Pentoxifylline
Funding Agency: None

Pharmacy
Category: Clinical

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Assessment of drug-drug interactions in outpatient prescriptions using the Micromedex drug interactions database

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Introduction:
The incidence of drug-drug interactions increases with the number of drugs a patient takes. Screening for such interactions may help to reduce the morbidity and mortality they cause. Several computerized drug databases have the ability to check for drug-drug interactions. In this study we used the Micromedex drug interactions database to examine the incidence of drug-drug interactions in a sample of outpatient prescriptions containing more than four drugs simultaneously.

Methods:
Retrospective evaluation of randomly selected outpatient prescriptions to check for drug-drug interactions was performed using the Micromedex drug interactions database. Interacting drugs were entered into the database and checked for severity, adequacy of documentation and the mechanism of the interaction. Data was assessed by simple counting and quantification of interactions rated according to severity and adequacy of documentation. For comparative purposes both severity and documentation were assigned a likert-type scale of 1-4 and 1-5 respectively.

Results:
The majority (82%) of prescriptions had at least one drug-drug interaction. A total of 48 specific drug-drug interactions were found in the 100 prescriptions assessed. The most serious interactions (16.8%) found were classified as major according to the database with a severity rating of 3. The majority (72.9) were classified as moderate with a severity rating of 2. Only 5 interactions were rated as minor. The largest number of interactions (39.5%) were between drugs used for cardiovascular or related conditions. This was followed by drugs for cardiovascular conditions and endocrine (22.9%), cardiovascular and musculoskeletal conditions (16.7%) and endocrine and musculoskeletal (10.4%).

Conclusions:
The Micromedex drug interactions database is a useful tool for screening prescriptions before the drugs are dispensed to patients.

Key Words: Computerised database; Morbidity; Drug interactions
Funding Agency: None

Pharmacy
Category: Basic Sciences

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Influence of rate controlling membrane and adhesive coat on the in vitro permeation of trimetazidine from nerodilol-based HPMC gel drug reservoir system

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Introduction:
Transdermal therapeutic systems (TTS) provide steady-state plasma concentrations for prolonged periods. The broad objective of the study was to design membrane-moderated TTS for trimetazidine. The present study was carried out to find the influence of rate controlling membrane and adhesive coat on the in vitro permeation of trimetazidine from nerodilol-based HPMC gel drug reservoir system.

Methods:
Either the rat epidermis (control), EVA2825 membrane, adhesive-coated EVA2825 membrane or adhesive-coated EVA2825 membrane-rat epidermis composite was mounted between the two compartments of Modified Keshary-Chien diffusion cell with stratum corneum facing the donor compartment. Two milliliters of 2% w/v HPMC gel drug reservoir containing 4% w/v of nerodilol and 2.5% w/v of trimetazidine was placed in the donor cell and 50 v/v ethanol-water was added to the receiver cell. The cells were maintained at 37.0°C, permeate samples were withdrawn, and analysed by HPLC. The amount of drug permeated upto 24 h was estimated and the relevant permeation parameters were calculated. The data were subjected to statistical analysis.

Results:
There was a significant decrease in the flux of trimetazidine across EVA2825 membrane when compared to control (rat epidermis). On coating with an acrylic adhesive emulsion, there was a further decrease in the flux of the drug. When the adhesive-coated EVA2825 membrane was stuck to rat epidermis, there was a significant decrease in the transdermal permeation of the drug as shown by decrease in the flux. This indicates that EVA2825 membrane is effectively controlling the transdermal permeation of trimetazidine from the nerodilol-based HPMC gel drug reservoir system.

Conclusions:
It is concluded that the chosen transdermal components (EVA2825 membrane and acrylic adhesive coat) are able to control the transdermal permeation of trimetazidine.

Key Words: Transdermal; Trimetazidine; EVA2825
Funding Agency: Kuwait University; # PP01/04

Pharmacy
Category: Basic Sciences

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Isolation and Quantitative Analysis of Yohimbine in Commercial Yohimbe Products by HPLC

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Introduction:
Yohimbe tree (Pausinystalia yohimbe, Coryanthe yohimbe) is native to West Africa, with the bark of the tree being the reservoir of the major alkaloid yohimbine. Within the past decade various over-the-counter yohimbine herbal preparations have become increasingly popular, primarily as natural aphrodisiacs. Because of the insufficient methods of standardization, there are highly variable quantities of yohimbine in commercially available yohimbe products. Identification and quantification of yohimbine is an important prerequisite for establishing standardization and quality control for these products.

Methods:
Yohimbine, the major indole alkaloid was isolated from yohimbe bark-containing tablets by moistening the powdered tablets with ammonium hydroxide, extraction with chloroform. The chloroform extract was subjected to simple chromatographic separation. Yohimbine in different yohimbe products was quantitatively determined by high performance liquid chromatography with ODS column, a mixture of KH_2 PO_4 :CH_3 CN (62:38, volume ratio) as mobile phase and UV detection at 220 nm.

Results:
The developed method of yohimbine analysis showed variable yohimbine concentrations in different products and was so sensitive that low concentrations were detected.

Conclusions:
The method is rapid, simple, accurate and reproducible. The method is proposed to be used for quality control of the commercially available yohimbe products.

Key Words: Yohimbine; Herbal Preparation; Standardization
Funding Agency: None

Pharmacy
Category: Clinical

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Therapeutic Drug Monitoring of Vancomycin: assessment of initial pharmacokinetic dosing equations at AL-Amiri hospital

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Introduction:
Vancomycin is a bactericidal antibiotic. Achieving and maintaining therapeutic blood levels is important for clinical efficacy. Population-based pharmacokinetic equations are commonly employed to predict volume of distribution (Vd) and clearance (Clvanco) in order to calculate doses required to achieve desired serum levels. The objective of this study was to compare three different population equations for: (a) their predictive ability in estimating Vd and Clvanco, and (b) the frequency with which the dosage from each method would yield simulated steady-state peak and trough concentrations within a specified range. Two of the equations used a fixed Vd, while the third took into account patient age as a possible variable of Vd.

Methods:
63 patients were studied. Based on vancomycin concentrations, Vd and Clvanco were calculated using a one-compartment model. These parameters were also estimated using population equations. The predictive ability of the estimated parameters from each equation was assessed using predictive performance analysis (precision and bias). In addition, the individual parameters were used to simulate steady state peak and trough levels, using first order kinetic equations from doses derived from the population equations. The frequency with which each equation would have achieved target peak and trough concentrations was determined.

Results:
The equation employing age and body weight found to be the least biased (ME=0.2, $p<0.05$ for Vd; ME=-5.0, $p<0.05$ for Clvanco) and most precise (SME=175 and RSME=10 for Vd; SME=665 and RSME=21 for Clvanco) method in predicting Vd and Clvanco values. This equation also produced a higher frequency of simulated steady-state peak and trough levels within the target ranges specified.

Conclusions:
The age and body weight equation proved the most reliable of those evaluated and could be easily applied in Kuwait to individualize dosing.

Key Words: Therapeutic Drug Monitoring; Vancomycin; Initial Dosing equations
Funding Agency: None

Pharmacy
Category: Clinical

214

A rapid tandem mass spectrometry method for steroid profiling of 17 alpha-hydroxyprogesterone, cortisol and androstenedione in human plasma: a proposed screening method for detection of congenital adrenal hyperplasia in young infants

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Introduction:
Congenital adrenal hyperplasia (CAH) is an inherited metabolic disorder of steroid biosynthesis due to 21-hydroxylase deficiency. It is characterized by elevation of 17alpha-hydroxyprogesterone, androstenedione and suppression of cortisol plasma levels. Life threatening salt-wasting crises and incorrect gender assignment in infancy make early diagnosis highly desirable. Screening was traditionally based on immunoassays whose drawbacks are low specificity and high rate of false-positive results. A rapid and specific tandem mass (MS/MS) method for the simultaneous determination of the steroid hormones in human plasma was developed and validated.

Methods:
Analytes and the internal standard were extracted from plasma samples by solid phase extraction procedure. After gentle evaporation of the eluting solvent, the residue was reconstituted in the mobile phase and was directly injected into the ionization probe of the mass spectrometer. The analysis run-cycle was 2-3 min injection-to-injection. Quantification of 17alpha-hydroxyprogesterone, cortisol and androstenedione was achieved using multiple reaction monitoring (MRM) at m/z 331.3>97, 363.7>121.5 and 287.8>97.4, respectively. The concentration of each compound was determined by the internal standard calibration method using dexamethasone (m/z 393>147) as an internal standard.

Results:
Validation studies showed good linearity (r: 0.99±0.013), accuracy (%DEVs: -16.2 to +15.6) and reproducibility (RSD%: 4.1-12.2) with LLOQ of 20.0 ng/ml (RSD: 0.08-0.14). Recovery studies of plasma samples spiked with known concentrations of the steroid hormones gave average percents of 100.6 % (17alpha-hydroxyprogesterone), 111.7 % (cortisol) and 101.6% (androstenedione).

Conclusions:
The results obtained suggest the utility of the described MS/MS method to screen for CAH and to confirm the results of conventional immnunoassays.

Key Words: Congenital adrenal hyperplesia; 17alpha-Hydroxyprogesterone; Androstenedione
Funding Agency: None

Pharmacy
Category: Clinical

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Opinion of depressive disorder patients' on two forms of pharmacist created educational interventions in Kuwait

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Introduction:
To assess patient's opinion toward receiving, either a written or verbal, pharmacist's interventions and to determine the effect of these interventions on patient's knowledge about antidepressants.

Methods:
150 newly diagnosed patients with unipolar depression were randomized into a control, leaflet and counselling groups. Assessment was done at initiation and after 6 weeks of treatment at the OPD, Psychiatric Hospital, Kuwait.

Results:
50% of respondents asserted that clinicians didn't give them sufficient information although 90% favoured the idea of receiving further information about medication. 53% patients returned for the 6 weeks scheduled follow up, majority were from the counselling (66%)and leaflets (58%) followed by 34% of the control (P>0.004). 97% support receiving leaflets and drug counselling. 94% of the counselling and 79% of the leaflets patients disclosed that they got adequate information compared to 47% of the control (P=0.001). Three quarters of the control patients considered 'psychiatrists' a source of information compared to a third of the intervention groups (P=0.012). More patients with either form of intervention demonstrated accurate knowledge concerning medicine name and strength, better understanding of how to deal with missed doses and how and when to take medication (P<0.026).

Conclusions:
Patients with depression appeared generally very comfortable with and very eager to receive additional drug information. Patients looked at the two forms of interventions in a very positive way and considered them as an aid in relieving worries and as a source of reassurance. More patients in the counselling group rated the counselling as helpful, sufficient, supportive and reassuring. Counselling was of greater effectiveness than leaflets and both were more informative than the control in conveying elemental drug information to patients. These data provided evidence that drug counselling and leaflets should be widely used.

Key Words: Antidepressant; Leaflet; Counselling
Funding Agency: None

Pharmacy
Category: Basic Sciences

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Preparation and characterization of probucol self-emulsified drug delivery system to enhance solubility and dissolution

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Introduction:
Self-emulsifying drug delivery system has proved its efficacy to improve the solubility and dissolution of poorly water soluble drugs. The objectives of this study were to prepare and characterize a self-emulsified drug delivery system of probucol (PBSEDDS) with enhanced dissolution and better chance for oral absorption.

Methods:
The solubility of probucol in different oils, surfactants and co-surfactants was demonstrated using saturation solubility method and HPLC for drug analysis. Based on that, Soybean oil (solvent), Labrafil (surfactant) and Capmul MCM-C8 (co-surfactant) were chosen to prepare PBSEDDS different formulations. The ingredients were tested for compatibility with the drug using DSC and FTIR. Different formulations were evaluated for spontaneity of emulsification, turbidity and particle size. Dissolution experiments of PBSEDDS filled in hydroxyl propyl methyl cellulose (HPMC) capsules in water were conducted using USP apparatus II. Ternary phase diagram was constructed to identify the best self-emulsified region.

Results:
The results showed higher solubility and compatibility of the drug with soybean oil, labrafil and Capmul MCM-C8. Oil to surfactant/co-surfactant ratio showed large influence on the characteristics of PBSEDDS formulations. The optimum oil concentration was found to be (20–40%) and surfactant/co-surfactant (1:4) concentration was 60–80%. With these concentrations, the resultant particle size ranged from 0.103–0.051um, turbidity ranged from 9.18-21.12NTU and t30 value (cumulative % drug dissolved in 30 min) ranged from 70.42–90.52. Several fold improvement of drug dissolution was observed compared to drug solution in soybean oil alone.

Conclusions:
The study revealed that the PBSEDDS increased the dissolution rate and has the potential to enhance the bioavailability without interaction or incompatibility between the ingredients.

Key Words: Self-emulsifying drug delivery system; Probucol; Preparation and characterization
Funding Agency: Kuwait University, # PP03/04

Pharmacy
Category: Basic Sciences

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Capillary electrophoretic enantioseparation of some anticonvulsants using native cyclodextrins as chiral selector and evaluating efficiency of smaller internal diameter capillaries

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Introduction:
The separation of enantiomers by capillary electrophoresis is an efficient and important method in the analysis of chiral compounds. In this investigation, the racemates of some anticonvulsant drugs; barbiturates and enamiNones, were separated using different native cyclodextrins (CDs); alpha-CD, beta-CD and gamma-CD.

Methods:
Separation of the enantiomers were done by capillary electrophoresis using native cyclodextrins as chiral selectors. Using a 50 µm internal diameter (id) fused silica capillary four of the six barbiturates studied could be resolved at a basic pH of 9.4 and using 100 mM phosphate buffer concentration. Optimum separation for the racemates is obtained by varying concentrations of the native CDs. Using the same conditions, 20 µm internal diameter capillary were used to separate the compounds partially resolved with the 50 µm internal diameter capillary.

Results:
There is an average two-fold increased in resolution when shifting to a 20 µm internal diameter fused silica capillary. When translated to a 20 µm id capillary conditions where only partial peak splitting was observed with the 50 µm id capillary gave successful resolutions. The enamiNones were only partially resolved using the native CDs with both the 50 and 20 µm id capillaries. It is indicated therefore that separation of the enamiNones may require the use of derivatized or substituted cyclodextrins.

Conclusions:
It is therefore concluded that the use of smaller id capillaries enhanced the resolutions of the samples with the added advantage of using only small amounts of sample volumes and reagents required for analysis.

Key Words: Enantioseparation; Capillary electrophoresis; Native cyclodextrins
Funding Agency: None

Pharmacy
Category: Basic Sciences

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EnamiNone pharmacophore as a requirement for novel anticonvulsant activity

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Introduction:
The enamiNone pharmacophore is a conjugated system of a carbonyl group joined to an amino group through a carbon-carbon double bond. All enamiNone compounds consist of the enamiNone pharmacophore.

Methods:
The reaction of beta-hydroxyketo compounds with appropriate amino compounds yielded aniline and benzylamino enamiNones which were evaluated in the maximal electroshock (MES) and subcutaneous pentylenetetrazole (scMet) tests in mice. The enamiNones were administered intraperitoneally in mice at 30, 100, and 300 mg/kg dosage levels with anticonvulsant activity noted 30 min and 4 h after administration. This was followed by the quantitative determination of the effective doses (ED50), and the toxic doses (TD50) of the anticonvulsant enamiNones.

Results:
Many anilino and benzylamino enamiNones provided anticonvulsant activity against electrically- and chemically-induced seizures, and were devoid of neurotoxicity. The most potent anilino enamiNone (E139) and benzylamino enamiNone (E81) were class 1 anticonvulsants. In the quantitative MES anticonvulsant evaluation, the ED50 for E139 and E81 were 6, and 65 mg/kg respectively; while the TD50 were 380 and >500 mg/kg respectively, providing high protective indices.

Conclusions:
The most potent anilino and benzylamino anticonvulsant enamiNones (E139 and E81) were devoid of neurotoxicity. Therefore, the enamiNone conjugated system is an important pharmacophore for desirable anticonvulsant activity.

Key Words: Anticonvulsant; EnamiNones; Synthesis
Funding Agency: Kuwait University Research Grant # PR 02/02

Physical Medicine and Therapy and Rehabilitation
Category: Clinical

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Therapeutic Lifestyle Changes and its positive effect on diabetics undergoing Coronary bypass graft surgery.

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Introduction:
Sedentary lifestyle, obesity and stress are risk factors contributing towards onset of coronary artery disease in diabetic population. Therapeutic Lifestyle changes (TLC) is a multifactor program aiming at lifestyle approach along with medicines to help diabetics to fight against the disease and its complications. This program is implemented by a team consisting of Physician, nurses, therapists, dietician and clinical psychologists. Objective: To evaluate the effectiveness of a structured TLC program in diabetics and non diabetic patients undergoing CABG surgery.

Methods:
This study was carried out on 74 patients who underwent CABG. Patients were evaluated prior to surgery and were initiated into lifestyle changes based on Diet, Relaxation, Exercise, Attitude and Motivation viz. DREAM concept. Dietary advices focused on secondary prevention and risk factor control. Patients received personalized diet plans, food diary and advice. Relaxation techniques including deep breathing exercises, visualization and meditation were taught to cope with stress and anxiety components. Exercises were prescribed in the form of range of motion exercises, and unsupervised aerobic progressive walking with a target heart rate of 60 – 75 % depending on age and symptoms. Attitude modifications were effectively addressed to patients with problems related to smoking, short temper, anxiety, alcoholism and worries. Frequent follow ups, every 15 days was emphasized to motivate and sustain motivation in patients enrolled for TLC program.

Results:
Pre and post operative comparitive analysis showed statistically significant favourable deviation in the FBS levels ($p=0.047$), TC/HDL ratio ($p=0.05$), WHR ($p=0.033$) and BMI (0.046). These changes achieved 3 months post operative are in conformity with the existing data on Western patients who undergo supervised exercises.

Conclusions:
The statistically significant results suggests an encouraging pattern for effective TLC program which can also be used for secondary prevention of complications in diabetics. Patients outside hospital can be motivated to make and sustain comphrensive lifestyle changes.

Key Words: Therapeutic Lifestyle Changes; CABG; Diabetes
Funding Agency: None

Physical Medicine and Therapy and Rehabilitation
Category: Clinical

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Management of musculoskeletal pain in female patients with non cardiac chest pain – A preliminary report

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Introduction:
Normally, patients suspected of having angina pectoris are admitted to cardiology ward because the heart is under suspicion as the pain source. In more than 50% of these patients, the pain is non cardiac. These patients are usually reassured and discharged. However, most of these patients continued to suffer from residual pain and demanded an answer. The musculoskeletal system is recognized as a possible source of pain in patients with chest discomfort. Objective :To diagnose the musculoskeletal causes of non cardiac chest pain.To assess the outcome of an appropriate pain management program for these patients

Methods:
Patients were evaluated using the American Rheumatology Association guidelines. Clinical examination was focused on Cervical spine, Dorsal spine, Shoulder and Tender points examination. Relevant investigations including Biochemical, Xrays and Musculoskeletal Ultrasound were performed and diagnosis was arrived at. The patients were prescribed appropriate treatment program including oral analgesics and NSAIDs, Local infiltrations, physical modalities (superficial and deep heating), exercise therapy and aqua therapy. Outcome was measured using Visual Analogue Scale and Quality of Life (QOL).The preliminary report on this ongoing study is presented.

Results:
Total number of patients=50. Mean age=58.82 years. 80% were Kuwaitis. 92% were females. The musculoskeletal causes of pain were 1) Shoulder disorders (supraspinatus tendinosis, subacromial bursitis, Adhesive capsulitis) in 40 % and 2) Fibromyalgia in 32%. 3) Myofascial pain 4) Spondylosis (Cervical, Dorsal) and 5) Costochondritis. 32% had associated Osteoporosis. More than one diagnosis was found in 60% of the patients.Treatment was individualized based on diagnosis. Mean VAS score was 82.3 and 40.1 before and after treatment respectively. Improvement in QOL was recorded in all patients

Conclusions:
Musculoskeletal pain is one of the most common cause of Non cardiac chest pain. Shoulder disorders and Fibromyalgia lead the spectrum. Accurate diagnosis and appropriate management relieves pain and anxiety and improves Quality of life in these patients

Key Words: Non cardiac Chest pain; Musculoskeletal; Quality of life
Funding Agency: None

Physiology
Category: Basic Sciences

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Estrogen Receptors Alpha and Beta in Rat Placenta: Detection by RT-PCR, Real Time PCR and Western Blotting

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Introduction:
High levels of estrogens during pregnancy not only retard placental and fetal growth but can lead to reproductive tract abnormalities in men. Estrogens act through estrogen receptors (ER) to modulate the transcription of target genes. These ER exist in two isoforms, ERalpha and ERbeta and recently several variants of these isoforms have been identified.

Methods:
The expressions of ER isoforms and variants have been studied in rat placenta at 16, 19 and 21 days gestation (dg). Gene expression was assessed using RT-PCR and real time PCR while protein expression was studied using Western blotting followed by immunodetection. Placental homogenates were probed with: a monoclonal antibody raised against the steroid binding domain of the ERalpha (ERalpha-S), a monoclonal antibody raised against the hinge region of ERalpha (ERalpha-H) and a polyclonal antibody raised against the amino terminus of ERbeta.

Results:
ERalpha and ERbeta mRNA and protein were detected from as early as 16 dg. Two PCR products were detected for ERalpha, one for the wild type ERalpha, and a smaller variant. Using real time PCR, results suggest the presence of a single product for ERbeta. The antibodies used for detection of ERalpha protein both identified a single 67 kDa isoform; however a second 54 kDa band, which may be an ERalpha variant, was identified when using the ERalpha-H antibody. The abundance of both ERalpha bands decreased significantly between 16 and 19 dg. As for ERbeta, four bands (76, 59, 54 and 41 kDa) were detected. The abundance of the 59 and 54 kDa bands decreased significantly between 16 and 19 dg.

Conclusions:
This study shows that both ER protein isoforms and their variants are present in rat placenta. The decrease in their expression near parturition suggests that the placenta may be relatively unresponsive to estrogens at this stage.

Key Words: Estrogen receptors; Pregnancy; Placenta
Funding Agency: Kuwait University Grant # MY02/99

Physiology
Category: Basic Sciences

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Physiological Profiles of Kuwaiti National Fencing Team

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Introduction:
Fencing is a sport as well as an art characterized by a combination of co-ordination and timing skill of correct movements. The aim of this study was to investigate the physiological characteristics of Kuwaiti National Fencing Team.

Methods:
The subjects were14 male Kuwaiti national fencing team players between the age of 18-35 yrs, G all (N=14), divided into three age groups:G1(N=4)<25 yr;G2(N=5) between25-29 yr and, G3(N=5)>30 yr. Each player signed a consent form before the start of the testing. Aerobic power was measured by COSMED Quarkb2 instrument. Body composition was measured using Harpenden skinfold caliper Height and weight were measured using health O meter scale.

Results:
The following results for the mean and standard error (SE) for all players (G all) and between each Group (G1, G2, G3).The mean and SE of age (yr); Ht (cm); Wt (kg); %Fat and VO2 max (ml.min-1.kg-1) for G all, G1, G2andG3 corresponds to 26.6±1.2; 21.5±1.2; 26.4±0.7; 31.0±1.0. 175.4±1.6; 173.5±1.4; 176.8±3.5; 175.6±3.0. 79.5±3.8; 75.7±5.0; 77.2±7.1; 84.8±7.5. 15.6±1.6; 14.6±1.8;13.6±2.6; 18.4±3.3. 47.7±1.8; 53.6±2.5; 45.2±2.7; 45.4±2.6 respectively.

Conclusions:
In this group of fencing athletes, it appear that they have lower average VO2max than endurance sports. Average%Fat was higher than that of endurance sports. Fencing therefore, is considered to be a power sport and the fencing athletes had lower average VO2 max and higher percentage of body fat than the average endurance athletes.

Key Words: VO2 max; Percent Fat; Fencing
Funding Agency: None

Physiology
Category: Basic Sciences

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Expression and functional activity of equilibrative nucleoside transporters in human choroid plexus

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Introduction:
This study investigated expression of human equilibrative human nucleoside transporters (hENTs) 1-4 in freshly isolated pieces of human choroid plexus (CP) at transcript and protein level. Their distribution between apical and basolateral membrane was assessed by the uptake studies.

Methods:
The tissue used represented a spare material which had to be dissected from the CPs in the Department of Neurosurgery, Clinical Centre, Belgrade, Serbia; this procedure has been approved by the local Ethic Committee. The expression at transcript level was assessed by RT-PCR and at protein level by immunoblotting, using the affinity-purified rabbit antibodies. Functional studies were performed by measuring tissue uptake of [^{3}H] inosine and [^{3}H] adenosine.

Results:
RT PCR revealed that transcripts of hENT2, hENT3 and hENT4 were present in the RNA extracts from the tissue. Immunoblots of the membrane extracts isolated from human CP revealed the presence of the nucleoside transporters, hENT1, hENT2 hENT3 and hENT4. The specificity of the antibodies for the cognate transporter was demonstrated by the lack of staining using primary antibodies that had been pre-incubated with the peptide sequences that were used for immunization. Uptake studies revealed that hENT1 is not functional at the apical CP side (facing the ventricles) so this transporter is probably confined to the CP's basolateral membrane. hENT2 was functionally active at the apical membrane, while hENT4 was active at the apical side at low pH of the buffer.

Conclusions:
These results revealed that the distribution of these transporters in the human CP is uneven (polar). Equilibrative uptake of nucleosides across the apical side of the CPs (i.e. from the cerebrospinal fluid (CSF) is mediated mainly via hENT2. However, when pH of the CSF decreases, hENT4 also mediates uptake of nucleosides, since this novel equilibrative transporter is pH dependent.

Key Words: Choroid plexus; Equilibrative transport; Nucleosides
Funding Agency: None

Physiology
Category: Graduate (PhD: Basic Sciences)

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$H_2 O_2$ -induced Oxidatvie Stress Alters IKDR

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Introduction:
The delayed rectifier potassium channel (K_{DR}) plays an essential role in the generation of electrical activity in the brain, and may be affected by oxidative stress conditions. In vitro, direct application of membrane permeable $H_2 O_2$ has been frequently used to induce oxidative stress conditions. We investigated the effects of $H_2 O_2$ -induced oxidative stress on the delayed rectifier current (IK_{DR}) in hippocampal CA1 neurons, known to be especially vulnerable to oxidative stress.

Methods:
The Whole Cell Patch-clamp technique was used to measure IK_{DR}. Measurements were obtained from freshly dissociated hippocampal CA1 neurons in control solution and from the same neurons after exposure to short-term and long- term $H_2 O_2$ external applications (at 0.1 mM, 1 mM, and 10 mM).

Results:
With short-term (6 minutes) $H_2 O_2$ (1 mM) treatment, IKDR measured in the $H_2 O_2$ -containing solution (778±23 pA, n=20), was smaller than that measured in the control Ca^{2+} - free Hepes solution (1112±38 pA, n=20). With long-term (40 minutes, 80 minutes) $H_2 O_2$ (0.1 mM, 10 mM) treatment, the neuron lost its distinctive shape (rounded up) and the neurite almost disappeared.

Conclusions:
These results show that oxidative stress inhibits IK_{DR} and thus may alter neural activity.

Key Words: Oxidative stress; Potassium Current; Hippocampus
Funding Agency: Kuwait University Grant # MY 01/04

Physiology
Category: Basic Sciences

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Transitory increase in baroreflex sensitivity during heat stress in rats.

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Introduction:
Baroreflex seems to play an important role in ensuring survival during heat exposure, but currently available information about heat dependent changes in the baroreflex sensitivity (BRS) is rather conflicting. It has been proposed that HSP70 induced by heat stress in nucleus tractus solitarii (NTS) may protect animals against heat-induced hemodynamic dysfunctions by amplifying the BRS. However, heat stress also stimulates expression of the c-Fos protein, which is known to be responsible for BRS attenuation in hypertension. The objectives of this study were to characterize effects of hyperthermia on hemodynamics, baroreflex sensitivity, and autonomic nervous system activity as well as on c-Fos and Hsp70 proteins expression in NTS.

Methods:
Wistar male rats were implanted with a telemetric device to monitor ECG, arterial blood pressure, core body temperature and animal activity. Core body temperature of freely moving animals was increased up to 41.5^{o}C for 15 minutes by heating in the climatic chamber. Hemodynamics, heart rate and arterial pressure variability as well as BRS were assessed. The c-Fos and Hsp70 proteins in NTS were determined with immunohistochemistry.

Results:
Outset of heating, up to 40^{o}C, was associated with increased vagal stimulation to the heart as well as augmented BRS. Further heating reduced the vagal activity and significantly elevated sympathetic stimulation to the heart and particularly arterioles. BRS returned to the pre-heating values. 4 hours after heating c-Fos and Hsp70 in the NTS were significantly elevated.

Conclusions:
Early augmentation of BRS is probably due to the amplified vagal activity and helps to stabilize circulation during heating. However, this change is only temporary and later reduction in the vagal stimulation may facilitate the transition to the heat stroke. Postulated inhibitory effect of c-Fos expression on BRS was probably reversed by the simultaneously elevated HSP70 expression.

Key Words: Heat stress; Baroreflex; Heart rate variability
Funding Agency: Department of Physiology

Psychiatry
Category: Basic Sciences

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Gender Differences in Depression among undergraduates from Gulf Cooperation Council (GCC) Countries.

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Introduction:
The Prevalence rate of depression is higher in women than men. A large number of studies provide strong evidence that gender differences contribute significantly to the higher prevalence of depression- disorders in women and men in industrials countries than in the developing countries (WHO, 2002). This study aims at examining gender difference in depression among undergraduates from GCC countries.

Methods:
The sample included 3, 028 respondents from the six GCC countries : King Saud University, Riyadh, Saudi Arabia (n=630); Kuwait University, Kuwait (n=510);Bahrain University, Manama, Bahrain (n=512); Qatar University, Doha, Qatar (n=500);United Arab Emirates University, Alain, UAE (n=350); and Sultan Qaboos University, Muscat, Oman (n=526).The ages of the participants ranged between 18-25 years. The Arabic version of the Beck Depression Inventory second edition BDI-II (Beck, et al, 1996 ; Alansari, 2003, 2006) was used for assessing depression.

Results:
Statistical Analysis: The data were analyzed using SPSS- V.14.Means; standard deviation, t-test, and univariate analysis of variance were calculated. Results: There were significant gender differences in four GCC countries. Females tended to have higher depression than the males - namely Saudi Arabia ($t=4.55$, $p<.001$), Oman ($t=3.25$, $p<.01$), Kuwait ($t=2.38$, $p<.02$), and Qatar ($t=2.32$, $p<.02$). However, no significant gender difference in depression was found in Bahrain ($t=0.06$, $p>.05$) or United Arab Emirates ($t=0.74$, $p>.05$).Moreover, the interaction effect of gender and culture with depression was found to be significant ($f=80.63$, $p<.001$) in all these countries.

Conclusions:
Gender differences in depression exist but vary between countries. This difference observed here in four of the six GCC countries may be attributable to cross-cultural factors, probably reflecting gender equality. This warrants further investigation.

Key Words: Gender; Depression; GCC Countries
Funding Agency: kuwait university, Research Administration grant # ORP001

Psychiatry
Category: Clinical

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Community living women with breast, cervical and ovarian cancers: comparison of their subjective quality of life with those of their family caregivers

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Introduction:
Quality of life (QOL) issues are important in cancer care as outcome measures because the effectiveness of modern treatments has resulted in increasing survival rates. QOL studies on cancer patients and their family caregivers are rare from Arabia. We assessed subjective QOL of stable Sudanese cancer patients and their family caregivers, using the WHO 26-item QOL Instrument, examined patient-caregiver concordance of ratings, and assessed the variables that impact on their QOL, with a view to delineating factors that can enhance quality of care.

Methods:
Responses of oncology outpatients with breast cancer (117), cervical cancer (46) and ovarian cancer (18) (mean age 44.6 SD 11.5) were compared with those of their family caregivers (mean age 43.1 SD13.1).

Results:
The three cancer groups had similar QOL domain scores (e.g., general facet: 8.4 SD1.8; 7.8 SD2.4; 8.4 SD1.7, respectively) which were significantly lower than those of the caregivers (9.3 SD 1.1, $P < 0.001$). Cancer patients had significantly higher QOL domain scores than psychiatric and diabetic patients studied previously in Sudan. Patients with higher education, better employment, longer duration of illness and lesser side effects had higher QOL. Patient and caregiver characteristics mutually interacted and impacted significantly on each other's QOL. Correlations between patient's ratings and caregiver impression of patient's QOL were high ($r=0.35$ to 0.64, $P < 0.001$). Caregiver impression was a significant predictor of patient's ($B =0.54$) and caregiver's ($B =0.24$) QOL.

Conclusions:
The patient-caregiver dyad should be regarded as a unit for treatment in cancer care. Attention to side effects, caregiver education and psychosocial support for patients and caregivers can improve patient's QOL, which should become an important outcome measure in the clinical setting.

Key Words: Breast - cervix - ovarian; Cancer - patient - caregiver; Quality - of - life
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Recurrent glomerulonephritis in renal allograft recipients.

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Introduction:
Recurrence of glomerulonephritis (GN) in the allograft continues to be a significant cause of morbidity and graft loss in the renal transplant population, even with the improvement in short and long term kidney survival in the last 2 decades.The current study was to evaluate the impact of recurrent GN in renal transplant recipients (RTR) in our centre.

Methods:
A retrospective analysis was done on 145 RTR with biopsy proven pre transplant diagnosis of GN for the prevalence and outcome of recurrent GN in the graft. The patients were followed up for an average of 5.1 years with a minimum period of 1 year. Recurrent GN (Group1) was diagnosed by renal biopsy and the data from these patients were compared with those without recurrence (Group2).

Results:
Recurrent GN (Group1) was diagnosed in 23 (15.8%) patients after an average period of 25.3 months and the diagnoses include Focal Segmental Glomerulosclerosis, IgA nephropathy, membranous nephropathy, membranoproliferative glomerulonephritis and lupus nephritis. The results of group1 were compared with those of group 2 (n=122). The demographic characteristics of the two groups were not significantly different.The mean period of follow up for these patients was 5.1 years with a minimum period of 1 year and the mean period to diagnosis of recurrent GN was 25.3 months. Graft loss occurred in 5 (21.7%) patients in group 1 compared to 6 (4.9%) in group2 and there were no patient loss in both the groups. Mean current serum creatinine was higher in group 1, 180 umol/L; compared to 123.8 umol/L in group 2.

Conclusions:
Recurrent GN is a significant problem after renal transplantation and is associated with increased incidence of graft loss and graft dysfunction

Key Words: Renal Transplantation; Recurrent glomerulonephritis; Graft loss
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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A Comparison of Specificity of Urine Cytology, Urinary Nuclear Matrix Protein 22 [NMP22] and Multi-target Fluorescent in Situ Hybridization [FISH] Assay in Bladder Cancer Patients with no Recurrence at Surveillance

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Introduction:
The UroVysion fluorescence in situ hybridization assay [FISH] is a multi-target assay that detects aneuploidy of chromosomes 3, 7 and 17 and loss of the 9p21 band in exfoliated cells in urine from patients with transitional cell carcinoma [TCC]. The nuclear matrix protein 22 [NMP22] detects elevated amounts of nuclear mitotic apparatus protein, a component of the nuclear matrix essential for cell division that is released into urine at cell death. Both tests have been reported to have higher sensitivity and specificity than urine cytology in patients with cystoscopic and histologic TCC either at initial diagnosis or recurrence. We compared the specificity of urine cytology, urinary NMP22 qualitative test [positive or negative] with those of FISH assay in patients with known TCC of bladder but without tumour recurrence during surveillance.

Methods:
Urine samples collected before cystoscopy in 275 patients with previously diagnosed TCC of the bladder was subjected to urine cytology, urinary NMP22 qualitative and FISH assay. Positive FISH result was defined as 5 transitional cells or greater with a gain of 2 or more chromosomes 3, 7 or 17; 12 cells or greater with 9p21 deletion. The specificity of urine cytology, NMP22, FISH assay was compared in patients without tumour recurrence after cystoscopy and bladder biopsy.

Results:
In 81 urine samples from 55 patients, there was no tumour recurrence during surveillance. The specificity of (a) urine cytology, (b) NMP22 and (c) FISH assay was 93.3%, 68% and 21% respectively (Fisher's exact test: a versus b $p=0.01$, a versus c $p=0.001$ b versus c $p=0.001$).

Conclusions:
Urine cytology has higher specificity than NMP22 and FISH in bladder cancer patients without tumour recurrence. FISH is not an ideal urinary marker for surveillance in patients with bladder cancer because of very low specificity. However, NMP22 appears to have great potential as it is cost effective and provides a rapid diagnosis.

Key Words: Urothelial cancer; Urine cytology; Urinary tumour marker
Funding Agency: This work was supported by Kuwait University Research Grant # MS 02/03

Surgery and Transplantation
Category: Clinical

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Post transplant haemolytic uraemic syndrome (HUS); Single center experience

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Introduction:
Therapy in post transplant HUS is debated in literature. We aimed at finding prevalence and outcome of HUS in our transplant population.

Methods:
We retrospectively analyzed our data from medical records of 950 kidney recipients under follow up in our center since December 1994. We looked at the risk factors and basic criteria for diagnosis of the syndrome in these cases. We reviewed the kidney biopsies performed for these patients to exclude other conflicting diagnoses like antibody mediated rejection.

Results:
HUS was diagnosed in 12 patients out of 950 following in our center (Prevalence 1.26%). 4 patients were male and 8 were females. None of them had HUS as the original kidney disease. Cyclosporine (CsA) was the primary immunosuppression in 10 and tacrolimus (Tac) in 2 patients. The median day of onset of HUS post transplant was 7 days. Criteria for diagnosis were anaemia (100%), thrombocytopenia (75%), elevated reticulocyte count (62.5%), fragmented red cells in blood smear (8.3%), elevated lactate dehydrogenase [LDH] enzyme (83.3%), increased fibrin degradation product [FDP] (83.3%), reduced haptoglobin level (42.9%) and hyperbilirubinemia (25%). Calcineurin inhibitor (CNI) elimination was the first step in the management. Transfusion of fresh frozen plasma [FFP] was used in 10 patients and plasma exchange [PE] using FFP as a replacement agent in the other two. All grafts recovered function. Two patients had reintroduction of CsA or Tac after complete clinical and laboratory recovery of CNI induced HUS. Both developed recurrence of HUS. While the former did not the later did recover on further treatment of HUS.

Conclusions:
Early CNI discontinuation and plasma replacement therapy can revert CNI induced HUS and save the graft. Reintroduction of CNI is deleterious to the graft and should be avoided.

Key Words: Kidney transplantation; Immunosuppression; Hemolytic uremic syndrome
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Hypomagnesemia in the Early Renal Transplant

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Introduction:
Magnesium the 2nd most abundant intracellular cation in the human body plays a key role in all enzymatic reactions involving ATP. The presence of hypomagnesemia should be suspected in the following situations: Chronic diarrhea, hypocalcemia, refractory hypokalemia, ventricular arrhythmia. Therapy with cyclosporin or tacrolimus increases the urinary Loses of magnesium in renal transplant recipients.The aim of the study was to analyze the effect of the hypomagnesium early post transplant and to identify its etiological factors.

Methods:
This is a retrospective study. Forty nine renal transplant recipients are selected, following blood tests were performed (Day O, 7, 14) total Mg, K, Albumin, Alkaline phosphatase, bicarbonate, FBS, cholesterol, PTH. These patients are assessed clinically in the early post operative periods for convulsion and cardiac (palpitation and chest pain) complications.

Results:
There is insignificant negative correlation between total magnesium and patients developing convulsions early post operative period at the beginning, middle and end of study (P value 0.06, 0.0078, 0.07 respectively).There is positive significant correlation between hypomagnesemia and improving renal function (beginning, middle and end of study (P value 0.002, 0.01, 0.03) and total cholesterol (at middle and end of study (P value 0.002, 0.05) respectively). There is significant negative correlation at the beginning and middle of study between total magnesium and Tacrolimus level (P value 0.04, 0.0002) respectively.

Conclusions:
Hypomagnesemia should be considered as an etiology for convulsion in early post operative period in RTR. Hypomagnesemia is associated with hypokalemia, glucose intolerance, and lipid abnormalities in RTR. Hypomagnesemia is more prominent in patients with Tacrolimus treatment compared to other immunosuppression in early post transplant.

Key Words: Renal; Transplantation; Magenesium
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Gender differences in mortality due to burns in Kuwait

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Introduction:
There are ample epidemiological and predictive studies concerning the incidence and mortality among burn patients worldwide. Though, hardly any studies have explored the association of gender differences and mortality in burns and this aspect remains a little researched area. Being the first gender-focused study on burn patients in Kuwait, our aim is to explore the association of gender differences with mortality concerning burn patients, in the light of demographic, clinical and outcome factors.

Methods:
A prospective study on burn patients, admitted at Al-Babtain Burn Center in Kuwait during 1993-2004, was conducted, comprising a total of 2690 cases. The data, from in-patients records included age, gender, nationality, as well as clinical factors, such as cause of burn, total body surface area (TBSA), duration of hospital stay and patient's outcome, for analysis.

Results:
The overall incidence rate, during 12-year period, was 10.8/100, 000 population and a mortality rate of 0.58/100, 000 population. From a total of 2690 burn patients, 145 (5.4%) died, giving a mortality rate of 0.526 in males and 0.674/100, 000 among females.The proportion of female deaths (8.2%) was significantly higher ($p<0.001$) than that in males (4.2%). The oveall median age, 20 years, in females was significantly lower, as compared to 26 years in males ($p<0.001$). Flame was the main cause of burns in both the gender. The multiple logistic regression model predicted that females, aged 60 years and above, flame burns and TBSA > 50%, are the most influencing risk factors for a fatal outcome at this center. The hospital stay was also found to be significantly higher ($p<001$) among females as compared to males (9 vs 4 days), in fatal cases.

Conclusions:
Female patients with flame burns, aged 60 years and above, and TBSA> 50%, need to be given special attention during in-patient care as they are more vulnerable with a high risk of mortality.

Key Words: Gender differences; Burn mortality; Logistic regression
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Necrotizing fasciitis of the neck: diagnosis and management in Kuwait

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Introduction:
Necrotizing fasciitis (NF) is a life-threatening, bacterial soft tissue infection characterized by progressive necrosis of skin, subcutaneous tissues, and fasciae. The abdominal wall, perineum and extremities are the most common sites of infection. The disease is more commonly seen in patients over forty years of age. The mortality rate ranges from 22 to 50%. Four patients are reported with NF of the head and neck, uncommon site for this rare infection. We present a retrospective study on patients who underwent radical surgical debridement (RSD) between 1995 and 2007.

Methods:
Records of patients with NF treated at Sabah and Jahra Hospitals between 1996 and 2007 were reviewed. The standard demographic data, clinical, radiologic and endoscopic evidences as well as the surgical procedures were noted. The outcome of surgery was analysed. All patients underwent RSD of the neck.

Results:
Total patients=4 (M=3, F=1). The age distribution was between 39 and 62 years. All patients were known diabetics. The infection was of dental origin in all cases. The diagnosis was made by plain film and C-T scan of the neck. Three patients were successfully treated with broad spectrum intravenous antibiotics and a RSD while one died of multi-organ system failure.

Conclusions:
Necrotizing fasciitis carries high morbidity and mortality rates. Early clinical diagnosis, broad spectrum antibiotics and an expeditious, radical surgical debridement remains the mainstay of optimal management. The place of hyperbaric oxygen in the treatment of necrotizing fasciitis is yet to be fully established and awaits longer-term follow-up results.

Key Words: Necrotizing fasciitis; Neck; Mediastinum
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Inferior turbinate hypertrophy: diagnosis and management in Kuwait

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Introduction:
The treatment of inferior turbinate hypertrophy (ITH) has incited considerable controversy. The premise of turbinate surgery is to treat nasal obstruction (NO) without affecting the vital functions of the nasal turbinates. Objective: to examine the safety and efficacy of partial inferior turbinectomy (PIT)and compare its outcome with other procedures such as electrocautery and laser turbinectomy (LT).

Methods:
Records of patients with ITH treated at Jahra Hospital between 1996 and 2007 were reviewed. The standard demographic data, clinical, radiologic and endoscopic evidences as well as the surgical procedures were noted.

Results:
Total patients=411 (M=227, F=184). The age distribution was between 8 and 57years.192 of the ITH were treated by PIT, 89 by submucosal resection (SMR), and 71 by submucosal diathermy (SMD) while the remainder required LT. 59% of cases underwent septoplasty and 24% FESS. The main outcome measurement was NO. Secondary outcome measurement included mean operative time (MOT) and the quality of convalescence QOC. While more than 93% experienced immediate improvement in NO(all techniques combined) only 74% showed long-lasting relief after a two-year follow-up. The latter were mainly treated by PIT. The MOT for PIT was shorter than most of the other techniques.The QOC was better after SMD and LT and bleeding was negligible. There were 27 conversions from the other techniques to a conventional PIT. There were four post-op bleeding that required packing.

Conclusions:
Partial turbinectomy is a safe and cost effective procedure. All techniques gave good short-term results. The choice of procedure depends on the surgeon's experience and the patient's preference. The advantages of SMD and LT were offset by the absence of long-lasting positive outcome. The importance of a long lasting positive outcome is underscored.

Key Words: Inferior turbinate hypertrophy; Partial turbinectomy; Endoscopy
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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The versatility of the medial thigh flap for coverage of large perineoscrotal defects

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Introduction:
Fournier's gangrene is a rare potentially fatal clinical entity. It is characterized by progressive spread of necrosis in the skin and subcutaneous tissue. Following aggressive surgical depridement, major scrotal and perineal defects with exposed testes are a challenge for reconstructive surgeons.

Methods:
This study presents the author's experience using the medial thigh flap for coverage of scrotal and perineal defects after depridement of Fournier's gangrene. Between July 2005 and October 2006 at Al-Babtain Center for Burns and Plastic Surgery, nine medial thigh fasciocutaneuos flaps were performed in seven male adult patients.

Results:
All flaps survived well, with the exception of partial distal necrosis in two cases. This was managed conservatively in one case, while the other case needed debridement and minimal advancement of the flap

Conclusions:
The medial thigh fasciocutaneuos flap offers a good option for Perineoscrotal defects. The flap provided a single stage, stable, well vascularized soft tissue coverage in our patients with no significant complications

Key Words: Medial thigh ; Fournies gangrene; Fasciocutaneous flap
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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The Effect of Green tea in normalization of Liver function test in experimental induced liver injury

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Introduction:
This study was carried out to understand the influence of green tea in preventing experimentally induced liver injury, and the involvement of trace elements and whether such changes could be normalized after treatment with green tea.

Methods:
Sixty male Wister rats weighing (220-280 g) were used. Liver injury was induced by subcutaneous administration of thioacetamide (200mg/Kg/wt) and the plasma level of Zn and Cu along with alanine aminotransferase (Alt) and asparate aminotransferase (Ast) studied. H and E stained liver sections were evaluated for pathological changes

Results:
Administration of green tea improved the plasma level of Zn, Cu and Cu/Zn ratio. Thioacetamide induced elevation of Ast in experimental animals; however, green tea administration improved both Ast level and Ast/Alt ratio significantly. Histopathological studies have shown that green tea administration showed improvement in hepatic architecture at the initial stages of the study.

Conclusions:
The present study shows that one dose of thioacetamide administration resulted in performed liver injury and supplementation of green tea has improved plasma level of Zn and Cu as well as Ast, Alt and Ast/Alt ratio.

Key Words: Green Tea ; Liver injury; Trace elements
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Steroid avoidance in renal transplantation – Preliminary report of a prospective open labeled controlled study

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Introduction:
Steroids have remained the mainstay of immunosuppression but recent data indicate steroid free regimens are feasible in renal transplant recipients, thereby reducing the side effects and improving compliance.

Methods:
A prospective open labeled controlled study to assess the safety and efficacy of steroid avoidance in renal transplants was initiated in our centre. Inclusion criteria were, severe diabetes, ischemic heart disease, gross obesity and bone complications and exclusion criteria included high risk patients with retransplants, PRA of >20 or previous positive cross match. Primary end point was biopsy proven acute rejection.Total number studied was 40 with 20 in the steroid free group and 20 in the control group.Induction therapy included either antithymocyte globulin or interleukin 2 receptor antibody. Steroids were given only for 5 days and then discontinued and the maintenance immunosuppression given was a combination of mycophenolate mofetil, Tacrolimus, Rapamicin or Cyclosporine.These subjects were compared to matched controls and were followed up for a median period of 8.8 months with a minimum of 3 months.

Results:
Demographic details were comparable in both groups. Patient survival and graft survival were 100% in both groups. Biopsy proven acute rejection episodes were 1 (5%) in the steroid group, compared to 3 (15%) in the control group with a mean serum creatinine of 118.8 umol/L and 108.2 umol/L respectively. Post transplant hypertension, higher number of antihypertensive medications, weight gain and post transplant diabetes mellitus were more common in the control group than the steroid free group.

Conclusions:
Steroid avoidance in selected patients using newer immunosuppressive protocols provides comparable graft survival, patient survival and rejection episodes and low incidence of steroid related morbidities.

Key Words: Renal Transplantation; Immunosuppression; Acute rejection
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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The Glidescope system: a clinical assessment of performance.

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Introduction:
The Glidescope is a new videolaryngoscope. It has a digital camera incorporated in the blade which displays a view of the vocal cords on a monitor. This allows the placement of a tracheal tube to be visualised.

Methods:
We describe its performance in 60 patients who required orotracheal intubations for elective surgery. Two Anaesthesiologists performed 30 intubations each. Intubation's with the Glidescope was successful in 58 of the 60 cases. The three failures occurred early in the series and were attributed to the initial learning curve.

Results:
The success rate after the first twenty patients in each series was 100%. The median (IQR [range]) time to intubations was 30 (20-45 [10-75]) s. The Glidescope provided a grade I view of the glottis in 54 cases and a grade II view in six cases. The view of the larynx was improved in more than 75 % (45) of the cases. The Glidescope improved the view by one grade in 32 and by two grades in five patients

Conclusions:
We conclude that the Glidescope is an effective device for tracheal intubation's and provides an improved view of the larynx. Further clinical studies are necessary to evaluate its role in airways that are difficult to manage.

Key Words: The Glidescope system; Tracheal intubation's; Performance
Funding Agency: Central Circirle Company, Kuwait

Surgery and Transplantation
Category: Clinical

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Preventing pain during injection of propofol: effects of a new emulsion with lidocaine addition

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Introduction:
Previous studies found that lidocaine addition to propofol long-chain triglyceride was associated with a lower incidence of injection pain than medium-chain triglyceride/long-chain triglyceride formulation, but the incidence was still high (30-45 %). Our study investigated whether the incidence of injection pain could be further reduced by the addition of lidocaine (10 mg, 20: 1) to propofol medium-chain triglyceride/long-chain triglyceride.

Methods:
In a randomized double-blind controlled trial 480 patients scheduled to undergoing for general anaesthesia were assigned to receive one of the following four options: Propofol medium-chain triglyceride/long-chain triglyceride+lidocaine; Propofol long-chain triglyceride +lidocaine;Propofol medium-chain triglyceride/long-chain triglyceride or ;Propofol long-chain triglyceride; Propofol was injected to reach grade 3 of the Observer's Assessment of Alertness/Sedation scale.

Results:
Incidence of injection pain was 18% in the propofol medium-chain triglyceride/long-chain triglyceride +lidocaine group, 31% in the propofol long-chain triglyceride +lidocaine group, 47% in the propofol medium-chain triglyceride/long-chain triglyceride group and 60% in the long-chain triglyceride group. Propofol medium-chain triglyceride/long-chain triglyceride + lidocaine was associated with a statistically significant reduced incidence of injection pain compared with propofol long-chain triglyceride +lidocaine (P =0.0249, number needed to treat =7.7).

Conclusions:
Premixing propofol medium-chain triglyceride/long-chain triglyceride with lidocaine is one of the most effective measures currently available to reduce the incidence of injection pain in sedated patients during regional anaesthesia.

Key Words: Pain; Propofol New Emulsion; Lidocaine
Funding Agency: B.Braun, Germany and Kuwait

Surgery and Transplantation
Category: Clinical

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Kidney Transplantation in the Elderly, Kuwait experience

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Introduction:
The number of elderly patients accepted in renal replacement programmes is increasing. There is a general agreement that age per se does not constitute a contraindication to transplantation. Yet many centres are still reluctant to accept patients >60 years old, as they are frail, have more comorbid conditions and their overall life expectancy is lower.The aim of this study was to investigate whether or not transplantation provides any survival benefit in this group of patients.

Methods:
This study is a retrospective case control analysis study in elderly patients (Group I; >60 years). Data were collected from 11/1993 till 5/2003.Data were compared to those obtained in patients (Group II) who were matched for HLA mismatches and time of follow up but not with recipients'age(20-50).Primary end points are Graft loss and/or patient death, while secondary end point are Cerebro-cardiovascular events, malignancies or rejection.

Results:
Thirty-two patients with mean age(±SD) 63.4(±3.2), ranged from 60 to 73 years old (11 females and 21 males) were compared with 32 patients with mean age(±SD) 33.5(±7.46) ranged from 21 to 50 (11 females and 21 males). There is no statistically significant difference between the 2 groups in the result of mean s.creatinine after 1 year while mean s.creatinine after 3 years in Gr II is significantly higher than Gr I ($p<0.003$)and prevalence of malignancy was similar in both groups (one patient in each group). Seven graft were lost in Gr I (6 due to patient deaths and 1 from trauma) while only 1 was lost in Gr II (due to renal vein thrombosis) ($p <0.01$).

Conclusions:
Elderly age was associated with lower number of graft losses due to rejection, while they had higher death rate resulting in significantly worse overall renal transplant survival.

Key Words: Renal transplantation; Elderly; Outcome
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Gastric Bypass: Early Experience

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Introduction:
Obesity is chronic disease with Major health problems. Failure rate of non-surgical treatment is up to 95%. Roux-n-Y gastric bypass (RYGBP) is the gold stander for maintaining weight loss.

Methods:
From April 2003 until October 2006 we conducted a prospective study in 63 patients (51 females and 12 males) diagnosed with morbid obesity. These patients fulfilled the criteria for weight loss surgery (WLS) according to the National Institute of Health (INH) and American Society of Bariatric Surgery (ASBS).

Results:
The mean age 33.59 years(range 17-54 years). The mean Body Mass Index was 46.27 (range 38-63.6).The most common preoperative co-morbidities were diabetus mellitus in 6 patients (9.5%), hypertension in 6 patients (9.5%), disc prolapse in 5 patients (7.9%) and Gall stones in 4 patients (6.3%). 29 patients (46.04%) had previous abdominal surgeries including laparoscopic cholecystectomy in 5 patients (7.9%), laparoscopic gastric banding in 11 patients (17.5%), laparoscopic gastric band removal in 5 patients (7.9%) and gynecological surgery in 7 patients (11.14%). Open Roux-n-Y gastric bypass (ORYGBP) done in 8 patients (12.7%), laparoscopic (LRYGBP) in 48 patients (76.2%), laparoscopic gastric band removal with RYGBP in 6 patients (9.52%), open bilopancreatic diversion and duodenal switch (BPDDS) in 1 patient (1.6%). There was one conversion in the laparoscopic group. The mean operative time was 135 minutes (range 90-165 minutes). The mean hospital stay was 3 days (range:2.5-4 days). The post operative complication including GIT bleeding in 5 patients (7.9%), Wernike's encephalopathy and psychological disorder in 2 patients (3.2%). There was no mortality. The mean follow up was 8.3 (range 1-22) months. The mean weight loss was 34.59 (range 76.04-10.8) kg. The excess weight loss (EWL%) was 27.3 (range 11.97-40.16)%.

Conclusions:
Gastric bypass surgery are safe and effective in achieving and maintaining weight loss.

Key Words: Morbid Obesity; Gastric bypass; Weight loss
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Turbinectomy Assisted by Videoendoscoopy and Mircrodebrider

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Introduction:
Nasal obstruction is the most common complaint in; ENT practice and it is associated with septal deviation or deformities of the lateral wall of the nose, as well as chronic inflammatory diseases of sinus and nasal cavities. Today the modern functional sinus surgery allows the one step management of structural deformities of the nose and of inflammatory diseases of nasal and paranasal cavities providing good respiratory function.Aim: The aim of this study is to show our experience in turbinectomies powered by videoendoscopy and microdebrider (soft tissue shaver) in Jahra Hospital. The trubinectomies were a supplementary procedure of nasal surgeries in 20 % patients with nasal obstruction.

Methods:
The trubinectomies were associated 45% with nasal septum surgery 40% with functional Endoscopic sinus surgery (FESS) and 15% isolated cases. The Turbinectomy was always partial removing all the soft tissue with the microdebrider, exposing the bone framework and then, cutting it partially, as conservative as possible if necessary. Bleeding areas were stopped by electro coagulation if needed. In all cases a septal nasal splint of sailastic was sutured in for 10 days in order to avoid nasal synechiae between the septum and the nasal lateral wall.

Results:
In this sample, we did not observe nasal bleeding after surgery. No nasal synechia between the nasal septum and the middle turbinate. Nasal crusts were common in the first six weeks after surgery, causing nasal obstruction; buffered isotonic saline nasal washings relieved them.

Conclusions:
Turbinectomy assisted by videoendoscoopy and microdebrider provided better control of this surgical procedure, lowering the rate of post-operative complications and enhancing respiratory nasal flow.

Key Words: Turbenectomy; FESS; Nasal obstruction
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Quadruple immunosuppression reduces acute rejection episodes in renal transplantation.

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Introduction:
Acute rejection episodes (ARE) have been one of the major causes of graft loss and morbidity in renal transplantation.This study investigates the impact of quadruple immunosuppression including induction with Antithymocyte Globulin (ATG) or interleukin 2 receptor antibody (IL2Rab), followed by maintenance therapy with steroids, mycophenolate mofetil (MMF) and a calcineurin inhibitor (CNI), on ARE in renal transplant recipients.

Methods:
175 renal transplants done over 2 years with a follow up period of 6 to 18 months were analyzed regarding immunosuppressive regimens, donor type, HLA mismatches and delayed graft function, to correlate with the incidence, severity and response to therapy of ARE. 82 patients received ATG, 87 patients received IL2Rab and 6 patients received no drug as induction therapy. Maintenance immunosuppression included triple drug therapy with steroid, MMF and CNI.There were 99 male and 76 female recipients of age groups, <18years (n=24), >60 years (n=26) and 18 to 60 years (n=125). 122 patients received kidneys from live donors while 53 received from deceased donors of which 15 had delayed graft function (DGF).

Results:
The acute rejection rate was 26/175 (14.8%) of which 17 (65.3%) occurred within the first 3 months. There were no significant differences in ARE among the different immunosuppression protocols. Subjects with 4 or more HLA mismatches displayed more ARE (25%) compared with those with 3or less (6.9%). Deceased donor recipients had a higher ARE (18.8%) compared with live donor recipients (13.1%) and subjects with DGF had a higher incidence of ARE (33.3%) than those without them (13.1%). Subjects below the age of 18 years had higher incidence of ARE (29.1%) compared to other age groups.

Conclusions:
Quadruple immunosuppression reduced ARE to below 15%. Higher HLA mismatches, deceased donor, DGF and recipient age below 18 were observed to be major risk factors for the development of ARE

Key Words: Renal transplantation; Quadruple immunosuppression; Acute rejection
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Joint departments in a provincial Irish setting

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Introduction:
The delivery of a safe, appropriate, efficient and timely acute hospital service continues to be a challenge for health service professionals. The medical professional and regulatory authorities have introduced strict safety criteria, best practice guidelines and revised standards of care. Within the above parameters the employing authorities are encouraging new work practices to facilitate more comprehensive and streamlined services for patients.

Methods:
Drogheda and Dundalk are the two principal towns, 35 kilometres apart, in County Louth on the East coast of the Republic of Ireland. In January 2005 a joint department of surgery was set up between Our Lady of Lourdes Hospital in Drogheda (OLLH) and the Louth County Hospital, Dundalk (LCH) where six consultant surgeons working in three teams provide elective and emergency services on two sites.

Results:
In parallel, a joint anaesthetic department provides for daily rotation of trainees. Most of the general elective surgery for both sites is now performed in the LCH. The OLLH site functions as a major trauma unit and is responsible for delivery of all specialised and major complex elective and emergency surgery. As a result of this new configuration there has been a significant increase in elective activity in LCH including a 2-fold increase in elective surgical procedures. This has reduced waiting times for these services (surgery, endoscopy and out-patients) to less than six weeks. A recent patient satisfaction survey revealed a 95% approval rating.

Conclusions:
This new development to date has achieved its objectives of improving services for patients and meeting the new quality benchmarks set by the profession.

Key Words: Joint; Surgery; Department
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Assessment of Moist Exposed Burn Ointment (MEBO) in the Healing of Pressure Ulcers: a Prospective Comparative Clinical Study

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Introduction:
Treatment modalities that promote wound healing are warranted. This study was conducted to assess the efficacy and safety of MEBO (Julphar Gulf Pharmaceutical Industries, UAE) as compared to topical antibiotic ointment (Fucidin, Leo Pharmaceutical, Denmark) in the healing of chronic pressure ulcers.

Methods:
From Jan 2003 to Jan 2006, 45 patients of both sexes with 88 pressure ulcers were categorized into 2 groups, those in group 1 (n=22) received MEBO while those in group 2 (n=23) received Fucidin. Their age ranged between 14 and 102 years with a mean of 69.5, b7.4 years. Patients had their ulcers prior to study entry for a mean of 10.55. Data collected included demographics, nutritional status, underlying predisposing disease and co-morbidities. Ulcer surface area (SA) and healing index (HI) were calculated and compared at twice weekly intervals for 3 months.

Results:
Patients in both groups had similar demographic and clinical features regarding age, gender, underlying predisposing factors, and co-morbidities. Ulcer characteristics were also similar with respect to number, site, size, duration, ulcer Departmenth and sepsis. There was a significant ($P<0.05$) increase in HI and reduction in ulcer SA on weeks two and four respectively, that was maintained through 12 weeks, in patients receiving MEBO as compared to those receiving Fucidin. Cumulative patient sample percentage showed that 55.8% of ulcers treated with MEBO had complete healing and None had a HI of <0.5 by 12 weeks, as opposed to 20.5% and 25% respectively, of those treated with Fucidin ($P<0.05$). Linear regression analysis showed that the change in ulcer size and HI can be attributed to ointment application ($r2 > 0.4$).

Conclusions:
Based on the data presented, it may be concluded that in addition to its safety, application of MEBO significantly promotes the healing of chronic pressure ulcers.

Key Words: Pressure ulcers; MEBO; Healing Index
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Vascular complications after renal transplantation

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Introduction:
One of the major complications that affect graft survival is Vascular. This includes vascular thrombosis, Arterial stenosis, Intra renal infarctions and Aneurysms.
Aim:
The Aim of the study is to evaluate the incidence and the various risk factors that would have lead to this complication at our center.

Methods:
A total of 678 renal transplants have been done during a period from November 1993 to May 2006.(487 live renal transplants and 191 cadaver). Retrospective analysis of the patient record was conducted.

Results:
A total of 32 recipients were detected to have vascular complication. Among these 13 were renal artery thrombosis (1.9%), 6 were renal vein thrombosis (0.8%), 6 were renal artery stenosis (0.8%), 6 were intra renal infarction (0.8%), 1 was a mycotic aneurysm (0.14%). Of these 17 Patients had cadaver renal transplant (8.9%) and 15 had Live renal transplants. Graft loss directly attributable to the vascular complication occurred in 16 patients (2.36%)

Conclusions:
The incidence of Vascular complication at our centre is 4.27%. There has been a significantly higher incidence noted in cadaver renal transplant. Almost all the patients were on Cyclosporine based immuno suppression protocol. The EGFR calculated at the time of the vascular complication was found to be low. All the patients were found to have a lower level of Hemoglobin. All these factors could be attributable as risk factors for the vascular complications. Maintaining proper hydration in the post operative period, correction of anemia, and starting all patients who are on Cyclosporine based regimen on low dose Aspirin would reduce the incidence further.

Key Words: Arterial thrombosis; Venous thrombosis; Renal transplantation
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Drinking green tea before fasting protects the intestinal mucosa of animals from free radical-induced damage

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Introduction:
Fasting is known to cause intestinal mucosal damage which could breach the intestinal barrier and contribute to migration of micro-organisms. In a previous histological study we showed that drinking green tea for two weeks protected the intestinal mucosa from fasting-induced damage in rats. However, the underlying protective mechanism was not understood. Therefore the objective of this project is to study the mechanisms involved in the protective effect of green tea on the intestinal mucosa.

Methods:
Four groups of male Wister rats were used (n=12 per group):
G1:Normal controls, on rat chow diet and water ad libitum.
G2:Animals on rat chow diet and water ad libitum were fasting for 3 days (only i.p. 10% glucose 40 ml/day).
G3:2 weeks of drinking green tea solution ad libitum (instead of water) and rat chow then fasted for 3 days.
G4: 2 weeks of drinking Vit. E-containing solution ad libitum (instead of water) and rat chow then fasted for 3 days.
On day 4 of fasting, blood was collected for biochemical analysis of total plasma antioxidants. After that the animals were euthanized and 2 inches of jejunum was removed for analysis of SOD, catalase and GPx by immunohistochemical methods and MPO by biochemical analysis.

Results:
Compared to G2 (fasting) group, G3 rats (pretreatment with green tea) showed: [1] A significant increase ($p<0.001$) in total plasma anti-oxidants, SOD and catalase in the intestinal mucosa, [2] A significant decrease ($p<0.001$) in the mucosal level of GPx and MPO. Although vitamin E pretreatment (G4) induced similar changes in the total antioxidant status, catalase and GPx as green tea; it was less effective in changing SOD and MPO.

Conclusions:
Pretreatment with green tea protects the intestinal mucosa of rats from fasting-induced damage by neutralizing free radicals.

Key Words: Green tea; Antioxidant; Free radicals in GIT
Funding Agency: Kuwait University Research Grant # MS 01/03

Surgery and Transplantation
Category: Basic Sciences

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Antioxidant and Anti-inflammatory Effects of Green Tea in The Repair of Fasting-Induced Intestinal Atrophy in Rats

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Introduction:
Previous histological studies from our laboratory showed that drinking green tea repairs the intestinal mucosal damage induced by fasting. However, the cellular and molecular mechanisms underlying the beneficial effects of green tea were not elucidated. Therefore this study is focused on investigating the mechanisms by which green tea helps in repairing the intestinal mucosa in the fasting-animal model.

Methods:
Five groups of male Wister rats were used (n=12 per group):
G1:Normal controls, on rat chow diet and water ad libitum.
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 allowed drinking water ad libitum for another 7 days.
G4:Same as G3 but on day 4 the animals were allowed drinking green tea solution ad libitum for another 7 days.
G5: Same as G3 but on day 4 the animals were allowed drinking vitamin E solution ad libitum for another 7 days.
On day 8, blood was collected for biochemical analysis of total plasma antioxidants following which the animals were euthanized and 2 inches of jejunum was removed for analysis of SOD, catalase, GPx and PCNA by immunohistochemical methods and MPO by biochemical analysis.

Results:
Compared to G3 (water group), the intestinal mucosa of G4 rats (green tea group) showed an increase ($p<0.001$) in total plasma anti-oxidants, SOD, catalase, GPx and PCNA and a decrease ($p<0.001$) in the level of MPO. Although G5 (vitamin E group) showed an increase the level of total plasma anti-oxidants; it was not as effective as green tea in inducing changes in the level of SOD, GPx and MPO.

Conclusions:
Drinking green tea after fasting repairs the intestinal mucosa of rats by inducing antioxidant mechanisms.

Key Words: Green Tea; Intestinal mucosa ; Free radicals in GIT
Funding Agency: Kuwait University Research Administration Grant # MS 01/03

Surgery and Transplantation
Category: Clinical

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Lymphocele following Renal Transplantation

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Introduction:
In this retrospective study we explore the incidence, clinical presentations, and outcome of lymphocele in renal recipients.

Methods:
677 patients (393 males and 284 females), aged 3 – 76 years, received renal allograft from 486 living and 191 cadaveric donors. 73 of recipients were under the age of 18 years, and the procedure was re-transplantation in 40 patients. Diagnosis of lymphocele was made basically by ultra sound examination, and symptomatic collections were drained either per continuously or into the peritoneal cavity.

Results:
68 instances of lymphocele collections were diagnosed at 2 weeks to 9 months after transplantation, in 40 male and 28 female recipients. Kidney grafts were obtained from 45 living and 23 cadaveric donors. 6 patients were children, and the procedure was re-transplantation in 3 patients. Symptomatic Lymphocele presented clinically as pelvi-abdominal swelling alone (45 cases), or as a swelling associated with manifestations of ureteric and/or venous compression (23 cases). It was treated by either Per cutaneous drainage or intraparitoneal drainage. All cases of lymphocele were successfully treated with no graft loss.

Conclusions:
lymphocele is an uncommon complication after renal transplantation, and it is formed during the early post transplantation period. Its incidence in the present series is similar to what is reported in literature. While the incidence was more common following cadaveric transplantation. Percutaneous aspiration has a high rate of recurrence and intraperitoneal drainage is the most effective management.

Key Words: Lymphocele; Complication; Renal transplantation
Funding Agency: None

Surgery and Transplantation
Category: Clinical

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Serum Zinc, Selenium, Manganese, and Magnesium in Zinc altered diet and burn wound healing

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Introduction:
To assess serum Zinc(Zn), Selenium(Se), Manganese(Mn) and Magnesium(Mg) following burn in different diets.

Methods:
The serum level of Zn, Se, Mn and Mg in 80 rabbits fed on variable zinc diet with burn or without burn form day 0 to 8 weeks was studied. There were twenty animals in each group either on normal zinc diet (Group-A)or supplemented zinc diet (Group-B), or depleted zinc diet (Group-C) and without burn but with normal zinc diet (Group-D). The Se, Mn, and Mg diet remained constant during control, pre-burn, and post burn period in all the groups.

Results:
The pre burn zinc was 1374+68µg/L in Group-A and 1334+76µg/L in Group-C respectively and remained low during post burn period ($p<0.05$). The pre burn zinc level in Group-B was 1471+107µg/L and it decreased up to 3 weeks post burn, but then onward significantly increased ($p<0.05$). The serum selenium in Group-A was found to be low up to 5 weeks post burn but increased from 6th weeks onward ($p<0.05$). In Group-B the serum selenium was low ($p<0.05$) through out the post burn period as compared to pre-burn level of 188.75+3.14µg/L. In Group-C the pre-burn selenium level was 191.2+6.3 µg/L, and it increased from two weeks post-burn ($p<0.05$). The significant decrease of serum manganese was only observed in Group-C ($p<0.05$) during post-burn period, while in rest of the Groups it remained unchanged. The serum magnesium level decreased up to 5 weeks post burn ($p<0.05$) in all three Groups-A, B, C but remained un-effected in Group-D. The rate of wound healing was faster ($p<0.05$) in Group-B (51 days) when compared to Group-A (55 days) and Group-C (64 days) in the altered zinc diet.

Conclusions:
Zinc supplementation favors burn wound healing. The study should be extended by modifying the selenium, manganese, and manganese diet in burn wound healing.

Key Words: Burn; Trace elements; Wound healing
Funding Agency: Kuwait University Grant # MS01/00

Surgery and Transplantation
Category: Clinical

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Disseminated varicella-zoster infection in renal allograft recipients

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Introduction:
Disseminated infection with varicella- zoster virus (VZV) is a rare but well recognized complication after renal transplantation. Infection develops either as primary varicella infection (chicken pox) or as a reactivation of the virus in the form of herpes zoster (disseminated shingles).We report our experience in 15 renal transplant recipients (RTR) with disseminated VZV infection.

Methods:
The records of 950 renal transplants performed during the last ten years were reviewed for the incidence of disseminated VZV infection. Diagnosis was made by clinical presentation, examination of the vesicle fluid for VZV by the polymerase chain reaction and by testing for IgM and IgG antibodies specific for VZV in the serum.

Results:
Disseminated VZV infection occurred in 15 RTR among 950 renal transplants of which 12 were primary varicella infection and 3 were disseminated herpes zoster. All the subjects were on triple immunosuppression with cyclosporin, prednisolone and azathioprine [2] or mycophenolate mofetil (13). The duration after transplantation at the time of development of VZV infection ranged from 7 to 102 months. All were treated with high dose intravenous acyclovir in addition to decrease/discontinuation of immunosuppressive medications. Presentation with severe abdominal pain was typically present in the 2 subjects who had severe disseminated disease leading to mortality. Severe disseminated intravascular coagulation, hepatic impairment, pneumonitis and graft dysfunction were characteristically present in the 2 RTR who expired.

Conclusions:
Disseminated VZV infection leads to high mortality in RTR. Post exposure prophylactic passive immunization and routine pretransplant active immunization in children and in adults with negative or low VZV antibodies should be recommended to prevent this life threatening infection.

Key Words: Renal Transplantation; Disseminated varicella zoster; Immunosuppression
Funding Agency: None

Transplantation
Category: Clinical

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Renal Re-Transplantation: Is it Justified?

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Introduction:
There is a dispute about the justification of renal re-transplantation in the presence of organ shortage, and the concept that patients who have lost a transplanted kidney are widely recognized as a high risk for re-transplantation. This is a retrospective study of the outcome of renal re-transplantation (Re-Tx) and to find out if renal re-transplantation is justified.

Methods:
Between 1993 and December 2006, 646 kidney transplantation procedures were performed in our centre, 193 were cadaveric kidney transplantation and 453 were from live donors, 39 of total number were Re-Tx (6%). 34 were 2nd graft(87%) and 5 were 3rd transplant (13%).The medical records of these patients were reviewed. They were 19 males and 20 females, aged 10 to 62 years (mean 36 years), nine of them were children. Kidney grafts were obtained from 16 living and 23 cadaveric donors. Induction immunosuppression was with ATG in 23 simululect in 4 and Zinapax in 1, Maintenance Therapy were prednisolone, azathioprine and Neoral in 9 patients while prednisolone, cellcept and Neoral were used in 27 patients.

Results:
Patients were followed up from 12 months to 134 months Post transplantation. Complications were in the form of: 14 instances of surgical complication (36%), 6 episodes of acute rejection (15%). Two recipients died with functioning graft at 4 months to 62 months after Tx. Seven more grafts were lost at one day to 84 months after Tx secondary to renal vessel thrombosis in 3, chronic dysfunction in 3, and graft infarction secondary to antiphospholipid syndrome in one recipient.

Conclusions:
It was observed in the present series that renal Re-Tx is associated with recipient survival rates which are similar, and graft survival rates which are 10-13 % lower than those in primary Tx. These results are still quite reasonable to justify renal re-transplantation

Key Words: Re-transplantation; Complications; Cadaveric
Funding Agency: None

Ultrasound Nuclear Medicine
Category: Clinical

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Loco-Regional Breast Cancer Recurrence Demonstrated On MIBI Scintigraphy: A Comparative Study Between Scintimammography, Mammography And Breast Ultrasound

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Introduction:
Breast cancer is the most common cancer among women and the second leading cause of death in women after lung cancer. Patients who have been treated for breast cancer may develop recurrence of primary cancer. The principle aim is to study the utility of Tc- MIBI scintimammography in evaluation of loco-regional recurrence of breast cancer in comparison with mammography and ultrasonography.

Methods:
All subjects received a 740-1000 MBq bolus i/v injection of 99mTc-sestamibi. 5-10min post injection planar lateral and anterior views were obtained in prone position using double head camera. Similarly, delayed planar images were acquired 1 hour after the injection followed by supine SPECT (64 projection, 64x 64 matrix, 30 sec/frame 180 degree arc per head). Only focal uptake was interpreted as positive. Semi-quantitative analysis of MIBI scans was performed and tumor to normal background ratio (T/B) was calculated.

Results:
A total of 33 patients (mean age, 42.5yr; age range, 22-77 yrs) with suspected loco-regional recurrence of breast cancer on clinical examination and/or at conventional imaging procedures were included in this study, 21 patients had confirmed as recurrence on histopathology/cytology. Planar SMM was found true positive in 18 patients and true negative in 11 patients with Sens. 85.7.3%, Spec. 91.6%, PPV 94.7%, NPV 78.5% and accuracy 87.8% ($p<0.001$). In comparison XMM had Sens. 53%, Spec. 66.66%, PPV 75% NPV 42.85% and accuracy 57.7% ($p<0.23$). and US had Sens. 61%, Spec. 66.66%, PPV 76.5% NPV 50% and accuracy 63.6% ($p<0.23$). No statistical difference in sensitivity, specificity and accuracy of planar and SPECT $p<0.001$ (McNemar results). ROC curve analysis demonstrates that SMM should be the test of choice for the investigation of suspected loco-regional recurrence.

Conclusions:
Scintimammography has better diagnostic accuracy than mammography and ultrasonography in the detection of loco-regional breast cancer recurrence.

Key Words: Scintimammography; Carcinoma breast; Locoregional recurrence
Funding Agency: None