

# **International Publications Awards**

## **Cairo University**

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**Dear colleagues,**

We are pleased to introduce vol. 7(1) issue of the international publications of Cairo University. It is a further step and distinct contribution, reflecting the scientific ability of staff members, which conforms to international quality standards.

The purpose of issuing these publications is mainly to introduce this work to the academic community, demonstrate the different research abilities of Cairo University researchers, and encourage them to increase the quality and quantity of their research.

We would like to assure you that the administration will spare no effort to support and reinforce these goals.

We congratulate all colleagues who were granted the awards for their international publications of the year 2012 and wish them all the best for their future endeavors.

We are also pleased to inform you that this policy will continue to be in effect for the years to come.

**Prof. Gamal Esmat**

**Vice - President for post-graduate  
studies and research  
Cairo university**

**Prof. Hossam Kamel**

**President  
Cairo university**



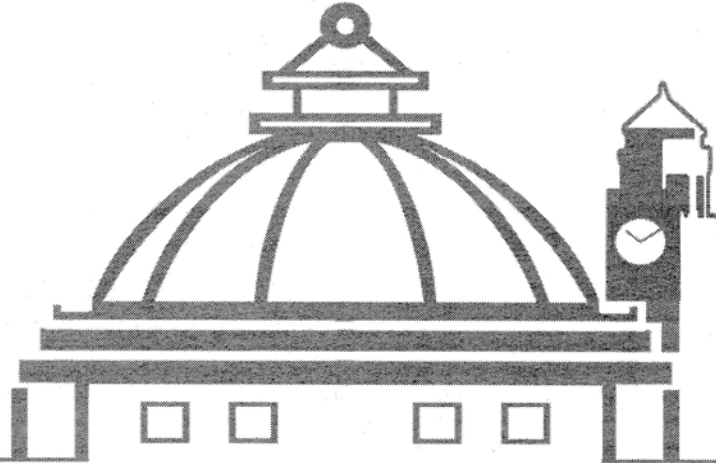
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**International Publications Awards  
Cairo University**



**(1)  
Medical  
Sciences Sector**

- 1-1 Faculty of Medicine**
- 1-2 Faculty of Oral and Dental Medicine**
- 1-3 Faculty of Nursing**
- 1-4 Faculty of Pharmacy**
- 1-5 Faculty of Physical Therapy**
- 1-6 National Cancer Institute**





## Faculty of Medicine

### Dept. of Andrology and Sexology

#### 1. Seminal Clusterin Gene Expression Associated with Seminal Variables in Fertile and Infertile Men

Adel Zalata, Ayman Z. El-Samanoudy, Dalia Shaalan, Youssef El-Baiomy, Mai Taymour and Taymour Mostafa

*J. Urology*, 188: 1260-1264 (2012) IF: 3.746

**Purpose:** CLU is a disulfide linked, heterodimeric protein associated with the clearance of cellular debris and apoptosis. We assessed the association of seminal CLU gene expression with seminal variables in fertile and infertile men.

**Materials and Methods:** A total of 124 men were divided into healthy, fertile men with normozoospermia, and men with asthenozoospermia, asthenoteratozoospermia and oligoasthenoteratozoospermia. History was obtained, and clinical examination and semen analysis were done. In semen we assessed sperm acrosin activity, sperm DNA fragmentation and seminal CLU gene expression.

**Results:** CLU RNA and CLU protein gene expression were significantly increased in semen samples of infertile men with oligoasthenoteratozoospermia, asthenoteratozoospermia, asthenozoospermia compared with healthy, fertile controls.

CLU gene expression significantly correlated negatively with sperm count, motility, acrosin activity index, linearity index and linear velocity, and significantly correlated positively with the percent of sperm abnormal forms and DNA fragmentation.

**Conclusion:** CLU gene expression was significantly increased in the semen samples of infertile men. It correlated negatively with sperm count, motility, acrosin activity, linearity index and linear velocity, and positively with the percent of sperm abnormal forms and DNA fragmentation.

**Keywords:** Testis; Infertility; Male; DNA Fragmentation; Spermatozoa; Clusterin.

#### 2. Ace Gene Insertion/Deletion Polymorphism Seminal Associations in Infertile Men

Adel A. Zalata, Heba K. Morsy, Abd El-Naser Badawy, Samir Elhanbly and Taymour Mostafa

*J. Urology*, 187: 1776-1780 (2012) IF: 3.746

**Purpose:** We assessed seminal associations of the ACE\* gene insertion/deletion polymorphism in infertile men.

**Materials and Methods:** A total of 405 men were investigated, divided into healthy fertile men, and those with asthenozoospermia, asthenoteratozoospermia and oligoasthenoteratozoospermia, respectively.

They underwent semen analysis, and assessment of sperm acrosin activity, hypo-osmotic swelling, seminal 8-iso-prostaglandin-F<sub>2α</sub>, total antioxidant capacity, alpha-glucosidase and ACE gene polymorphisms.

**Result:** the ACE\* insertion/insertion genotype was noted in 182 men, including 76.5% of healthy fertile men, and 47.4%, 39.8% and 17.6% of those with asthenozoospermia, asthenoteratozoospermia and oligoasthenoteratozoospermia, respectively. The ACE\* insertion/deletion genotype was noted in 133 men, including 13.7% of healthy fertile men, and 42.3%, 27.5% and 47.2% of those with asthenozoospermia, asthenoteratozoospermia and oligoasthenoteratozoospermia,

respectively. The ACE\* deletion/deletion genotype was identified in 90 men, including 9.8% of healthy fertile men, 10.3%, 32.70% and 35.2% of those with asthenozoospermia, asthenoteratozoospermia and oligoasthenoteratozoospermia, respectively. Men with the ACE\* deletion/deletion and insertion/deletion genotypes showed a significant decrease in sperm count, motility, linear velocity and normal forms, acrosin activity index, hypo-osmotic swelling test and seminal alpha-glucosidase, and significantly increased seminal 8-iso-prostaglandin-F than those with the ACE\* insertion/insertion genotype.

**Conclusions:** ACE gene deletion polymorphism is associated with abnormal seminal variables, such that carriers of the ACE\* deletion/deletion genotype have higher seminal oxidative stress.

**Keywords:** Testis; Infertility; Male; Spermatozoa; Peptidyl-Dipeptidase A; Oxidative Stress.

#### 3. Shaer's Glans Augmentation Technique: A Pilot Study

Osama Shaer

*J. Sex Med*, 9: 3264-3269 (2012) IF: 3.552

**Introduction:** Augmentation of the glans penis may be indicated for cosmetic reasons, lack of glans tumescence following implantation of a penile prosthesis, or asymmetry following girth augmentation of the shaft.

Many augmentation techniques have been offered to increase the length and girth of penile shaft, but not the glans penis, with the exception of hyaluronic acid gel injection that is known to decrease sensitivity of the glans and is restricted for cases with premature ejaculation.

**Aim:** This work is the first report on glans augmentation by grafting.

**Main Outcome Measures:** Maximum circumference of the glans, self-reported impression of the augmented volume and glans sensitivity.

**Methods:** Ten males requesting augmentation of the glans were selected for the study after failing counseling, with normal erectile function and ejaculatory control.

Two ventral incisions were cut along the ventral aspects of the coronal sulcus, one on either side of the frenulum. Lateral glans flaps were dissected on either side. The urethra was circumvented, creating a plane all around it. A dermal fat graft was inserted into the space created. The flaps were closed by simple absorbable sutures.

**Results:** Maximum circumference of the glans increased by 16.6%, declining to 14.2% by the last follow-up visit (10–12 months), a 2.3% decline. Self-reported impression of the augmented volume was high and well maintained over the follow-up period. Glans sensation, engorgement, erectile function, and ejaculatory control were preserved.

**Conclusion:** This pilot study on glans augmentation by grafting reports promising results with retention of the added volume at 1-year follow-up, preservation sensitivity and engorgement, and no adverse effects on erectile function or ejaculatory control. Shaer O. Shaer's glans augmentation technique: A pilot study.

**Keywords:** Glans; Augmentation; Size; Graft.

#### 4. The Global Online Sexuality Survey (GOSS): the United States of America in 2011 Chapter 1

Osama Shaeer

*J. Sex Med*, 9: 3264-3269 (2012) IF: 3.552

**Introduction:** The Global Online Sexuality Survey (GOSS) is a worldwide epidemiologic study of sexuality and sexual disorders, based on validated questionnaires and applying age adjustment to the World Standard Population (WSP) by the World Health Organization. In 2010, the first report of GOSS came from the Middle East, describing an erectile dysfunction (ED) prevalence rate of 47%.

**Aim:** This report studies the prevalence rate of ED in the United States as of 2011–2012 and evaluates risk factors for ED. Main Outcome Measures. Prevalence of ED.

**Methods.** GOSS was randomly deployed to English-speaking male web surfers in the United States via paid advertising on Facebook, comprising 146 questions including the abbreviated 5-item International Index of Erectile Function.

**Results:** Two thousand twenty-two males participated; with a mean age was 52.38 years 14.5. Prevalence of ED was 37.7%, adjusted to 33.7% according to WSP, comparable across ethnic groups. The following risk factors were associated with higher risk for ED: diabetes mellitus, hypertension with and without antihypertensive treatment, coronary heart disease, obesity (defined by body mass index), difficult micturition, subjectively reported depression, interpersonal distress, subjectively reported impotence, in addition to novel factors such as subjectively reported premature ejaculation (PE) and concerns over genital size (not a smaller penis per se), low libido, and irregular coitus. Frequency of smoking and alcohol were not associated with higher prevalence of ED, although duration of smoking was.

**Conclusion:** Adjusted to WSP, prevalence rate of ED in the United States of America is 33.7% in the year 2011, in contrast to the adjusted prevalence in the Middle East (47%). Most of the classical risk factors for ED play the same role in the United States and the World, including diabetes, hypertension, and aging. Concerns over genital size and PE are emerging risk factors for ED. Shaeer O and Shaeer K. The Global Online Sexuality Survey (GOSS).

**Keywords:** Epidemiology; Survey; Erectile Dysfunction; Usa; United States Of America; Prevalence

#### 5. Effects of Female Genital Cutting on the Sexual Function of Egyptian Women. A Cross-Sectional Study

Tarek H. Anis, Samah Aboul Gheit, Hossam H. Awad and Hanan S. Saied

*J. Sex Med*, 9: 2682-2692 (2012) IF: 3.552

**Introduction:** the existing literature is conflicting regarding effects of female genital cutting (FGC) on sexual functions. Several studies from Africa over the past 20 years have challenged the negative effect of genital cutting on sexual function as defined by performance on the following domains: desire, arousal, lubrication, orgasm, satisfaction, and sexual pain. Other studies however indicated that sexual function of genitally cut women is adversely altered.

**Aim:** the aim of the study was to investigate the effects of FGC on the female sexual function of Egyptian women.

**Methods:** This is a cross-sectional study conducted between February and May 2011 at the outpatient clinic of Cairo University Hospitals. the study included 650 Egyptian females between 16 and 55 years of age (333 genitally cut women and 317 uncut women). Participants were requested to complete the Arabic Female Sexual Function Index (ArFSFI) and were then subjected to clinical examination where the cutting status was confirmed.

**Main Outcome Measures:** the total score of the ArFSFI and its individual domains.

**Results:** the mean age of cutting was 8.59 ( $\pm 1.07$ ) years. of the cut participants, 84.98% showed signs of type I genital cutting, while 15.02% showed signs of type II genital cutting. After adjusting for age, residential area, and education level, uncut participants had significantly higher ArFSFI total score ( $23.99 \pm 2.21$ ) compared with cut participants ( $26.81 \pm 2.26$ ). the desire, arousal, lubrication, orgasm, and satisfaction domains were significantly higher in the uncut participants ( $4.02 \pm 0.78$ ,  $4.86 \pm 0.72$ ,  $4.86 \pm 0.75$ ,  $4.86 \pm 0.68$ ,  $5.04 \pm 0.71$ , respectively) compared with those of the cut participants ( $3.37 \pm 0.89$ ,  $4.13 \pm 0.71$ ,  $4.16 \pm 0.84$ ,  $4.50 \pm 0.79$ ,  $4.69 \pm 0.92$ , respectively). No significant difference between the two groups was found regarding the sexual pain domain.

**Conclusion:** in Egyptian women, FGC is associated with reduced scores of ArFSFI on all domain scores except the sexual pain domain.

**Keywords:** Female Genital Cutting; Female Sexual Function Index; Female Sexual Function; Egyptian Population.

#### 6. Pheromones in Sex and Reproduction: Do they Have A Role in Humans?

Taymour Mostafa, Ghada El Khoully and Ashraf Hassan

*Journal of Advanced Research*, 3 (1): 1-9 (2012) IF: 3

Pheromones are found throughout the living world and are a primal form of communication. These chemical messengers are transported outside the body and have a direct developmental effect on hormone levels and/or behaviour.

This review article aims to highlight the role of human pheromones in sex and reproduction. A review of published articles was carried out, using PubMed, medical subject heading (MSH) databases and the Scopus engine. Key words used to assess exposure, outcome, and estimates for the concerned associations, were; olfaction; sex; pheromones; libido; behaviour; reproduction; humans; and smell.

Although there are studies to support this phenomenon, they are weak because they were not controlled; others have proposed that human olfactory communication is able to perceive certain pheromones that may play a role in behavioural as well as reproductive biology. Unfolding the mysteries of smells and the way they are perceived requires more time and effort as humans are not systems that instinctively fall into a behaviour in response to an odour, they are thinking individuals that exercise judgment and subjected to different motivations.

**Keywords:** Olfaction; Sex; Pheromones; Libido; Behaviour; Reproduction.

## 7. Effect of Smoking on Sperm Vitality, Dna Integrity, Seminal Oxidative Stress, Zinc in Fertile Men

Emad A. Taha, Azza M. Ez-Aldin, Sohair K. Sayed, Nagwa M. Ghandour and Taymour Mostafa

*Urology*, 80 (4): 822-825 (2012) IF: 2.428

**Objective:** to assess the effect of smoking on sperm vitality, sperm DNA integrity, semen reactive oxygen species, and zinc levels in fertile men.

**Methods:** One-hundred sixty men were investigated. They were divided into 2 equal groups: healthy fertile nonsmokers and healthy fertile smokers. They were subjected to history taking, clinical examination, and semen analysis. in their semen, sperm hypo-osmotic swelling test, sperm DNA fragmentation test, seminal reactive oxygen species, and zinc were assessed.

**Results:** Compared with fertile nonsmokers, fertile smokers were significantly associated with lower hypo-osmotic swelling test and seminal zinc levels and significantly associated with higher sperm DNA fragmentation percent and seminal reactive oxygen species levels.

**Conclusion:** Smoking (cigarettes/day and duration) has detrimental effects on sperm motility, viability, DNA fragmentation, seminal zinc levels, and semen reactive oxygen species levels, even in fertile men, and it is directly correlated with cigarette quantity and smoking duration.

## 8. Androgen Receptor-Cag Repeats in Infertile Egyptian Men

T. Mostafa, L. H. El-Shahid, A. A. El Azeem, O. Shaker, H. Gomaa and H. M. Abd El Hamid

*Andrologia*, 44: 147-151 (2012) IF: 1.546

This study aimed to assess the androgen receptor (AR) codon amino acids glutamine (CAG) repeats in 185 Egyptian men divided into fertile controls (n =30), oligoasthenoteratozoospermic (OAT) men (n = 35), nonobstructive azoospermic (NOA) men (n = 120; 18 successful testicular sperm extraction (TESE) and 102 unsuccessful TESE cases).

They were subjected to history taking, genital examination, semen analysis, testicular biopsies for NOA cases, serum hormones and CAG repeats by PCR. the mean AR-CAG repeats showed significant difference between NOA group compared with fertile controls or OAT groups. Nonsignificant difference was elicited between OAT group and fertile controls. in NOA cases, CAG repeats demonstrated nonsignificant difference between unsuccessful and successful TESE. AR-CAG repeats elicited significant negative correlation with sperm count, significant positive correlation with sperm normal forms percentage and nonsignificant correlations with sperm motility per cent, tested serum hormones or testicular volume. It is concluded that AR-CAG repeats in Egyptian infertile men are in the range of other international or regional studies. AR-CAG repeats have demonstrated nonsignificant difference regarding TESE outcome in NOA cases.

**Keywords:** Azoospermia; Cag; Male Infertility; Semen; Tese; Testis.

## 9. Ultrasonographic Parameters of the Spermatic Veins at the Inguinal and Scrotal Levels in Varicocele Diagnosis and Post-Operative Repair

S. El-Haggar, S. Nassef, A. Gadalla, A. Latif and T. Mostafa

*Andrologia*, 44: 210-213 (2012) IF: 1.546

Varicocele has been identified as an important cause of male infertility where its influence on men's reproductive capacity is due to its markedly diverse effects on the testicles. This study aimed to assess the value of ultrasonographic parameters of the spermatic veins at the inguinal and scrotal levels in varicocele diagnosis and post-operative evaluation. Forty-five infertile men associated with varicocele and 15 fertile men were subjected to history taking, genital examination and semen analysis. in addition, inguinal and scrotal ultrasonography was carried out pre-varicocelectomy and 3 months post-varicocelectomy. at both the scrotal or inguinal levels, the mean spermatic vein diameter demonstrated significant post-operative decrease compared with the pre-operative resting condition and on Valsalva' manoeuvre. the mean diameters of the pampiniform plexus of veins also demonstrated significant decreases post-operatively compared with the pre-operative resting condition or on Valsalva' manoeuvre. It is concluded that colour Doppler ultrasound is a reliable and noninvasive method that is useful not only for diagnosis but also for post-varicocele repair follow-up.

**Keywords:** Colour Doppler; Male Infertility; Semen; Ultrasonography; Varicocele.

## 10. Seminal Plasma Reactive Oxygen Species–Antioxidants Relationship with Varicocele Grade

T. Mostafa, T. Anis, A. El Nashar, H. and Imam, I. Osman

*Andrologia*, 44 (1): 66-69 (2012) IF: 1.546

This work aimed to assess seminal plasma reactive oxygen species (ROS)- antioxidants relationship with varicocele grade in infertile men with oligoasthenoteratozoospermia (OAT). the study included 89 infertile OAT men with varicocele divided into grade I (n = 22) and grade II (n = 43), grade III (n = 24) and compared with 20 healthy fertile controls. in their seminal plasma, two ROS parameters (malondialdehyde [MDA], hydrogen peroxide [H<sub>2</sub>O<sub>2</sub>]) and four antioxidants (superoxide dismutase [SOD], catalase [Cat], glutathione peroxidase [GPx], vit.C) were estimated.

There was significant increase in seminal MDA, H<sub>2</sub>O<sub>2</sub> and significant decrease in seminal SOD, Cat, GPx, vit.C in varicocele-associated OAT cases when compared with the controls. Compared with grade I cases, varicocele cases with grades II, III demonstrated significant increase in estimated seminal MDA, H<sub>2</sub>O<sub>2</sub> and significant decrease in seminal SOD, Cat, GPx, vit.C. It is concluded that seminal oxidative stress (OS) is related to increased varicocele grade in infertile OAT men associated with varicocele.

**Keywords:** Antioxidants; Male Infertility; Oxidative Stress; Ros; Semen; Varicocele.

### 11. Effect of Testosterone and Frequent Low-Dose Sildenafil/ Tadalafil on Cavernous Tissue Oxidative Stress of Aged Diabetic Rats

T. Mostafa, L. Rashed, K. Kotb and M. Taymour

*Andrologia*, 1-5 (2012) IF: 1.546

This study aimed to assess the effect of testosterone (T) administration and chronic low-dose sildenafil/tadalafil on cavernous tissue oxidative stress (OS) of aged diabetic rats. In all, 140 Sprague-Dawley aged rats were subdivided into the following: controls; streptozotocin (STZ)-induced diabetic rats; diabetic rats injected with T every 4 weeks; diabetic rats on sildenafil orally daily; diabetic rats on T and daily sildenafil; diabetic rats on tadalafil orally every other day; diabetic rats on T and tadalafil; diabetic rats on alternate sildenafil/tadalafil; and diabetic rats on alternate sildenafil/tadalafil with T. After 12 weeks, the rats were euthanized where in dissected cavernous tissues malondialdehyde (MDA), glutathione peroxidase (GPx) and cGMP (cyclic guanosine monophosphate) were estimated. Compared with controls, aged diabetic rats demonstrated significant increase in cavernous tissue MDA and significant decrease in GPx and cGMP where diabetic rats injected with T had marked improvement of these parameters. Diabetic rats on sildenafil, tadalafil or alternate sildenafil/tadalafil demonstrated significant increased cavernous tissue GPx, cGMP and decreased cavernous MDA that was further improved when supplemented with T. It is concluded that frequent low-dose use of sildenafil and/or tadalafil supplemented with T has a marked impact on ameliorating cavernous OS in aged diabetic rats.

**Keywords:** Ageing; Antioxidants; Cavernous Tissue; Diabetes; Erectile Dysfunction; Pde-5 Inhibitors; Testosterone.

### 12. Serum Testosterone Levels in Diabetic Men with and Without Erectile Dysfunction

S. Ghazi, W. Zohdy, Y. ElKhat and R. Shamloul

*Andrologia*, 44: 373-380 (2012) IF: 1.546

Diabetes mellitus is a common chronic disease, affecting 0.5–2% worldwide. The Massachusetts Male Aging Study reported that up to 75% of men with diabetes have a lifetime risk of developing ED. Type 2 diabetes is associated with low total serum testosterone (TT) identified in several cross-sectional studies and systemic analyses. There is a lack of consensus regarding what constitutes the lowest level of testosterone within the boundaries of normality. In this retrospective study, we sought to evaluate the effect of associated co-morbidities on serum total testosterone (TT) level in men with type 2 diabetes DM, either with or without erectile dysfunction (ED). Three hundred and ninety-one patients were evaluated for erectile function using an abridged, five-item version of the International Index of Erectile Function-5. Measurements of TT, fasting lipid profile, blood sugar and glycated haemoglobin (HbA1c) were conducted. Penile hemodynamics was assessed using intracavernosal injection and penile duplex study. Hypogonadism was found in 126 cases (33.2%), and normal TT was observed in 254 (66.8%). ED was detected in 119 cases in the hypogonadal group (94.4%) as compared to 155/254 (61.0%) in the eugonadal group,  $P = 0.0001$ . TT was lower in diabetic men with ED as compared to those with normal erectile function (EF),  $392.4 \pm 314.9$  versus  $524.3 \pm 140.2$  ng dl<sup>-1</sup>, respectively,  $P < 0.0001$ . After exclusion of patients with hypertension and dyslipidaemia, 185 men were evaluated, and

there was no difference in the mean TT level among men with ED  $490.6 \pm 498.2$  ng dl<sup>-1</sup> versus normal EF  $540.6 \pm 133.4$  ng dl<sup>-1</sup> although, HbA1c remained lower in men with normal erectile function. Receiver operating characteristic (ROC) curve of TT in men without associated co-morbidities showed that EF was compromised at TT = 403.5 ng dl<sup>-1</sup> or less. Sensitivity of 63.3% and a specificity of 94.0% were detected. At this level, ED was found in 33/38 (86.8%) men with TT 403.5 ng dl<sup>-1</sup>, whereas ED was observed in 57/147 (38.8%) men with TT 403.5 ng dl<sup>-1</sup> ( $P < 0.0001$ ). We propose a cut-off value of 403.5 ng dl<sup>-1</sup> of TT blood levels as an indicator for initiation of testosterone replacement therapy in diabetic men with ED. Further prospective controlled trials are recommended.

**Keywords:** Diabetes mellitus; Erectile dysfunction; Testosterone.

### 13. Prevalence of Late-Onset Hypogonadism in Men with Type 2 Diabetes Mellitus

M. Arafa, W. Zohdy, S. Aboulsoud and R. Shamloul

*Andrologia*, 44: 756-763 (2012) IF: 1.546

Late-onset hypogonadism (LOH) or age-associated testosterone deficiency syndrome is defined as a clinical and biochemical syndrome associated with advancing age and characterised by symptoms and a deficiency in serum testosterone levels. This condition may result in significant detriment in the quality of life and adversely affect the function of multiple organ systems. It has been suggested that sex steroid hormones may play a causal role in the development of insulin resistance and type II diabetes. This comparative study was aimed at determining the prevalence of LOH in diabetic men with erectile dysfunction and investigating the effect of testosterone replacement therapy on erectile function and on glycaemic control.

**Keywords:** Hypogonadism; Diabetes; Testosterone.

### 14. Relation of Color Doppler Parameters with Testicular Size in Oligoasthenoteratozoospermic Men with A Varicocele

Emad A. Tahaa, Saad R. Abd El-Wahed and Taymour Mostafa

*Hum Androl*, 2: 6-11 (2012)

**Purpose:** to assess the relation of color Doppler ultrasound (CDU) parameters with testicular size in oligoasthenoteratozoospermic (OAT) men with a varicocele (Vx). Patients and methods: in all, 500 OAT men were investigated: men without Vx ( $n = 100$ ), men with left-sided Vx ( $n = 150$ ), and men with bilateral Vx ( $n = 250$ ). They were subjected to history taking, clinical evaluation, and scrotal CDU examination.

**Results:** there was a significant decrease in testicular sizes and a significant increase in size discrepancy in OAT men with left-sided and bilateral Vx compared with OAT men without Vx. Maximum vein diameter, vein numbers, and venous reflux duration of OAT men with bilateral Vx demonstrated a significant increase compared with OAT men with left-sided Vx and OAT men without Vx. Maximum vein diameter, vein numbers, and venous reflux duration in OAT men with left-sided Vx demonstrated a significant increase compared with OAT men without Vx. Maximum vein diameter on the left side demonstrated significant negative correlations with ipsilateral testicular size, right testis size, and total testicular size and a significant positive correlation with size discrepancy. CDU

parameters were associated with significant decreased total testicular size in OAT men with bilateral Vx and increased size discrepancy in OAT men with left-sided Vx.

**Conclusion:** Vx is associated with a significant decrease in ipsilateral, total testicular size, and increased size discrepancy. CDU parameters were associated with a significant decrease in total testicular size in OAT men with bilateral Vx and a significant increase in size discrepancy in OAT men with left-sided Vx.

**Keywords:** Color doppler ultrasound; Male infertility; Oligoasthenoteratozoospermia; Testis; varicocele

#### Dept. of Anesthesiology

### 15. The Friday of Rage of the Egyptian Revolution: A Unique Role for Anesthesiologists

Ahmed Mukhtar, Ahmed Hasanin, Akram El-Adawy, Safinaz Osman, Abeer Ahmed, Heba Nassar, Dalia Saad, Ahmed Zaghoul, Mohamed Sarhan and Michael Reda

*Anesth Analg*, (2012) IF: 3.286

On Friday 28 January, called by some "the Friday of Rage" clashes between Egyptian protesters and security forces have happened resulted in significant injuries and even deaths among the protesters. In this article we described the challenges that we have faced during early days of revolution. Such challenges not caused only by mass casualty incident, but also security vacuum that spread chaos in the country.

**Keywords:** Egyptian Revolution; Mass Casualty.

### 16. Efficacy and Cardiovascular Tolerability of Continuous Venovenous Hemodiafiltration in Acute Decompensated Heart Failure: A Randomized Comparative Study

Sahar S.I. Badawy and Ahmed Fahmy

*J Crit Care*, 27(1): 106-113 (2012) IF: 2.127

**Background and Objectives:** recently, continuous venovenous hemodiafiltration (CVVHDF) has received increased attention in the treatment of congestive heart failure (CHF). The aim of this study is to assess the safety and efficacy of CVVHDF compared with intravenous furosemide in patients with CHF.

**Methods:** Forty patients having CHF were included in this prospective, randomized, comparative trial. We randomized patients to treatment for 72 hours with CVVHDF or intravenous furosemide. Outcomes assessed were weight loss, total fluid output, length of stay (LOS) in the intensive care unit (ICU), 30-day mortality, and cardiovascular stability.

**Results:** Demographic data were comparable in both groups. Weight loss ( $P \leq .05$ ) and total fluid output ( $P \leq .01$ ) were greater in the CVVHDF group. Length of stay in the ICU was significantly reduced in the CVVHDF group ( $P \leq .05$ ). The mortality rates were comparable in both groups. The cardiac output and the stroke volume significantly increased, whereas the pulmonary capillary wedge pressure significantly decreased ( $P \leq .05$ ) in both groups compared with the baseline. A transient attack of hypotension occurred in 1 patient in the CVVHDF group.

**Conclusion:** in CHF, the use of CVVHDF effectively and safely produced greater weight and fluid loss and decreased LOS in the

ICU more than the intravenous furosemide with no hemodynamic instability.

**Keywords:** Heart failure; Continuous veno; Venous hemodiafiltration; Furosemide.

### 17. The Association of Promoter Gene Polymorphisms of the Tumor Necrosis Factor-Alpha and Interleukin-10 with Severity of Lactic Acidosis During Liver Transplantation Surgery

O. Farahat, M. Salah, A. Mokhtar, F. Abouelfetoh, D. Labib, and H. Baz

*Transplantation Proceedings*, 44: 1307-1313 (2012) IF: 1.005

**Background:** Orthotopic liver transplantation (OLT) is a major operation, causing cytokine release and other inflammatory responses that can contribute to postreperfusion syndrome occurrence. During the systemic inflammatory response syndrome, increased lactate levels result from excessive cytokine production despite normal oxygen delivery and carbohydrate metabolism. The goal of the study was to determine the relationship between genetic polymorphisms in interleukin (IL)-10 (1082G/A) or tumor necrosis factor (TNF)- $\alpha$  (-376 G/A) and lactate levels in patients during OLT surgery.

**Patients and Methods:** This prospective observational study in 40 consecutive adult patients who underwent OLT documented lactic acid levels at 5 times: Immediately after induction of anesthesia, at the end of the pre-anhepatic phase, at the end of the anhepatic phase, 1 hour after reperfusion, and at the end of surgery. Polymerase chain reaction (PCR; RFLP methodology) was used to examine IL-10 (1082G/A) and TNF- $\alpha$  (-376 G/A) gene polymorphisms.

**Results:** Carriers of the IL-10/TNF- genotype combination GG/GG showed significantly different changes in lactate levels at 1 hour after reperfusion and at the end of surgery. Lactate levels were significantly higher among patients heterozygous for TNF- $\alpha$  (AG genotype) compared with patients homozygous for TNF- $\alpha$  (GG genotype) at same times. In contrast, there was no significant difference among IL-10 polymorphic genotypes (-1082G/A).

**Conclusion:** Genetic factors play a role in the development of lactic acidosis after OLT. IL-10 (1082G/A) and TNF- $\alpha$  (-376 G/A) gene polymorphisms could influence the variability of lactate levels after liver transplantation surgery.

**Keywords:** Tnf-; Gene polymorphisms; Interleukin-10; Lactic acidosis

### 18. Comparison between Prostaglandin E1, and Esmolol Infusions in Controlled Hypotension During Scoliosis Correction Surgery A Clinical Trial

Hala Mostafa Goma

*Middle East Journal of Anesthesia*, 21 (4): 599-604 (2012)

**Background:** scoliosis correction surgery is common in children, and adolescents. Deliberate hypotension is indicated in scoliosis correction procedures, because bloodless field is needed for exposure of the nerve roots, and to decrease the need for blood transfusion. Protection of the kidneys during deliberate hypotension is essential. The ideal hypotensive drug maintains the renal function and the urine output during the period of hypotension. Aim of this study is to compare Prostaglandin E1,

and Esmolol hypotensive effects, bleeding score, and their effects on the serum creatinine, and urine output.

**Patients and methods:** Twenty patients under went hypotensive anesthesia during scoliosis correction procedure, were enrolled in this clinical trial. in group 1 (n = 10) (Esmolol infusion), group 2 (n = 10) (prostaglandin E1 infusion), Parameters were measured: Mean arterial blood pressure, Heart rate, (preoperative, just after induction, 15 minutes, 30 minutes, 60 minutes after starting the infusions, and 15 minutes after discontinuation of infusions). the bleeding score was assessed at (15 minutes, 30 minutes, 60 minutes after starting the infusions).

**Results:** heart rate was significantly higher in prostaglandin E1 group than Esmolol group at 15, 30, 45, and 60 minutes. There was significant difference in the bleeding score only after 30 minutes, the target mean blood pressure (50 mmHg) was achieved at 30 minutes in group 2 (prostaglandin E1), while it was achieved at 60 minutes in group 1 (Esmolol group). There were significant differences in Mean blood pressure between both groups at 15, 30, 45, 60 minutes after starting the infusions. Creatinine level was significantly lower in prostaglandin E1 group, while the introperative urine output was significantly higher in prostaglandin E1 group.

**Conclusions:** Prostaglandin E1 hypotensive effects started earlier than Esmolol and its bleeding score is better than esmolol especially at thirty minutes after initiation of the infusion. Prostaglandin E1 can maintain renal function and urine output more than Esmolol. This study recommended using Prostaglandin E1 to induce hypotensive anesthesia in scoliosis correction surgery.

**Keywords:** Prostaglandine; Esmolol; Scoliosis; Surgery.

#### Dept. of Cardiology

### 19. Hypertension in Developing Countries

M Mohsen Ibrahim; and Albertino Damasceno

*The Lancet*, 380: 611-619 (2012) IF: 38.278

Data from different national and regional surveys show that hypertension is common in the developing world particularly in urban areas, while rates of awareness, treatment and control are low.

A number of hypertension risk factors seem to be more common in developing countries. Serial surveys showed increasing prevalence of hypertension possibly due to urbanization, aging of population, changing dietary habits and social stress. on the other hand, high illiteracy rates, lack of access to health facilities, bad dietary habits, poverty and high cost of drug therapy are factors behind poor blood pressure control. the health system in many of the developing countries is inadequate because of limited funds, lack of infrastructure and inexperience. Priority is given to care of acute conditions, child and maternal health care and control of communicable diseases.

Governments together with medical societies and non-governmental organizations should support and promote preventive programs aiming at increasing public awareness, physician education and limiting salt intake. Regulations regarding food industry, production and availability of generic drugs should be reinforced.

**Keywords:** Hypertension; Developing Countries; Prevalence; Treatment; Control; Risk Factors and Salt.

### 20. Prevalence and Severity of Pulmonary Hypertension in Asymptomatic Rural Residents with Schistosomal Infection in the Nile Delta

Azza Farrag, Wafaa El-Aroussy, Salah Zaghloul, Mohamed El-Guindy and Magdi Yacoub

*Tropical Medicine and International Health*, 17 (1): 112-118 (2012) IF: 2.795

**Objectives:** Millions of people in the developing world may suffer from pulmonary hypertension (PHTN) because of preexisting infectious conditions. Schistosomiasis can cause pulmonary lesions that eventually lead to PHTN. the aim of this study was to assess the prevalence of PHTN together with assessment of right ventricular (RV) function in asymptomatic rural residents previously infected with schistosomiasis.

**Methods:** Three hundred and seventy asymptomatic people from an endemic area in the Nile Delta were screened for antibodies against schistosomiasis. All were scheduled for transthoracic echocardiographic study to assess pulmonary artery systolic (PASP) and diastolic (PADP) pressures as well as RV function. PASP >40 mmHg was considered elevated.

**Results:** Seropositive (SP) and seronegative (SN) groups had comparable age and body mass index. PASP >40 mmHg was met in 18 subjects (Range 42–72 mmHg) (8.6%) of SP group and in no subject in SN group (P = 0.000). Compared with SN group, the SP group had higher mean values of PASP (30 ± 10 vs. 24 ± 7 mmHg, P < 0.000) and PADP (12 ± 4 vs. 9 ± 3 mmHg, P < 0.000). the SP group had lower values of RV ejection fraction.

**Conclusion:** Prevalence of PHTN as detected by echocardiography in asymptomatic rural residents with schistosomiasis in Nile Delta is low with mild affection of RV function.

**Keywords:** Schistosomiasis; Pulmonary Hypertension; Echocardiography.

### 21. Ventricular Function in Patients with End-Stage Renal Disease Starting Dialysis Therapy: A Tissue Doppler Imaging Study

Karim Said, Mohamed Hassan, Essam Baligh and Bahaa Zayed.

*Echocardiogr-J Card*, 29: 1054-1059 (2012) IF: 1.239

**Background:** Heart failure is prevalent in end-stage renal disease (ESRD) patients on long-term dialysis. Detection of right ventricular (RV) dysfunction before starting dialysis may help to identify patients at a higher risk of developing heart failure.

**Aim:** to assess RV function in predialysis patients using tissue Doppler imaging (TDI) derived myocardial performance index of RV (MPI-RV). **Methods:** Echocardiography including pulsed TDI of lateral tricuspid annulus was performed in 41 patients with ESRD before starting dialysis therapy and 12 age and gender matched healthy controls. RV dysfunction was defined as MPI > 0.4; a value above the median MPI in controls.

**Results:** Compared to controls, ESRD patients had significantly higher blood pressure and lower hemoglobin level. MPI-RV was significantly impaired in ESRD patients compared to control (0.6 vs. 0.4, P < 0.001). RV dysfunction was identified in 23 ESRD patients (56%). ESRD patients had significantly lower e' velocity and e'/a' ratio as compared with controls. Pulmonary hypertension was detected in 15 (36.5%) patients. Among ESRD patients, no correlation was detected between MPI-RV and calculated mean pulmonary artery pressure (r = -0.13, P = 0.47),

pulmonary artery systolic pressure ( $r = -0.12$ ,  $P = 0.6$ ), left ventricular ejection fraction ( $r = 0.294$ ,  $P = 0.06$ ), or MPI of left ventricle ( $r = 0.3$ ,  $P = 0.065$ ). ESRD patients with and without pulmonary hypertension had similar MPI-RV (0.6 vs.0.62,  $P = 0.32$ ).

**Conclusion:** Subclinical RV dysfunction—as estimated by TDI derived MPI—is highly prevalent among ESRD patients even before starting dialysis therapy. Pulmonary hypertension is not significantly associated with RV dysfunction in these patients

**Keywords:** End-Stage renal disease; Myocardial performance index; Right ventricle; Tissue doppler imaging.

## 22. Value of Conventional and Tissue Doppler Echocardiography in the Noninvasive Measurement of Right Atrial Pressure

Karim Said, Ahmed Shehata, Zainab Ashour and Sherif El-Tobgi

*Echocardiogr-J Card*, 779-784 (2012) IF: 1.239

**Background:** Evaluation of right atrial pressure (RAP) provides useful diagnostic, therapeutic, and prognostic information.

**Aim:** to assess the utility of several conventional and tissue Doppler parameters in the estimation of RAP.

**Methods:** Among 50 consecutive patients (median age: 50 years; all in sinus rhythm),

invasively measured RAP was simultaneously correlated with pulsed Doppler of tricuspid inflow (peak E and A velocities, E-wave deceleration time) and pulsed tissue Doppler of lateral tricuspid annulus (peak E' and A' velocities, isovolumic relaxation time [IVRT], acceleration time and rate of E'-wave, deceleration time and rate of E'-wave). These ratios were calculated: E/A, E'/A', E/E', and E/IVRT.

**Results:** the median RAP was 14 mmHg (range 1–27 mmHg) with 29 patients (58%) having an elevated RAP (>10 mmHg).

Among all studied Doppler variables, E/E' ratio showed the strongest correlation with RAP ( $r = 0.84$ ,  $P < 0.001$ ) with the following regression equations:  $RAP = 1.24 + (1.69 \times E/E')$ . the mean difference between Doppler and invasively measured RAP was  $0.21 \pm 2.6$  mmHg. E/ E' ratio  $\geq 4.5$  provides 89% sensitivity and 100% specificity for detection of elevated RAP (receiver operating characteristic area 0.95;  $P < 0.001$ ).

**Conclusion:** of all echocardiographic variables investigated, tricuspid annular E/E' ratio is identified as the best index for noninvasive determination of RAP.

**Keywords:** Right Atrial Pressure; Tissue Doppler Imaging.

## 23. Coronary Artery Disease in Africa and the Middle East

Wael Almahmeed, Mohamad Samir Arnaout, Rafik Chettaoui, Mohsen Ibrahim, Mohamed Ibrahim Kurdi, Mohamed Awad Taher and Giuseppe Mancina

*Therapeutics and Clinical Risk Management*, 8 65-72 (2012)

Countries in Africa and the Middle East bear a heavy burden from cardiovascular disease. the prevalence of coronary heart disease is promoted in turn by a high prevalence of cardiovascular risk factors, particularly smoking, hypertension, dyslipidemia, diabetes, and sedentary lifestyles. Patients in Africa and the Middle East present with myocardial infarction at a younger age, on average, compared with patients elsewhere. the projected future burden of mortality from coronary heart disease in Africa

and the Middle East is set to outstrip that observed in other geographical regions.

Recent detailed nationally representative epidemiological data are lacking for many countries, and high proportions of transient expatriate workers in countries such as Saudi Arabia and the United Arab Emirates complicate the construction of such datasets. However, the development of national registries in some countries is beginning to reveal the nature of coronary heart disease.

Improving lifestyles (reducing calorie intake and increasing physical activity) in patients in the region will be essential, although cultural and environmental barriers will render this difficult.

Appropriate prescribing of pharmacologic treatments is essential in the prevention and management of cardiovascular disease. in particular, recent controversies relating to the therapeutic profile of beta-blockers may have reduced their use. the current evidence base suggests that beta-blockers are as effective as other therapies in preventing cardiovascular disease and that concerns relating to their use in hypertension and cardiovascular disease have been overstated.

**Keywords:** Coronary heart disease; Beta-blockers; Cardiovascular risk factors; Cardiovascular disease; Heart failure.

## Dept. of Chemical Pathology

### 24. A Prospective Surveillance of Surgical Site Infections: Study for Efficacy of Preoperative Antibiotic Prophylaxis

Wassef M. A., Hussein A., Abdul Rahman E. M, and El-Sherif R. H.

*African Journal of Microbiology Research*, 6 (12): 3072-3078 (2012) IF: 0.539

To estimate the incidence and risk factors of surgical site infections, to determine the antimicrobial susceptibility pattern among the organisms isolated and to assess the ability of our protocol for preoperative antibiotic prophylaxis to prevent surgical site infections (SSI), a prospective SSI surveillance in Cairo University hospital using the criteria of the Centers for Disease Control of elective procedures, 881 patients were recruited in six months.

Data of surgical procedures, and preoperative antibiotic prophylaxis were collected. Patients were followed up for 30 days after surgery. The incidence of SSI infections was 9.2%. A significant increase was associated with a prolonged preoperative hospital stay, prolonged surgery, contaminated wounds and presence of the drain.

The most common organism was *Staphylococcus aureus* (24.3%) then *Klebsiella pneumoniae* (18.5%). MRSA constituted 68% of *S. aureus*, ESBL-producing Gram negative bacilli 41.8% and multidrug-resistant 25.4%. This is an insight to risk factors associated with SSI, the causative pathogens and their sensitivity in our hospital that can help in updating the preoperative antimicrobial prophylaxis.

**Keywords:** Surgical site infection; Surveillance; Preoperative antibiotics policy; Antimicrobial prophylaxis.

**Dept. of Clinical & Chemical Pathology**

**25. Enhanced Interpretation of Newborn Screening Results Without Analyte Cutoff Values**

Melanie Downing, Yannis Dotsikas and Yannis L. Loukas

*Genetics in Medicine*, 14 (7): 648-655 (2012) IF: 4.762

To improve quality of newborn screening by tandem mass spectrometry with a novel approach made possible by the collaboration of 154 laboratories in 49 countries.

**Methods:** A database of 767,464 results from 12,721 cases affected with 60 conditions was used to build multivariate pattern recognition software that generates tools integrating multiple clinically significant results into a single score. This score is determined by the overlap between normal and disease ranges, penetration within the disease range, differences between conditions, and weighted correction factors.

**Results:** Ninety tools target either a single condition or the differential diagnosis between multiple conditions. Scores are expressed as the percentile rank among all cases with the same condition and are compared to interpretation guidelines. Retrospective evaluation of past cases suggests that these tools could have avoided at least half of 279 false-positive outcomes caused by carrier status for fatty-acid oxidation disorders and could have prevented 88% of known false-negative events.

**Conclusion:** Application of this computational approach to raw data is independent from single analyte cutoff values. In Minnesota, the tools have been a major contributing factor to the sustained achievement of a false-positive rate below 0.1% and a positive predictive value above 60%.

**Keywords:** Cutoff values; False-positive rate; Inborn errors of metabolism; Newborn screening; Positive predictive value.

**26. Evaluation of Blood Supply Operation and Infectious Disease Markers in Blood Donors During the Egyptian Revolution**

Eiman Hussein and Jun Teruya

*Transfusion*, 52: 2321-2328 (2012) IF: 3.217

**Background:** the Egyptian revolution took place on January 25, 2011. Millions of protesters demanded the overthrow of the Egyptian president's regime. Many people suffered from life-threatening injuries after violent clashes between police and protesters.

**Study Design and Methods:** the overall management of the blood bank operation at Cairo University Hospital was described, in an attempt to evaluate blood safety and establish a standard effective plan to manage blood supply during crisis.

**Results:** Three days after the uprising, thousands of Egyptians rushed to the hospital to alleviate the blood shortage. A total of 3425 units were collected in 3 days and thousands of donors were turned away. an error delayed processing of 1000 units and they were used as stored whole blood. Apheresis platelets were donated by protesters who were particularly motivated to donate for two victims with liver injury. the usual positive rate of hepatitis C virus (HCV) antibody in Egyptian donors is 3.8%. However, the positive rate of HCV markers in the collected units was only 1.6%. the mean age of donors during the revolution was 31.7 10.4 years while the usual mean age of donors is 39.2 8.5 years. Operating theaters were used only for emergencies. A blood surplus developed that met the hospital needs for 1 month.

**Conclusion:** Revolution resulted in an influx of firsttime donors with a relatively low positive rate of HCV antibody. to be prepared for disasters, a systematic approach to spread donors evenly on a daily basis is needed.

**Keywords:** Hcv; Hbv; Hiv; Blood supply operation; Disasters.

**27. Socioeconomic Impact on Device-Associated Infections in Pediatric Intensive Care Units of 16 Limited-Resource Countries: International Nosocomial Infection Control Consortium Findings**

Victor D. Rosenthal, William R. Jarvis, Silom Jamulitrat, Cristiane Pavanello Rodrigues Silva, Bala Ramachandran, Lourdes Dueñas, Vaidotas Gurskis, Gulden Ersoz, Maria Guadalupe Miranda Novales, Ilham Abu Khader, Khalid Ammar, Nayide Barahona Guzmán, Josephine Anne Navoa-Ng, Zeinab Salah Seliem, Teodora Atencio Espinoza, Cheong Yuet Meng and Kushlani Jayatilake

*Pediatr Crit Care Med*, 13 (4): 1-8 (2012) IF: 3.129

**Objectives:** We report the results of the International Nosocomial Infection Control Consortium prospective surveillance study from January 2004 to December 2009 in 33 pediatric intensive care units of 16 countries and the impact of being in a private vs. public hospital and the income country level on device-associated health care-associated infection rates. Additionally, we aim to compare these findings with the results of the Centers for Disease Control and Prevention National Healthcare Safety Network annual report to show the differences between developed and developing countries regarding device-associated health care-associated infection rates.

**Patients and Methods:** A prospective cohort, active device-associated health care-associated infection surveillance study was conducted on 23,700 patients in International Nosocomial Infection Control Consortium pediatric intensive care units. the protocol and methodology implemented were developed by International Nosocomial Infection Control Consortium. Data collection was performed in the participating intensive care units. Data uploading and analyses were conducted at International Nosocomial Infection Control Consortium headquarters on proprietary software. Device-associated health care-associated infection rates were recorded by applying Centers for Disease Control and Prevention National Healthcare Safety Network device-associated infection definitions, and the impact of being in a private vs. public hospital and the income country level on device-associated infection risk was evaluated.

**Interventions: None. Measurements and Main Results:** Central line-associated bloodstream infection rates were similar in private, public, or academic hospitals (7.3 vs. 8.4 central line-associated bloodstream infection per 1000 catheter-days [ $p < .35$  vs. 8.2;  $p < .42$ ]). Central line-associated bloodstream infection rates in lower middle-income countries were higher than low-income countries or upper middle-income countries (12.2 vs. 5.5 central line-associated bloodstream infections per 1000 catheter-days [ $p < .02$  vs. 7.0;  $p < .001$ ]). Catheter-associated urinary tract infection rates were similar in academic, public and private hospitals:

(4.2 vs. 5.2 catheter-associated urinary tract infection per 1000 catheter- days [ $p .41$  vs. 3.0;  $p .195$ ]). Catheter-associated urinary tract infection rates were higher in lower middle-income countries than low-income countries or upper middle-income countries (5.9 vs. 0.6 catheter-associated urinary tract infection per 1000



catheter-days [ $p < .004$  vs. 3.7;  $p < .01$ ]). Ventilator-associated pneumonia rates in academic hospitals were higher than private or public hospitals: (8.3 vs. 3.5 ventilator-associated pneumonias per 1000 ventilator-days [ $p < .001$  vs. 4.7;  $p < .001$ ]). Lower middleincome countries had higher ventilator-associated pneumonia rates than low-income countries or upper middle-income countries: (9.0 vs. 0.5 per 1000 ventilator-days [ $p < .001$  vs. 5.4;  $p < .001$ ]). Hand hygiene compliance rates were higher in public than academic or private hospitals (65.2% vs. 54.8% [ $p < .001$  vs. 13.3%;  $p < .01$ ]).

Conclusions: Hospital type and country socioeconomic level influence device-associated infection rates in developing countries and need to be considered when comparing device-associated infections from one country to another.

**Keywords:** Bacteremia; Bloodstream Infection; Catheter-Associated; Urinary Tract Infection.

### 28. The Association between Hepatitis C Virus Infection, Genetic Polymorphisms of Oxidative Stress Genes and B-Cell Non-Hodgkin'S Lymphoma Risk in Egypt

Hala Farawela, Mervat Khorshied, Iman Shaheen, Heba Gouda, Aya Nasef, Nelly Abulata, Hebat-Allah Mahmoud, Hamdy M. Zawam and Somaia M. Mousa

*Infect Genet Evol*, 12: 1189-1194 (2012) IF: 3.128

Hepatitis C virus (HCV) has been postulated to be an etiological agent for lymphoid malignancies. Polymorphisms in oxidative stress genes as; superoxide dismutase (SOD2), glutathione peroxidase (GPX1), catalase (CAT), myeloperoxidase (MPO) and nitric oxide synthase (NOS2) may influence non-Hodgkin's lymphoma (NHL) risk. HCV screening and polymorphisms in these five genes coding for antioxidant enzymes were studied in 100 Egyptian patients with B cell-NHL and 100 controls to clarify the association between HCV infection, oxidative stress genes polymorphisms and B cell-NHL risk.

A significantly higher prevalence of HCV infection was detected among NHL patients relative to controls and this carried a 14-fold increased NHL risk (odds ratio (OR) = 14.3, 95% confidence interval (CI) = 5.4–38.3,  $p < 0.0001$ ). GPX1 and MPO genetic polymorphisms conveyed increase in B-NHL risk (OR = 3.3, 95% CI = 1.4–7.4,  $p = 0.004$  and OR = 4.4, 95% CI = 1.3–14.2,  $p = 0.009$  respectively).

Further analyses stratified by HCV infection revealed that concomitant HCV infection and GPX1 gene polymorphism had a synergetic effect on NHL risk with an OR of 15 (95%CI = 2.2–69.6,  $p < 0.0001$ ). In addition, combined HCV infection and MPO gene polymorphisms had a pronounced NHL risk (OR = 9.2, 95%CI = 2.5–33.9,  $p < 0.0001$ ). SOD2, CAT and NOS2 genetic polymorphisms were not found to confer increased NHL risk. This study revealed that HCV infection is a risk factor for NHL in Egypt. Polymorphisms in GPX1 and MPO genes may influence NHL risk in HCV infected Egyptian patients. Larger scale studies are warranted to establish this genetic susceptibility for NHL.

**Keywords:** Hcv; Oxidative stress genes; Genetic polymorphism; Antioxidant enzymes; B-Nhl; Nhl; Risk.

### 29. Viral Etiologies of Lower Respiratory Tract Infections among Egyptian Children Under Five Years of Age

Caroline F Shafik, Emad W Mohareb, Aymen S Yassin, Madgy A Amin, Amani El Kholy, Hanaa El-Karakasy and Fouad G Youssef

*Bmc Infectious Diseases*, (2012) IF: 3.118

**Background:** Lower respiratory tract infections (LRTI) are responsible for a considerable number of deaths among children, particularly in developing countries. In Egypt and the Middle East region, there is a lack of data regarding the viral causes of LRTI. In this study, we aimed to identify the relative prevalence of various respiratory viruses that contribute to LRTIs in young children. Although, nucleic acid-based methods have gained importance as a sensitive tool to determine the viral infections, their use is limited because of their prohibitive cost in low-income countries. Therefore, we applied three different laboratory methods, and presented the different virus prevalence patterns detected by each method.

**Methods:** We collected nasopharyngeal aspirate samples, demographic data and, clinical data from 450 children under five years of age who presented with LRTI at Abou El Reesh hospital in Cairo during a one-year period. To identify the viral causes of the LRTI we used direct fluorescence assay, real-time reverse-transcriptase polymerase chain reaction (rt-RT-PCR), and shell vial culture. We tested for eight major respiratory viruses.

**Results:** Two hundred sixty-nine patients (59.9%) had a viral infection, among which 10.8% had a co-infection with two or more viruses. By all three methods, respiratory syncytial virus (RSV) was the most predominant, and parainfluenza virus type 2 (HPIV-2), influenza B virus (FLUBV) were the least predominant. Other viral prevalence patterns differed according to the detection method used. The distribution of various viruses among different age groups and seasonal distribution of the viruses were also determined.

**Conclusions:** RSV and human adenovirus were the most common respiratory viruses detected by rt-RT-PCR. Co-infections were found to be frequent among children and the vast majority of co-infections were detected by nucleic acid-based detection assays.

**Keywords:** Egypt, Direct fluorescence assay, Lower respiratory tract infections, Pediatric, Polymerase chain reaction, Respiratory viruses, Shell vial culture.

### 30. Tumor Necrosis Factor Alpha-308 and Lymphotoxin Alpha+252 Genetic Polymorphisms and the Susceptibility to Non-Hodgkin Lymphoma in Egypt

Azza Ibrahim, Hala Abdel Rahman, Mervat Khorshied, Rania Samia, Nelly Nasra and Ola Khorshid

*Leukemia Res*, 36 ( 6 ): 694-698 (2012) IF: 2.923

Genetic polymorphism within the regulatory regions of tumor necrosis factor-alpha (TNF- $\alpha$ ) and Lymphotoxin-alpha (LT- $\alpha$ ) may be involved in the development of lymphoid malignancies. The aim of the current study was to investigate the effect of TNF $\alpha$ -308 and LT $\alpha$ +252 genetic polymorphism on susceptibility to non-Hodgkin lymphoma (NHL) in Egypt. Genotyping of the studied genes by restriction fragment length polymorphism polymerase chain reaction was conducted on 84 NHL and 100 healthy controls and revealed that TNF $\alpha$ -308 homotype (AA) was significantly higher in NHL patients and conferred sixfold increased risk of NHL (OR = 5.9, 95%CI = 2.3–16.1). Moreover,

TNF $\alpha$ /LT $\alpha$  high-producer haplotypes were significantly higher in NHL patients and conferred increased risk of NHL (OR = 4.59, 95%CI = 2.19–9.42).

**Keywords:** Tumor necrosis factor; Alpha (Tnf- $\alpha$ ) lymphotoxin; Alpha (Lt-  $\alpha$ ) Nhl; Pcr- Rflp; Egypt.

### 31. The Link between Genetic Polymorphism of Glutathione-S-Transferases, Gstm1, and Gstt1 and Divise Large B-Cell Lymphoma in Egypt

Hala A. Abdel Rahman, Mervat M. Khorshied, Haidy H. Elazzamy and Ola M. Khorshid

*Journal of Cancer Research and Clinical Oncology*, 138: 1363-1368 (2012) IF: 2.558

**Background:** Divise large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma. A number of studies have examined the role of genetic polymorphisms in the risk of DLBCL, and several variants have been identified as potential susceptibility genes, of those glutathione-S-transferases T1 and M1 (GSTT1 and GSTM1).

**Aim of the work:** the aim of the current study was to investigate the influence of inherited genetic polymorphisms of GSTM1 and GSTT1 genes on the susceptibility to DLBCL in Egypt.

**Methods:** Genotyping of the candidate genes was performed for 71 Egyptian DLBCL patients and 100 age- and gender-matched healthy controls by multiplex polymerase chain reaction technique.

**Results:** the frequencies of GSTT1 null, GSTM1 null, and dual null genotypes among DLBCL patients were 47.9, 52.1, and 23.9 % respectively.

**Conclusion:** GSTT1 null genotype conferred almost fourfold increased risk of DLBCL (OR = 3.9, 95 % CI = 1.97–7.75), and the risk increased when confined to male patients (OR = 4.4, 95 % CI = 1.57–12.63), while GSTM1 null genotype was not associated with DLBCL risk. Further studies on the functional consequences of GSTT1 and GSTM1 genetic polymorphisms would pave the way to declare their role in the pathogenesis of DLBCL or as possible predictors for response to therapy.

**Keywords:** Dlbcl; Gstt1; Gstm1; Genetic Susceptibility; Egypt.

### 32. Device-Associated Nosocomial Infection Rates in Intensive Care Units at Cairo University Hospitals: First Step Toward Initiating Surveillance Programs in A Resource-Limited Country

El-Kholy A, Saied T, Gaber M, Younan MA, Haleim MM, El-Sayed H, El-Karakasy H, Bazara'a H. and Talaat M.

*Am J Infect Control*, 40 (6): 216-220 (2012) IF: 2.396

**Background:** Device associated infections (DAIs) have major impact on patient morbidity and mortality.

**Methods:** This study involved active prospective surveillance to measure the incidence of DAIs, evaluate microbiological profiles, and investigate excessive mortality in intensive care units (ICUs) in 3 hospitals of Cairo University applying the US Centers for Disease Control and Prevention's National Healthcare Safety Network case definitions for ventilator-associated pneumonia (VAP), catheter-associated urinary tract infection (CAUTI), and central-line associated bloodstream infection (CLABSI). Data were collected between March 2009 and May 2010.

**Results:** A total of 1,101 patients were hospitalized for a total of 10,869 days, had 4,734 device-days, and acquired 97 DAIs, with an overall rate of 20.5/1,000 ICU days. VAP was the most commonly identified infection (88.7%); followed by CLABSI (8.2%) and CAUTI (3.1%). Excess mortality was 48% (relative risk, 1.9; P < .001) for CAUTI, 12.9% (relative risk, 1.2; 95% confidence interval, 1.1-1.4; P < .05) for VAP, and 45.7% for CLABSI. *Acinetobacter baumannii* was the most frequently isolated pathogen (36.1%), followed by *Klebsiella pneumoniae* (29.2%) and *Pseudomonas aeruginosa* (22.2%). High antimicrobial resistance was identified, with 85% of *A baumannii* isolates resistant to ciprofloxacin and imipenem, 76% of *K pneumoniae* isolates were extended-spectrum  $\beta$ -lactamase producers, and 56.3% *P aeruginosa* isolates resistant to imipenem (56.3%).

**Conclusion:** High rates of DAI and antimicrobial resistance require strengthening infection control, instituting surveillance systems, and implementing evidence-based preventive strategies.

**Keywords:** Device associated infection; Icu infection; Surveillance; Clabsi; Vap; Cauti.

### 33. DNA Methyltransferase 3B (Dnmt3b -579 G>T) Promotor Polymorphism and the Susceptibility to Pediatric Immune Thrombocytopenic Purpura in Egypt

Mervat Mamdooh Khorshied and Mona Kamal El-Ghamrawy

*Gene*, 511 (2012): 34-37 (2012) IF: 2.341

Idiopathic thrombocytopenic purpura (ITP) is an autoimmune disease characterized by increased platelet destruction. Although the etiology of ITP remains unclear, it is accepted that both environmental and genetic factors play an important role in the development of the disease. The present study aimed at exploring a novel molecular determinant that may influence the susceptibility and course of ITP in Egyptian children. To achieve our aim, genotyping of DNMT3B-579 G>T promotor polymorphism by polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP) assay. The current study was conducted on 140 ITP patients and 150 age and gender matched healthy controls. The results obtained revealed that DNMT3B 579 TT homotype was significantly higher in ITP patients and conferred almost three fold increased risk of ITP (OR=3.16, 95%CI=1.73–5.79). There was no statistically significant difference between ITP patients with wild or mutant genotypes as regards their clinical or laboratory data. Furthermore, there was no statistical difference in the distribution of DNMT3B -579 G>T genotypes between acute and chronic ITP patients.

In conclusion, DNMT3B-579 G>T promotor polymorphism represents a novel genetic risk factor for ITP but not a predictor for tendency to chronicity in pediatric ITP in Egypt.

**Keywords:** Itp; Dnmt3b -579 G>T Promotor; Polymorphism.

### 34. Angiotensin Converting Enzyme (Ace) Serum Level and Gene Polymorphism in Egyptian Patients with Systemic Lupus Erythematosus

D Abbas, Y Ezzat, E Hamdy and M Gamil

*Lupus*, 21: 103-110 (2012) IF: 2.337

**Objectives:** to investigate the association of angiotensin-converting enzyme (ACE) gene polymorphism and serum ACE

level among Egyptian SLE patients and its relation to disease activity parameters.

**Subjects and methods:** we enrolled 50 Egyptian female systemic lupus erythematosus (SLE) patients and 29 healthy controls. Measurement of serum ACE level was done using ELISA, and the ACE genotype was determined by polymerase chain reaction using genomic DNA from peripheral blood.

**Results:** a significant difference was found in ACE genotypes between SLE patients and controls (2/47.84, p/40.02). the frequency of ACE DD versus (DI and II) genotypes was significantly higher in SLE patients compared with controls (2/45.57, p /4 0.018 and OR for risk of SLE was 3.1 with 95% confidence interval: 1.198.06). Mean serum ACE level was significantly higher in the SLE group compared with controls (p/40.006). Subjects with DD genotype had a significantly higher mean level than those with DI ( p/40.015) and II genotypes (p/40.02). Lupus nephritis patients had a significantly higher frequency of DD versus DI and II genotypes compared with lupus patients without nephritis (Fisher's exact test, p/40.025) and controls (2 /48.74, p/40.003). SLE patients with vasculopathy had a significantly higher frequency of DD versus DI/II genotypes compared with SLE patients without vasculopathy (Fisher's exact test, p/40.04) and controls (2/49.84 and p/40.002). Mean serum ACE level was significantly higher in the lupus nephritis and SLE patients with vasculopathy compared with controls (p/40.008, p/40.001, respectively).

Significant positive correlations were found between serum ACE level and serum creatinine and 24 h proteinuria (p/40.03, 0.009, respectively). SLE patients with DD genotype had a statistically significant higher mean SLEDAI score than those with (DI/II) genotypes ( p/40.02). Significant positive correlation was found between serum ACE levels and SLEDAI scores ( p/40.04).

**Conclusion:** ACE genotype and subsequently serum ACE level could be associated with the disease activity of Egyptian SLE patients; in addition, ACE deletion polymorphism might be used as one of the predictive factors for the activity of SLE. Further studies on a larger number of patients should be done to determine the exact prevalence of ACE gene polymorphism among Egyptian SLE patients. *Lupus* (2012) 21, 103–110.

**Keywords:** Ace I/D Gene Polymorphism; Lupus Nephritis; Serum Ace Level; Sle; Sledai; Vasculopathy.

### 35. Evaluation of Multiplex Nested Polymerase Chain Reaction for Routine Hepatitis C Virus Genotyping in Egyptian Patients

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*Hepat Mon*, 12(4): 265-270 (2012) IF: 2.19

**Background:** at least six HCV (hepatitis C virus) genotypes are unequally distributed worldwide. HCV genotyping guides the selection of treatment regimens and provides important epidemiological markers that enable the outbreak source to be traced and the spread of disease to be controlled. In Egypt, there is an increasing need for cost-effective, fast, and easily performable HCV genotyping assays. Recently, a multiplex PCR assay was developed to determine HCV genotypes. It employs genotype-specific primers, based on sequences of the entire core region and part of the 5'UTR of the genome.

**Objectives:** in this study, we compared a simple, new, modified multiplex PCR system for HCV genotyping with a commercially

available line probe assay (INNO-LiPA) that is based on reverse hybridization.

**Patients and Methods:** Serum samples from chronic HCV Egyptian patients (n = 73) were genotyped using the modified multiplex PCR assay, and genotypes were verified using the INNO-LiPA HCV II assay.

**Results:** the modified multiplex PCR method was able to type HCV-4 in 65 of 70 typeable samples (92.86%) and had 100% concordance with the INNO-LiPA assay.

**Conclusions:** Genotype 4 was the most prevalent genotype in our study. Based on our results, the modified multiplex nested PCR assay is a sensitive and inexpensive alternative for HCV genotyping and can be used in routine diagnostic laboratories. INNO-LiPA may be useful as a second-line assay for genotyping samples that are indeterminate by multiplex PCR. This approach will effect better treatment optimization and a reduction of the spread of HCV.

**Keywords:** Hepatitis C; Multiplex polymerase chain reaction; Branched DNA signal amplification; Assay.

### 36. Association of Folate Intake, Dietary Habits, Smoking and Cox-2 Promotor 765G > C Polymorphism with K-Ras Mutation in Patients with Colorectal Cancer

Manal M. Kamal, Omar Z. Youssef, Ahmed N. Lotfy, Eman T. Elsaed and May M.T. Fawzy

*Journal of the Egyptian National Cancer Institute*, 24: 115-122 (2012) IF: 2

**Background:** Understanding the role of environmental and molecular influences on the nature and rate of K-ras mutations in colorectal neoplasms is crucial. COX-2 polymorphisms 765G >C may play a role in carcinogenic processes in combination with specific life-style conditions or dependent on the racial composition of a particular population.

If mutational events play an important role in colorectal carcinogenesis sequence, one can hypothesize that modification of these events by life-style or other factors would be a useful prevention strategy.

**Aim of work:** to explore the association between K-ras mutation and potential variables known or suspected to be related to the risk of colorectal cancer (CRC) as well as determining the possible modulating effect of the COX-2 polymorphism, 765G > C.

**Subjects and methods:** the study was conducted on 80 patients with colorectal cancer from Tropical Medicine and Gastrointestinal Tract endoscopy Departments and those attending clinic of the National Cancer Institute, Cairo University during the period extending from April 2009 to March 2010. Full history taking with emphasis on the risk factors of interest, namely age, sex, family history, smoking and dietary history. Serum CEA and CA19-9, RBCs folic acid and occult blood in stool were done to all samples. K-ras protooncogene mutation at codon 12 (exon 1) and cyclooxygenase 2 (COX-2) 765G > C polymorphism were determined by PCR-RFLP.

**Results:** the K-ras mutation was positive in 23 (28.7%) patients. COX-2 polymorphism revealed GG in 62.5%, GC in 26.2 % and CC genotype was found in 11.3 % of cases. the mean red blood cell folic acid level was lower in the K-ras positive group (100.96 ± 51.3 ng/ml) than the negative group (216.6 ± 166.4 ng/ml), (P < 0.01). Higher folate levels were found in males than females

(median= 173 ng/ml and 85 ng/ml; respectively, P = 0.002) with adjusted odds ratio (OR) of 0.984.

Only, the RBCs folate (P = 0.0018) followed by gender (P = 0.036) contributed significantly in the discrimination between patients prone to develop K-ras mutation and those who are not.

**Conclusion:** RBC folic acid was significantly deficient in CRC (colorectal cancer) patients with Kras mutations in comparison with CRC patients free of the mutations, suggesting that folic acid may be a risk factor for K-ras mutation development.

**Keywords:** Folate; Colorectal cancer; K-Ras; Cyclooxygenase2.

### 37. Hematopoietic Stem Cell Mobilization Into the Peripheral Circulation in Patients with Chronic Liver Diseases

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*J Digest Dis*, 13: 571-578 (2012) IF: 1.589

**Objective:** the present study was aimed to investigate and compare the kinetics of bone marrow derived hematopoietic stem cells (BMHSC) migration in the peripheral blood and liver in response to liver injury in patients with chronic liver disease (CLD).

**Methods:** in all, 45 CLD patients staged with Child–Pugh A, B and C and 15 healthy participants were evaluated for the concentration of circulating BMHSC by a flow cytometric analysis of CD133+/ CD34+ cells. in addition, homing BMHSC and hepatic progenitors were assessed by the immunohistochemical detection of CD133+ and OV6+ cells in liver biopsy specimens from Child–Pugh A and B patients.

**Results:** No significant difference in the percentage of circulating CD133+/CD34+ cells was observed among all groups of patients. in liver tissues, OV6+ cells increased significantly in Child–Pugh B cases (P < 0.05), while CD133+ cells were distributed sparsely in the periportal region in Child–Pugh A and B patients. OV6+ cells were significantly correlated with CD34+ cells but not with CD133+ cells in Child–Pugh A and B patients (P < 0.01 and P < 0.05, respectively).

**Conclusions:** Various degrees of severity in CLD neither evoked the mobilization of BMHSC into the circulation nor triggered their homing into liver tissue, thus excluding extrahepatic stem cell-mediated repair. the recovery process seems to be dependent on proliferating endogenous liver progenitors (OV6+ cells).

**Keywords:** Liver diseases; Hepatic progenitors; Oval cells; Hematopoietic stem cells.

### 38. Mesenchymal Stem Cells are A Rescue Approach for Recovery of Deteriorating Kidney Function

Mervat El-Ansary, Gamal Saadi and Samah M Abd El-Hamid

*Nephrology*, 17 (2012): 650-657 (2012) IF: 1.311

**Aim:** Stem cell (SC) therapy for chronic kidney disease (CKD) is urgently needed. the use of mesenchymal stem cells (MSC) is a possible new therapeutic modality. Our work aimed to isolate human MSC from adult bone marrow to improve kidney functions in CKD patients.

**Methods:** in our study 30 patients with impaired kidney function were included, their ages ranged from 22 to 68 years. They

included 10 inactive glomerulonephritis patients due to systemic lupus erythromatosus (SLE) (group I), 10 renal transplantation cases (group II) and 10 patients of other aetiologies as the control group. Fifty millilitres of bone marrow was aspirated from the iliac bone, for separation of MSC.

**Results:** There was a highly statistically significant difference between both CD271 and CD29 before and after culture with increase of both markers at end of culture, P < 0.01. Finally 50–70 million MSC in 10 mL saline (0.7–1.0 ¥ 10<sup>6</sup> MSC/kg body weight) were infused intravenously in two divided doses one week apart. There was a highly statistically significant difference between each of serum creatinine and creatinine clearance levels before and after MSC injection at 1, 3 and 6 months post-infusion with SLE cases showing a greater decline of their serum creatinine and elevation of mean creatinine clearance levels after injection than transplantation and control groups, P < 0.05.

**Conclusion:** Mesenchymal stem cells therapy is a potential therapeutic modality for early phases of CKD.

**Keywords:** Chronic Kidney Disease; Glomerulonephritis; Mscs; Renal Transplantation; Tissue Repair.

### 39. FcgrIIa and FcgrIIa Genetic Polymorphisms in A Group of Pediatric Immune Thrombocytopenic Purpura in Egypt

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*Blood Coagul Fibrin*, 23 (1): 64-68 (2012) IF: 1.238

Immune thrombocytopenic purpura (ITP) is an acquired autoimmune disorder caused by the production of antiplatelet antibodies. the current case-control study aimed at detecting the frequency of FcgrIIa-131H/R and FcgrIIa-158F/V genes polymorphism in Egyptian children with ITP as genetic markers for ITP risk, and to clear out their possible role in choosing the treatment protocols of ITP. to achieve this aim, FcgrIIa genotyping was tested by PCR-restriction fragment length polymorphism (RFLP) technique, whereas FcgrIIa genotyping was tested by nested PCR followed RFLP analysis. the current casecontrol study was conducted on 92 children with ITP; 12 acute and 80 chronic cases and 90 controls. the V allele and FcgrIIa FV heterotype were significantly higher in ITP patients and conferred increased ITP risk [odds ratio (OR)U1.96 and 2.55, respectively]. the frequency of FcgrIIa H allele was significantly higher among chronic ITP patients. in conclusion, FcgrIIa gene polymorphism may contribute to susceptibility to ITP. Moreover, analysis of the Fcgr polymorphisms in ITP patients could influence the effectiveness of medications and selection of the line of treatment.

**Keywords:** Childhood itp; Fcgr Iia; Fcgr Iiia; Pcr-Restriction Fragment length polymorphism.

### 40. Role of Soluble P-Selectin and Methylenetetrahydrofolate Reductase Gene Polymorphisms (677C>T) in Egyptian Patients with Venous Thromboembolism

Nehad M. Tawfik, Manal El. Deeb and Aml S. Nasr

*Blood Coagul Fibrin*, 23 (6): 537-542 (2012) IF: 1.238

Venous thromboembolism (VTE) is a significant problem for surgical and medical hospitalized patients, leading to the

possibility of serious illness and risk of death. the aim of the present study was to investigate soluble P-selectin levels and genetic polymorphisms in 5, 10-methylenetetrahydrofolate reductase (MTHFR 677C/T) and to evaluate its associations with VTE was the aim of work. the study involved 49 patients diagnosed as having VTE (as a patients group) as well as 24 apparently healthy volunteers (as controls group). All the participants included in the study were assessed for soluble serum P-selectin levels using the enzyme-linked immunosorbant assay technique. All the participants included in the study were genotyped for detection of MTHFR gene polymorphisms (677C >T) by restriction fragment length polymorphism. Concerning the results of soluble P-selectin, there were statistically significant differences between the two groups (P U0.0210). Concerning the results of MTHFR gene polymorphisms, there were no statistically significant differences between the two groups regarding CT allele (P U0.8790), but there were highly statistically significant differences between the two groups regarding CC, TT alleles as well as CC/CT and TT/CT alleles (P <0.0001). According to our study, elevated soluble P-selectin levels as well as MTHFR gene polymorphisms are to be considered as independent risk factors for development of VTE, so it may be recommended to include P-selectin assay and detection of MTHFR gene polymorphisms when considering patients with thromboembolism even in the absence of any other predisposing factor.

**Keywords:** Enzyme-linked immunosorbant assay technique; Methylenetetrahydrofolate reductase; P-Selectin; Polymorphisms by restriction fragment length polymorphism; Thromboembolism.

#### 41. Methylenetetrahydrofolate Reductase Gene Polymorphisms (677C > T and 1298A > C) in Egyptian Patients with Non-Hodgkin Lymphoma

Aml S. Nasr, Rania M. Sami and Noha Y. Ibrahim

*Journal of Cancer Research and Therapeutics*, 8 (3): 355-360 (2012) IF: 0.656

**Background:** Folate metabolism plays an essential role in Deoxyribonucleic acid (DNA) synthesis and methylation processes. Deviations in the flux of the folate may affect the susceptibility to various cancers including lymphoma.

**Aim:** the aim of this study was to investigate the genetic polymorphisms in 5, 10-methylenetetrahydrofolate reductase (MTHFR 677C/T and 1298A/C) and to evaluate its associations with the risk of Non Hodgkin lymphoma.

**Materials and Methods:** the study included 50 patients with diffuse large B cell lymphoma (DLBCL) as well as 50 age matched apparently healthy volunteers (as control). All the subjects included in the study were genotyped for the detection of the MTHFR gene polymorphisms (677C > T and 1298A > C) by using restriction fragment length polymorphism (PCR-RFLP).

**Results:** There were highly statistically significant differences between the 2 groups with respect to results of PCR-RFLP for MTHFR677C?T polymorphism for CC genotype ( P value = 0.001), statistically significant differences for CT (P value = 0.048) and TT ) P value = 0.038) genotypes; however, no statistically significant differences regarding CC/CT or TT/CT alleles (P value = 0.052). Also, there were highly statistically significant differences between the patient and control groups with regards to the results of MTHFR1298 A/C polymorphism for the AA, AC genotypes as well as the AA/AC and CC/AC alleles (

P value < .0001), and statistically significant difference regarding CC genotype) P value 0.0192).

**Conclusion:** in conclusion, this study demonstrated a significant association between the MTHFR polymorphisms and the risk of DLBCL. Thus the study could support that folate intake together with the genetic basis may help in modifying the risk to lymphoma.

**Keywords:** Methylenetetrahydrofolate reductase; Methylenetetrahydrofolate reductase gene polymorphisms; Non hodgkin lymphoma; Promoter polymorphisms; Restriction fragment length polymorphism; Risk.

#### 42. GSTP1 and Cyp1a1 Gene Polymorphisms and Nonhodgkin Lymphoma

Noha Y. Ibrahim, Rania M. Sami and Aml S. Nasr

*Lab Medicine*, 43 (4): 12-16 (2012) IF: 0.359

**Objective:** to determine the association between genetic variants of GSTP1 and CYP1A1 enzymes and individual susceptibility to diffuse large B-cell lymphoma (DLBCL), as well as correlations with tobacco smoking.

**Methods:** Fifty patients with DLBCL and 50 apparently healthy volunteers were genotyped for detection of GSTP1 and CYP1A1 polymorphisms by the restriction fragment length polymorphism (RFLP) technique.

**Results:** for GSTP1 313 A?G polymorphism, statistically significant differences were observed between the DLBCL and control groups for the AA, AG, and GG genotypes, as well as the G allele. for CYP1A1 4889 A→G (M2) polymorphism, statistically significant differences were observed for the AA and AG genotypes and the G allele. the relationship of smoking status to susceptibility to DLBCL in the presence of these genetic polymorphisms revealed that smoking status had no effect.

**Conclusion:** GSTP1 313 A→G polymorphism is associated with a decreased risk of lymphoma, whereas CYP1A1 4889 A→G (M2) polymorphism is associated with an increased risk of lymphoma regardless of smoking status.

**Keywords:** Drug-metabolizing genes; Nonhodgkin lymphoma; Gstp1 and Cyp1a1 promoter polymorphisms; Risk; Tobacco smoking; Smoking status.

#### 43. Studying the Effect of rhBAFF and BAFF-R-Fc Fusion Protein on Lymphocytes and Platelets in Children with Itp

Sahar Kamal, Nadia Sewelam, Doha Mokhtar, Rania Fawzy and Nouran Nabil

*Life Science Journal*, 9 (4): 2363-2369 (2012) IF: 0.075

**Introduction:** B cell activating factor, a member of tumor necrosis factor family, is a crucial homeostatic cytokine for B cells. It has been shown to enhance the expression of CD19+ cells and mediate the maturation of autoreactive B cells. BAFF is elevated in several autoimmune diseases including immune thrombocytopenic purpura (ITP). Increased survival of CD8+ T cells also may promote the apoptosis of platelets through cytotoxic T lymphocyte-mediated platelet lysis. Blockade of BAFF receptor has demonstrated a clinical benefit in immunologic diseases.

**Methods:** PBMCs and platelets from 15 acute ITP patients and 15 healthy controls were cultured with rhBAFF or a combination of

rhBAFF and BR3-Fc and then analyzed by flow cytometry for apoptosis of autologous platelets and/or CD19+, CD8+ and CD4+ cells. Results Blockade of BAFF receptor by BR3-Fc significantly increased the apoptosis of CD19+ cells in patients only and decreased the apoptosis of platelets in both patients and controls. Apoptotic CD8+ cells were significantly increased in patients only, following the addition of BR3-Fc.

**Conclusion:** These findings suggest that blockade of BAFF receptor (BR3-FC) could successfully correct the effects of BAFF by promoting the apoptosis of CD19+ and CD8+ cells and decreasing the apoptosis of platelets. Further research will indicate whether blocking BAFF-BR3 will have a therapeutic applicability in the management of ITP or not.

**Keywords:** Immune thrombocytopenic purpura; Baff; Cd19;- Cd8;- Cd4;- Platelets.

#### 44. Study of Survivin and X-Linked Inhibitor of Apoptosis Protein (Xiap) Genes in Acute Myeloid Leukemia (Aml)

Azza Mostafa Ibrahim, Iman Maher Mansour, Manal Michel Wilson, Doha Abdel-Hamid Mokhtar, Amani Mohamed Helal and Hanan Mohamed Al Wakeel

*Lab Hematol.*, 18 (1): 1-8 (2012)

Apoptosis deregulation is important for cancer development, chemotherapy response, and prognosis. Survivin and X-linked inhibitor of apoptosis protein (XIAP) are 2 members of the inhibitor of apoptosis proteins family (IAP). We used semi-quantitative reverse transcriptase polymerase chain reaction (RT-PCR) to determine the levels of expression of survivin and XIAP in 30 patients with de novo acute myeloid leukemia (AML) and 20 age- and sex-matched healthy volunteers. Survivin and XIAP overexpression were detected in 36.7% and 43.3% of cases, respectively. Patients with overexpression of either survivin or XIAP showed unfavorable response to chemotherapy in 81.2% and 91.7%, respectively. Also, these cases showed shorter median survival time (30 days) compared to patients with normal expression of either survivin or XIAP (150 days and 180 days). Patients with overexpression of both survivin and XIAP showed unfavorable response to induction therapy in 100% of the patients and the shortest median survival (30 days). These findings suggest that survivin and XIAP may have a role in leukemogenesis and provide prognostic information.

**Keywords:** Apoptosis; Survivin; X-Linked inhibitor of apoptosis protein (Xiap); Acute myeloid leukemia (Aml).

#### 45. Role of Serum Anti-C1q Antibodies as A Biomarker for Nephritis Activity in Pediatric and Adolescent Egyptian Females with Sle

Mohamed Salah Eldin Mohamed Abdel Kader, Mohamed Momtaz Abd Elaziz and Dina Hisham Ahmed

*Expert Opinion on Medical Diagnostics*, 6 (6): 489-498 (2012)

**Objective:** to evaluate serum anti-C1q antibodies as a biomarker of systemic lupus erythematosus (SLE) flare and as a proposed noninvasive alternative to renal biopsy which is still the "gold standard" to determine renal activity in SLE.

**Methods:** Serum anti-C1q antibodies were measured in our patients (all were females), they were followed at the nephrology and pediatric nephrology units at the Faculties of Medicine of

Cairo University and Misr University for science and technology (MUST). Our study included 120 patients in the pediatric and adolescent age group and they were categorized into three groups with (mean  $\pm$  SD of 16.7  $\pm$  3, 16.1  $\pm$  2, 15.9  $\pm$  3) respectively: Group 1 including 40 patients with SLE and active lupus nephritis; Group 2 including 40 patients with SLE and without active lupus nephritis, but with some extra renal activity mainly arthritis; and Group 3 including 40 healthy subjects.

**Results:** Anti-C1q antibodies were found to be significantly higher in patients with active lupus nephritis than those without active nephritis than control individuals with a median (range) of [27.5 (14 – 83), 9 (2.5 – 30), 7 (2 – 13)] respectively. In those with active lupus nephritis, anti-C1q was found to correlate significantly with other parameters assessing lupus nephritis activity like C3 ( $r = -0.33$ ,  $p < 0.04$ ), C4 ( $r = -0.32$ ,  $p < 0.044$ ), daily urinary protein excretion ( $r = 0.32$ ,  $p < 0.036$ ), renal SLEDAI ( $r = 0.64$ ,  $p < 0.001$ ), and activity index ( $r = 0.71$ ,  $p < 0.001$ ).

**Conclusions:** Anti-C1q antibodies can be used as a considerable marker for LN activity in that age group with 97.5% sensitivity and 65% specificity with the cutoff level 12 U/l. These levels are clearly higher than those for traditional markers of disease activity such as C3/C4 consumption and anti-dsDNA.

**Keywords:** anti-C1q antibodies, anti-dsDNA, C3, C4, ELISA, juvenile systemic lupus erythematosus, lupus nephritis, renal SLEDAI, urinary proteins.

#### 46. Device-Associated Infection Rates in Adult and Pediatric Intensive Care Units of Hospitals in Egypt. International Nosocomial Infection Control Consortium (Inicc) Findings

Ossama Rasslana, Zeinab Salah Seliemb, Islam Abdullorziz Ghazic, Muhamed Abd El Saboura, Amani Ali El Kholyb, Fatma Mohamed Sadeqc, Mahmoud Kalila, Doaa Abdel-Azizb, Hosnia Yousif Sharafc, Adel Saeeda, Hala Aghab, Sally Abd El-Wadood Zein El-Abdeenc, Maha El Gafareya, Amira El Tantawyb, Lamia Fouada, Mona M. Abel-Haleimb, Tamer Muhameda, Hedya Saeeda and Victor D. Rosenthal

*J. Infect Public Health*, 5: 394-402 (2012)

**Purpose:** to determine the rate of device-associated healthcare-associated infections (DA-HAIs) at a respiratory intensive care unit (RICU) and in the pediatric intensive care units (PICUs) of member hospitals of the International Nosocomial Infection Control Consortium (INICC) in Egypt.

**Materials and Methods:** A prospective cohort DA-HAI surveillance study was conducted from December 2008 to July 2010 by applying the methodology of the INICC and the definitions of the NHSN-CDC.

**Results:** in the RICU, 473 patients were hospitalized for 2930d and acquired 155 DA-HAIs, with an overall rate of 32.8%. There were 52.9 DA-HAIs per 1000 ICU-days. in the PICUs, 143 patients were hospitalized for 1535d and acquired 35 DA-HAIs, with an overall rate of 24.5%. There were 22.8 DA-HAIs per 1000 ICU-days. the central line-associated blood stream infection (CLABSI) rate was 22.5 per 1000 line-days in the RICU and 18.8 in the PICUs; the ventilator-associated pneumonia (VAP) rate was 73.4 per 1000 ventilator-days in the RICU and 31.8 in the PICUs; and the catheter-associated urinary tract infection (CAUTI) rate was 34.2 per 1000 catheter-days in the RICU.

**Conclusions:** DA-HAIs in the ICUs in Egypt pose greater threats to patient safety than in industrialized countries, and infection control programs, including surveillance and guidelines, must become a priority.

**Keywords:** Device associated infection; Icu infection; Surveillance; Clabsi; Vap; Cauti.

#### 47. Prevalence of Occult Hepatitis C Virus in Egyptian Patients with Chronic Lymphoproliferative Disorders

Samar Samir Youssef, Aml S. Nasr and Taher El Zanaty

*Hepatitis Research and Treatment.*, (2012)

**Background:** Occult hepatitis C virus infection (OCI) was identified as a new form of Hepatitis C virus (HCV), characterized by undetectable HCV antibodies and HCV RNA in serum, while HCV RNA is detectable in liver and peripheral blood cells only. **Aim:** the aim of this study was to investigate the occurrence of OCI in Egyptian patients with lymphoproliferative disorders (LPDs) and to compare its prevalence with that of HCV in those patients.

**Subjects and Methods:** the current study included 100 subjects, 50 of them were newly diagnosed cases having different lymphoproliferative disorders (patients group), and 50 were apparently healthy volunteers (controls group). HCV antibodies were detected by ELISA, HCV RNA was detected in serum and peripheral blood mononuclear cells (PBMCs) by reverse transcription polymerase chain reaction (RT-PCR), and HCV genotype was detected by INNO-LIPA.

**Results:** OCI was detected in 20% of patients group, compared to only 4% OCI in controls group. HCV was detected in 26% of patients group with a slightly higher prevalence. There was a male predominance in both HCV and OCI. All HCV positive patients were genotype 4.

**Conclusion:** Our data revealed occurrence of occult HCV infection in Egyptian LPD patients at a prevalence of 20% compared to 26% of HCV.

**Keywords:** Hcv; Chronic Lymphoproliferative Disorders; Hcv Antibodies; Hcv Rna; Rt-Pcr.

#### 48. Iron Load and Serum Hepcidin in Hepatitis C Virus-Related Hepatocellular Carcinoma

Nehad M. Tawfik, Mona A. Hegazy, Inas A. Abdel Maksoud and Aml S. Nasr

*Euroasian Journal of Hepatology and Gastroenterology*, 2 (1): 24-27 (2012)

Hepatocellular carcinoma (HCC) is a major cause of death worldwide, and chronic inflammatory stress caused by hepatitis viruses plays a major role in HCC carcinogenesis. the aim of the present study was to investigate the expression of serum hepcidin and its correlation with iron overload in HCC.

**Study Design:** the study was carried out on 50 hepatitis C virus (HCV) related HCC cirrhotic patients (Group I) and 20 age-matched non-HCC liver cirrhosis patients as control (Group II).

**Results:** There was no relationship between the serum hepcidin level and the histological grade of HCC ( $P = 0.1492$ ), or multiplicity of focal lesion ( $P = 0.0719$ ), however, hepatic iron

deposition was significant higher in HCC than non HCC cirrhotic patients ( $P < 0.005$ ).

**Conclusion:** the current study suggests a positive association of hepatic iron score, but the role of hepcidin in this context remains to be elucidated.

**Keywords:** Hepatocellular carcinoma; Serum hepcidin level; Hcv.

#### 49. The Clinical Significance of Methylenetetrahydrofolate Reductase (Mthfr) Polymorphisms in Acute Lymphoblastic Leukemia

Hanaa H. Arnaout, Mervat M. Khorshied, Iman A. Shaheen, Heba M. Gouda, Noha Y. Ibrahim and Naglaa F. Koura

*Comparative Clinical Pathology*, (2012)

Acute lymphoblastic leukemia (ALL) is the most common pediatric malignancy. Genetic polymorphisms in the folate metabolic pathway may contribute to the susceptibility to childhood ALL because they affect the DNA synthesis, methylation, and repair. the most common polymorphisms are methylenetetrahydrofolate reductase (MTHFR) C677T and A1298C. the current study aimed at detecting the frequency of these two genetic polymorphisms in de novo ALL patients, and to clarify their impact on the response to induction chemotherapy, as well as treatment toxicity. MTHFR C677T and A1298C polymorphisms were tested in 30 de novo ALL patients by restriction fragment length polymerase chain reaction technique. Thirty normal age- and sex-matched subjects were subjected to the same analysis as a control group. the frequency of MTHFR A1298C gene polymorphism was significantly lower in ALL patients than the controls thus showing a protective effect. the two polymorphisms had no effect on the response to induction chemotherapy.

as regards the treatment toxicity, MTHFR C677T polymorphism was associated with marked thrombocytopenia, while A1298C polymorphism was associated with hepatic toxicity. Identifying predictors of methotrexate sensitivity may lead to the development of individualized treatment strategies with improved efficacy and reduced toxicity as well as adjusting the initial methotrexate dose.

**Keywords:** Mthfr gene polymorphism C677t; A1298c; Pcr; All.

#### 50. Association of Caspase 8 and Caspase 10 Genetic Polymorphisms with B-Cell Non Hodgkin's Lymphoma in Egypt: A Case-Control Study

Hanaa Hamed Arnaout, Mervat Mamdooh Khorshied, Ola M. Reda Khorshid and Mona Hazem El-Nagdy

*Journal of Cancer Science & Therapy*, 4: 249-253 (2012)

Non-Hodgkin lymphomas are closely related diseases with distinctive morphologic, immunophenotypic, genetic, and clinical features. Genetic susceptibility studies of NHL are mandatory to identify at risk populations and to clarify important disease mechanisms. Caspase genes play a key role in regulation of apoptotic cell death, and dysregulation of this signaling pathway has been shown to participate in tumorigenesis. the current study aimed at defining the role of Caspase 8-D302H, Caspase 8-652 6N ins/del and Caspase 10-I522L genetic polymorphisms as risk factors for NHL and their possible role as genetic prognostic markers.

**Methods:** the present study included 100 Egyptian B-cell NHL patients and 100 healthy controls. Genotyping of the studied genes was performed by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique. Data was analyzed using SPSS statistical package version 15.

**Results:** the study revealed that CASP8-D302H mutant genotypes were significantly higher in NHL patients when compared to the controls and conferred increased risk of NHL. for CASP8-652 6N ins/del and Casp10-I522L, there was no statistical difference in the distribution of the different genotypes between NHL cases and the controls. Furthermore, there were no statistical differences between NHL patients harboring the wild or mutant genotypes of the studied genes as regards their response to therapy.

**Conclusions:** CASP8-D302H genetic polymorphism represents a genetic risk factor for NHL in Egyptian population. Hopefully, better understanding of the functional consequences of caspase genes polymorphism would provide a foundation for future studies of the possible role of these genes in lymphomagenesis.

**Keywords:** Caspase; Polymorphisms; Non hodgkin'S lymphoma.

### 51. The Osteogenic Differentiation Potentials of Umbilical Cord Blood Hematopoietic Stem Cells

Mervat M. Khorshied, Heba M. Gouda, Iman A. Shaheen and Tarek N. Al Bolkeny

*Comparative Clinical Pathology*, (2012)

Under specific culture conditions, umbilical cord blood derived mesenchymal stem cells (MSCs) can differentiate into osteogenic, adipogenic, and chondrogenic lineages. the purpose of the current study was to assess the differentiation potential of osteogenic umbilical cord blood derived hematopoietic stem cells (HSCs) and to develop an appropriate osteogenic differentiation medium for in vitro differentiation of umbilical cord blood derived HSCs. the study was conducted on 20 cord blood samples. the cells were cultured in osteogenic differentiating medium for 3 weeks. the HSCs differentiated into osteoblasts, which expressed osteoblast-associated genes (osteocalcin and bone sialoprotein), which were detected by RT-PCR. They showed alkaline phosphatase activity and a positive Alizarin red-S (AR-S) stain (calcium phosphate deposition). Umbilical cord blood is a rich source of hematopoietic stem cells that can be differentiated into osteoblasts; thus, it can be used for therapeutic strategies in the context of regenerative therapy.

**Keywords:** Umbilical cord blood; Hematopoietic stem cells; Osteogenic differentiation.

### 52. Flow Cytometric Detection of Leukemic Stem Cells (Lscs) in Egyptian Pediatric B-Acute Lymphoblastic Leukemia

Manal W. El-Masry, Mervat M. Khorshied, Iman A. Shaheen, Nelly N. Abulata and Tarek A. Hashem

*Comparative Clinical Pathology*, (2012)

Identifying leukemia stem cells (LSCs) is a challenge and a critical step in understanding their respective biology and may provide insights into a more efficient treatment of acute lymphoblastic leukemia (ALL). This cohort study aimed at detecting LSCs expressing CD19, CD34, and CD38Low in the bone marrow of 20 de novo Egyptian pediatric B-ALL patients at the time of the diagnosis and after the induction of chemotherapy.

LSCs were detected in 80% of cases at the time of diagnosis and in 70% of the cases after the induction of chemotherapy. Patients were followed up for 12–18 months. No statistically significant difference was encountered between LSC-positive and LSC-negative patients as regards their clinical and laboratory data at the time of diagnosis. Furthermore, there was no statistically significant difference between the percentages of LSC-positive patients before or after induction of therapy. on follow-up, two patients died; they had residual LSCs after the induction therapy. However, the existence of LSCs did not affect the patient's 1-year disease-free survival rate. LSC may resist the traditional lines of treatment applied for childhood B-ALL; it may be used in minimal residual disease monitoring as well as being a target for new therapeutic lines to improve the outcome of treatment especially in patients with high-risk and relapsed ALL.

**Keywords:** Lscs; B-All; Multicolor flow cytometry.

### 53. Glutathione S-Transferase T1 (Gstt1) and M1 (Gstm1) Genes Polymorphism and Risk of Bronchial Asthma in Children

Asmaa Ahemed Abd El-Aal, Mostafa M. El-Nashar and Amal H. El-Sissy

*Comparative Clinical Pathology*, (2012)

Oxidative stress is thought to be involved in the pathogenesis of asthma. Glutathione-S-Transferase (GST) enzymes play an important role in the antioxidant defence mechanism and therefore may influence asthma risk. Polymorphism of GSTT1 and GSTM1 genes has been associated with asthma in children and adults, but results are inconsistent across studies. the aim of the present study was to examine the association of GSTT1 and GSTM1 gene genotype and the risk of asthma among 44 stable asthmatic children in comparison to 30 healthy control subjects. Genotyping was performed using the multiplex PCR technique. GSTT1 null genotype was significantly associated with an increased risk of asthma by more than 9 fold. GSTM1 polymorphism did not appear to play a major role in the development of bronchial asthma in children. Neither was associated with patients' phenotype.

**Keywords:** Asthma; Gsst; Gstm; Polymorphism.

### 54. Differentiation of Insulin-Producing Cells from Human Cord Blood-derived Haemopoietic Stem Cells in Vitro

Manal El-Masry, Heba Gouda, Rania Fawzy and Nihal Salah El-Din

*Comparative Clinical Pathology*, 21: 1707-1711 (2012)

the use of stem cells in regenerative medicine holds great promise for the cure of many diseases, including type 1 diabetes mellitus, which, despite of the advances in current therapeutic approaches, remains to be one of the most serious health care problems. in addition to the traditional sources of adult stem cells, human umbilical cord blood has provided an important source of stem cells for research due to its unique advantages compared to other sources. in this study, we aimed at optimizing culture conditions for obtaining insulin-producing cells from cord blood hematopoietic stem cells. Twenty cord blood samples were subjected to short-term, liquid static culture that favors the proliferation of CD34+ hematopoietic stem cells. A duplicate



culture was set for each sample, one with high glucose concentration and the other with low glucose concentration. Then these cells were subsequently induced to transdifferentiate into insulin-producing cells via a biphasic liquid culture using exendin-4. the expression of human insulin was then tested using RT-PCR. at the end of the culture, 17 out of the 20 samples (85%) cultured in high glucose concentration showed positive human insulin mRNA expression, while culture media with low glucose concentration failed to induce transdifferentiation into insulin-producing cells in any of the 20 samples. in brief, our study demonstrate that hematopoietic cord blood stem cells can transdifferentiate into insulin-producing cells in short-term liquid culture supplemented with high glucose concentration, nicotinamide, and exendin-4 in vitro.

**Keywords:** Insulin-Producing Cells; Diabetes Mellitus.

### 55. Clinical Relevance of Angiopoietin-1, Angiopoietin-2, and their Receptor Tie-2 Expression in Acute Myeloid Leukemia

Safaa M. El Karaksy, Nancy M. El Guindy, Heba M. Gouda, Mervat M. Khorshied, Iman A. Shaheen, Reham E. Abu Khalil and Noha Y. Ibrahim

*Comparative Clinical Pathology*, 21: 1171-1177 (2012)

The angiogenic-related factors: angiopoietin-1 and -2 and their receptor Tie-2 have wide-ranging effects on tumor behavior that includes angiogenesis and, inflammation. These multifaceted pathways present a potential target in developing novel inhibition strategies for cancer therapy. the present work aimed at detecting the prevalence of expression of: angiopoietin-1, angiopoietin-2, and their receptor Tie-2 in 56 Egyptian de novo acute myeloid leukemia (AML) patients by conventional RT-PCR to verify the prognostic impact of their expression on the response to induction chemotherapy. Thirty age- and sexmatched healthy volunteers were subjected to the same analysis as a control group. High expression of angiopoietin-1 (Ang-1) was detected in the patient group but not the control group. AML patients expressing angiopoietin-2 (Ang-2) either solely or in combination with high Ang-1 and/or Tie-2 showed unfavorable response to induction chemotherapy; either failed induction or death during induction. These data provide evidence that the alternation of angiopoietin balance in favor of Ang-2 may play a critical role in the pathophysiology of AML. Furthermore, positive pre-therapeutic expression of Ang-2 indicates valuable unfavorable prognostic marker in AML patients and may be used as a prognostic tool in the risk-adaptive management of AML.

**Keywords:** Aml; Ang-1; Ang-2; Tie-2; Rt-Pcr.

### 56. DNMT3B Promoter Polymorphism and Risk of Immune Thrombocytopenic Purpura in Pediatric Egyptians

Iman A. Shaheen, Reham E. Abukhalil, Dina K. Ali and Rasha A. Afifi

*Blood Coagulation Fibrin*, 23: 636-639 (2012) IF: 1.238

Idiopathic (immune) thrombocytopenic purpura (ITP) is a heterogeneous clinical disorder characterized by immunemediated platelet destruction. Epigenetic changes in gene expression, including DNA methylation and histone modifications, might contribute to autoimmunity. Polymorphisms of the DNA

methyltransferase 3B (DNMT3B) gene may influence DNMT3B activity on DNAmethylation and increase the susceptibility to several diseases. the current study investigated the association between a single nucleotide polymorphism (SNP) in the promoter of DNMT3B gene and the risk for ITP in pediatric Egyptians. DNMT3B SNP was genotyped by PCR– restriction fragment length polymorphism in 71 pediatric ITP patients and 82 healthy controls matched for age and sex.

the C/C wild genotype was not detected in ITP patients or in the controls. the frequencies of the T/T and C/T genotypes were 93.9 and 8.5% in the controls and 91.5 and 8.5% in ITP patients, respectively. There was no significant difference in either genotypes or allelic distribution between ITP patients and the controls. in conclusion, this polymorphism was almost equally distributed between ITP patients and the controls. These results demonstrated that this SNP may not be used as a stratification marker to predict the susceptibility to childhood ITP in Egypt.

**Keywords:** Children; DNA methyltransferase 3B; Idiopathic thrombocytopenic purpura; Pcr–Restriction fragment length polymorphism.

### Dept. of Clinical Oncology and Nuclear Medicine

### 57. Clinical Relevance of Different Dose Calculation Strategies for Mediastinal Imrt in Hodgkin's Disease

A. Y. Abo-Madayan

*Strahlenther Onkol*, 653-659 (2012) IF: 3.561

Continuing progress in diagnosis and therapy has led to high cure rates of Hodg-kin lymphoma. Survivors carry, however, the risk of long-term complications such as second malignancies and cardiovascular disease, especially when the mediastinum is involved [1, 2, 3, 4, 5]. Intensity-modulated radiotherapy (IMRT), image-guided radiotherapy (IGRT), and stereo-tactic body radiotherapy (SBRT) facilitate optimization of dose to target, lung, breasts and heart in radiotherapy for me-diastinal Hodgkin lymphoma, lung cancer or breast cancer [6,7, 8, 9,10]. in an effort to assess these issues for both 3D-CRT and IMRT, we analyzed the differences in calculated dose between calculation with a PB algorithm vs. a collapsed cone (CC) algorithm for 3D-CRT and between PB vs. a Monte Carlo (MC) algorithm (with a MC calculation basis already during the second optimization step) on CT datasets of thoracic targets drawn from the clinical routine within the framework of the German Hodgkin Study Group (GHSG) focusing on target coverage and organs at risk (OAR) doses. as recalculation of IMRT plans with the CC algorithm and MC recalculation of 3D-CRT plans were technically not feasible, a CC vs. MC comparison was not performed within the framework of this study.

### 58. Physiological <sup>18</sup>F-FDG Uptake by the Spinal Cord: is it A Point of Consideration for Cancer Patients?

Amr Amin, Sandra J. Rosenbaum and Andreas Bockisch

*J. Neurooncol*, 107: 609-615 (2012) IF: 3.214

It is essential to be familiar with normal patterns of <sup>18</sup>F FDG distribution in the whole body for accurate PET interpretation.

We assessed FDG uptake by the spinal cord to evaluate its characteristics in cancer patients.

For 101 cancer patients who underwent 18F FDG PET/CT the spinal cord along its segments was visually assessed for FDG uptake, regarding MaxSUV-measurement C1 as cutoff point. This assessment was correlated with the patient's database variables. MRI and FDG PET-CT follow-up were included in the evaluation of positive subjects with FDG cord uptake. Forty-nine (48.5%) were positive for FDG cord uptake. the most encountered sites were the eleventh and twelfth dorsal vertebrae (36/49; 73.5%), all cervical (24/49; 49%), and the first lumbar segments (19/49; 38.7%). 38/49 (77.6%) and 11/49 (22.4%) were detected in the winter and summer, respectively (P = 0.007). MRI was available for 25 of the positive FDG cord uptake patients and showed no cord abnormalities, and in follow-up FDG PET-CT studies within 3–6 months 41/49 (83.7%) faded completely, while stationary or reduced uptake was observed for the remainder (8/49; 16.3%). FDG uptake in multiple consecutive segments of the spinal cord is not uncommon in cancer patients.

This must be recognized as physiological, to avoid misdiagnosis as malignant involvement. Such physiological uptake is mostly encountered in the cervical, last two dorsal, and first lumbar levels, and quite frequently in winter.

**Keywords:** Fdg; Pet-Ct; Spinal cord; Fdg uptake by the spinal cord.

### 59. Glioma Residual or Recurrence Versus Radiation Necrosis: Accuracy of Pentavalent Technetium-99m-Dimercaptosuccinic Acid [Tc-99m (V) DMSA] Brain Spect Compared to Proton Magnetic Resonance Spectroscopy (<sup>1</sup>H-MRS): Initial Results

Amr Amin, Hosna Moustafa, Ebaa Ahmed and Mohamed El-Toukhy

*Journal of Neuro-Oncology*, 106: 579-587 (2012) IF: 3.214

We compared pentavalent technetium-99m dimercaptosuccinic acid (Tc-99m (V) DMSA) brain single photon emission computed tomography (SPECT) and proton magnetic resonance spectroscopy (<sup>1</sup>H-MRS) for the detection of residual or recurrent gliomas after surgery and radiotherapy. A total of 24 glioma patients, previously operated upon and treated with radiotherapy, were studied. SPECT was acquired 2–3 h post-administration of 555–740 MBq of Tc-99m (V)DMSA. Lesion to normal (L/N) delayed uptake ratio was calculated as: mean counts of tumor ROI (L)/mean counts of normal mirror symmetric ROI (N). <sup>1</sup>H-MRS was performed using a 1.5-T scanner equipped with a spectroscopy package. SPECT and <sup>1</sup>H-MRS results were compared with pathology or follow-up neuroimaging studies. SPECT and <sup>1</sup>H-MRS showed concordant residue or recurrence in 9/24 (37.5%) patients. Both were true negative in 6/24 (25%) patients. SPECT and <sup>1</sup>H-MRS disagreed in 9 recurrences [7/9 (77.8%) and 2/9 (22.2%) were true positive by SPECT and <sup>1</sup>H-MRS, respectively]. Sensitivity of SPECT and <sup>1</sup>H-MRS in detecting recurrence was 88.8 and 61.1% with accuracies of 91.6 and 70.8%, respectively. A positive association between the delayed L/N ratio and tumor grade was found; the higher the grade, the higher is the L/N ratio (r = 0.62, P = 0.001). Tc-99m (V) DMSA brain SPECT is more accurate compared to <sup>1</sup>H-MRS for the detection of tumor residual tissues or recurrence in glioma patients with previous radiotherapy. It allows early and non-invasive differentiation of residual tumor or recurrence from irradiation necrosis.

**Keywords:** Glioma; Post-Radiation Necrosis; Tc-99 M.

### 60. Targit-E (Lderly) - Prospective Phase II Study of Intraoperative Radiotherapy (Iort) in Elderly Patients with Small Breast Cancer

Ahmed Yasser Ahmed

*Bmc Cancer*, (2012) IF: 3.011

Patients [greater than or equal to 70 years with small, low-risk breast cancer who are operated but not irradiated show local relapse rates around 4% after 4 years. with adjuvant whole breast radiotherapy (WBRT) the local relapse rate drops to 1% after 4 years under Tamoxifen (5). It has been demonstrated (6, 12) that the efficacy of radiotherapy of the tumor bed only in a selected group can be non-inferior to WBRT.

**Methods:** This prospective, multicentric single arm phase II study is based on the protocol of the international TAKGIT-A study. the TARGIT-E study should confirm the efficacy of a single dose of intraoperative radiotherapy (IORT) in a well selected group of elderly patients with small breast cancer and absence of risk factors. Patients will receive IORT (20 Gy with Intra-beam system/Carl Zeiss) during breast conserving surgery. in presence of risk factors postoperative WBRT will be added to complete the radi otherapeutic treatment according to international guidelines. Endpoints are the local relapse rate (within 2 cm of the tumor bed), Ipsilateral in breast relapse, cancer-specific and overall survival and contralateral breast cancer as well as documentation of quality of life and cosmetic outcome. the expected local relapse rates are 0.5/1/1.5% after 2,5/5/7.5 years, respectively. Discontinuation of the trial is scheduled if rates of local relapse rates rise to 3/4/6% after 2.5/5/7.5 years. Power calculations result in 540 patients with a calculated dropout rate of 20% and loss to follow-up of 20%, an alpha of 0.01 and a beta 0,05. There will be a pre- and a post-pathology stratum (n=270 each).

### 61. Tc-99m Diethylenetriamine Pentaacetic Acid (DTPA) Renal Function Reserve Estimation: is it A Reliable Predictive Tool for Assessment of Preclinical Renal Involvement in Scleroderma Patients?

Amr Amin, S. El-Sayed, N. Taher, M. Sedki and H. Nasr

*Clin Rheumatol*, 31: 961-966 (2012) IF: 1.996

Prognosis of systemic sclerosis (SSc) depends on internal organ involvement. We assessed the value of renal function reserve (RFR) for the detection of preclinical nephropathy in scleroderma. Thirty SSc patients with normal serum creatinine and 30 healthy controls were included. Medsger disease severity score, glomerular filtration rate (GFR), and microalbuminuria were measured. Tc-99m DTPA was utilized for GFR measurement at baseline and after oral protein overload (stimulated GFR). RFR was calculated as the percentile increase of stimulated GFR. SSc patients had lower means of baseline GFR (P=0.001), stimulated GFR (P=0.004), RFR (P=0.046), and higher microalbu- minuria (P=0.009) than controls. According to baseline GFR, SSc patients showed three categories—normal baseline GFR (n=12), hyperfiltration GFR (n=3), and reduced baseline GFR (n=15). in the former category, RFR was normal in 6/12 patients and abnormal in the remainders (50%). Hyperfiltration patients and those with reduced baseline GFR showed abnormal RFR. A statis- tically significant negative association was found between microalbuminuria versus

stimulated GFR and RFR ( $r=-0.5$ ,  $P=0.007$  and  $r=-0.45$ ,  $P=0.013$ , respectively). The majority of SSc patients with abnormal RFR had disease duration of  $\geq 48$  months (60% vs. 20%,  $P=0.008$ ). All SSc patients with pulmonary hypertension had abnormal RFR, while reduced baseline GFR was noted in only 60%. A significant negative correlation was found between reduced baseline GFR and cumulative dose of corticosteroids in SSc patients ( $r=-0.4$ ,  $P=0.022$ ). RFR estimation could be a useful predictive marker for preclinical renal involvement in SSc patients so that early prophylactic measures and therapy modifications could be considered.

**Keywords:** Early Nephropathy; Glomerular Filtration Rate; Microalbuminuria; Renal Function Reserve; Systemic Sclerosis; Tc-99M DTPA.

### 62. The Palliative Prognostic Index for the Prediction of Survival and in-Hospital Mortality of Patients with Advanced Cancer in Kuwait

Salem Alshemmari, Hanan Ezzat, Zainab Samir, Samar Refaat and Samy A. Alsirafy

*J Palliat Med*, 15 (2): 200-204 (2012) IF: 1.849

**Introduction:** Prognostic scoring systems are increasingly used in cancer care. One of these systems is the Palliative Prognostic Index (PPI) which is based on clinical findings. Few studies validated the PPI in different settings. Our aim was to test the predictive value of the PPI in an acute cancer care setting.

**Methods:** Prospective study that included patients with advanced cancer admitted to a tertiary cancer center in Kuwait. Patients were divided according to the PPI score into three groups: A ( $PPI \leq 3$ ), B ( $PPI > 3 - \leq 6$ ), and C ( $> 6$ ).

**Results:** the study included 91 hospitalized patients. at the time of PPI assessment, the plan of treatment was best supportive care only in 70 (77%) patients. the majority (80%) of included patients died in-hospital. the in-hospital mortality rate for patients with a  $PPI > 6$  was significantly higher than those with  $\leq 6$  (93% versus 56%,  $p < 0.001$ ). Using a cutoff point of  $PPI > 6$ , in-hospital mortality was predicted with a 73% sensitivity, 78% specificity, 93% positive predictive value, and 41% negative predictive value. the median survival was 61 days (95% confidence interval [CI]: 25.8-96.2) for group A, 20 days (95% CI: 4.5-35.5) for group B, and 6 days (95% CI: 4-8) for group C. the difference in survival was highly significant ( $p < 0.001$ ).

**Conclusion:** the results suggest that the PPI may be helpful for oncologists in predicting survival and in-hospital mortality of patients with advanced cancer in the acute care setting.

**Keywords:** Advanced cancer; Prognosis; in-Hospital Mortality; Palliative prognostic index; Kuwait.

### 63. Palliative Care: An Unexplored Aspect of Schistosomiasis Neglect?

Samy A. Alsirafy, Somaia M. Mousa and Stuart M. Brown

*American Journal of Hospice and Palliative Medicine*, 29 (1): 7-8 (2012) IF: 1.153

the World Health Organization defines palliative care as “an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of

early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.

Although the palliative care needs of patients with lifethreatening noncancer diseases are comparable to those of patients with cancer, they are largely unmet. Schistosomiasis is one of the neglected tropical diseases which are considered “a symptom of poverty and disadvantage.” It is estimated that more than 207 million people are infected with schistosomiasis, and the majority (85%) are in Africa. the estimated number of deaths per year due to schistosomiasis is more than 200 000 in sub-Saharan Africa alone. the provision of palliative care services for those with the late effects of schistosomiasis is an area that needs exploration.

**Keywords:** Schistosomiasis; Neglect; Palliative care; Quality of life.

### 64. Opioid Consumption Before and After the Establishment of a Palliative Medicine Unit in an Egyptian Cancer Centre

Samy A. Alsirafy, Noha Y. Ibrahim, and Enas N. Abou-Elela

*J Palliat Care*, 135-140 (2012) IF: 0.931

Opioid consumption before and after the establishment of a palliative medicine unit (PMU) in an Egyptian cancer centre was reviewed. A comparison of consumption during the year before the PMU was established to consumption during the third year after the PMU's establishment revealed that morphine consumption increased by 698 percent, fentanyl by 217 percent, and tramadol by 230 percent. Expressed in defined daily dose (DDD) and adjusted for 1,000 new cancer patients, consumption increased by 460 percent, from 4,678 DDD/1,000 new patients to 26,175 DDD/1,000 new patients. Expressed in grams of oral morphine equivalent (g OME), consumption increased by 644 percent, from 233 g OME/1,000 new patients to 1,731 g OME/1,000 new patients. the establishment of the PMU was associated with an increase in opioid consumption, especially morphine, which is an indicator of improvement in cancer pain control. the expression of opioid consumption in OME in addition to DDD may provide further information, especially when weak opioids are included in the analysis.

**Keywords:** Cancer pain; Opioid consumption; Palliative medicine; Quality of life; Egypt.

### 65. Detection of Orphan Receptor Tyrosine Kinase (Ror-1) Expression in Egyptian Pediatric Acute Lymphoblastic Leukemia

Iman Shaheen and Noha Ibrahim.

*Fetal and Pediatric Pathology*, 1-7 (2012) IF: 0.613

Receptor tyrosine kinases, a group of tumor-associated antigens, were introduced as targets for cancer intervention strategies. the human orphan receptor tyrosine kinase-1 (ROR-1) is a member of this family. Overexpression of ROR1 has been reported in B-cell chronic lymphocytic leukemia. the aim of this study was to detect the expression profile of ROR1 in 54 pediatric acute lymphoblastic leukemia (ALL) patients. ROR1 was overexpressed in ALL as the ROR1/ $\beta$ -actin ratio was higher in ALL children than in control group ( $P = 0.024$ ). ROR1 is a potential tool for targeted immunotherapy in pediatric ALL patients.

**Keywords:** Acute Lymphoblastic Leukemia (All); Ror-1; Semi-Quantitative Rt-PCR.

### 66. Capecetabine Plus Oxaliplatin as Adjuvant Therapy for Colon Cancer

Wael Makar, Noha Ibrahim, Ibtessam Saad El Din and Dalia Darwish

*Austral - Asian Journal of Cancer*, 11 (3): 175-180 (2012)

Adjuvant chemotherapy improves overall survival (OS) in patients with locally advanced, node-positive (stage III) colon cancer.

**Methods:** This study was designed to compare capecitabine/oxaliplatin (XELOX) with FU/LV/oxaliplatin (FOLFOX4) as adjuvant treatment for patients with high risk stage II and stage III colon carcinoma in terms of toxicity, patient convenience, event-free survival (EFS) and overall survival. Patients were followed up for a median period of 39 months ranging from 30 to 48 months.

**Results:** Sixty four patients were enrolled in each arm. the overall survival at 36 and 48 months for the XELOX group was 73.8% and 62% respectively. While the overall survival for FOLFOX group was 72% and 58% respectively (HR 0.8338, 95%CI= 0.2557-2.719). the difference was not statistically significant. Grade 3/4 neutropenia was more significant with FOLFOX 22% versus 9.4% (p=0.01). XELOX was associated with more G3/4 diarrhea 17.2% versus 11% (p=0.25), and hand and foot syndrome 9.4% versus 1% (p=0.04).

**Conclusion:** This study reveals that XELOX is as effective and safe as FOLFOX and has a manageable tolerability profile in the adjuvant setting with more convenience to the patients.

**Keywords:** Xelox; Folfox; Adjuvant; Advanced Cancer Colon.

### 67. Potential Toxicities of Prophylactic Toxicities of Prophylactic Cranial Irradiation

Ahmed Yasset Ahmed Abd Elatif Abumedyan

*Tran Stat Ional Lung Cancer Research*, (2012)

Prophylactic cranial irradiation (PCI) with total doses of 20-30 Gy reduces the incidence of brain metastasis (BM) and increases survival of patients with limited and extensive- disease small-cell lung cancer (SCLC) that showed any response to chemotherapy. PCI is currently not applied in non-small-cell lung cancer (NSCLC) since it has not proven to significantly improve OS rates in stage IIIA/B, although novel data suggest that subgroups that could benefit may exist. Here we briefly review potential toxicities of PCI which have to be considered before prescribing PCI. They are mostly difficult to delineate from pre-existing risk factors which include preceding chemotherapy, patient age, paraneoplasia, as well as smoking or atherosclerosis. on the long run, this will force radiation oncologists to evaluate each patient separately and to estimate the individual risk. Where PCI is then considered to be of benefit, novel concepts, such as intensity-modulated radiotherapy and/or neuroprotective drugs with potential to lower the rates of side effects will eventually be superior to conventional therapy. This in turn will lead to a re-evaluation whether benefits might then outweigh the (lowered) risks.

**Keywords:** Prophylactic cranial irradiation (Pci); Potential toxicities; Brain metastasis (Bm); Small-cell lung cancer (Sclc); Non-small-Cell Lung cancer (Nsclc).

### 68. A Comparative Study of Mucinous and Serous Adenocarcinomas of the Ovary: Are they the Same Disease?

Emmad E. Habib

*Austral - Asian Journal of Cancer*, 11 ( 2): 143-151 (2012)

Ovarian cancer is the most lethal gynecological malignancy, with epithelial tumours being the largest group (90%).

**Aim of this Study:** the objective of this study was to identify the clinical and treatment outcome differences between stage 3 and 4 mucinous and serous ovarian carcinomas with regard to survival and disease free survival and the impact of the histological grade on prognosis.

**Results:** Between June 2005 and December 2009, 186 serous ovarian carcinoma patients and 36 mucinous patients were diagnosed and treated at the gynecology unit of the clinical oncology department, faculty of medicine, Cairo University, Egypt. Those cases were included in the present study with a minimal follow up period of 2 years. for the serous group the number of relapsing cases after achieving a complete remission was 12 within the first year of follow-up (6.6%). Salvage surgery was performed to 21 cases (11.5%) not achieving initial CR, with 18 of those (85.7%) performing optimal debulking. After the first year 51 cases achieving CR relapsed (27.4%). Peritoneal relapse was in 42 cases (82.4%), liver metastases in 6 cases (11.8%)

**Keywords:** Ovarian cancer; Mucinous; Serous; Surgery.

### 69. Management of Neuroblastoma: A Study of First- and Second-Line Chemotherapy Responses, A Single Institution Experience

Emmad E. Habib, Amr T. El-Kashef and Ezzat S. Fahmy

*Oncology Reviews*, 6 ( e3 ): 11-15 (2012)

Neuroblastoma is a high-grade malignancy of childhood. It is chemo- and radio-sensitive but prone to relapse after initial remission. the aim of the current study was to study the results of the first- and second-line chemotherapy on the short-term response and long-term survival of children, and to further describe the side effects of treatment.

Ninety-five children with advanced neuroblastoma were included in the study, divided into two groups according to the treatment strategy: 65 were treated by first-line chemotherapy alone, and 30 children who were not responding or relapsed after first-line chemotherapy were treated by second-line chemotherapy. External beam radiotherapy was given to bone and brain secondary cancers when detected. Staging workup was performed before, during and after management. Response was documented after surgery for the primary tumor. Median follow up was 32 months (range 24-60 months). Chemotherapy was continued until toxicity or disease progression occurred, indicating interruption of chemotherapy. Patients received a maximum of 8 cycles. Toxicity was mainly myelo-suppression, with grade II-III severity in 60% of the firstline and 70% of the second-line chemotherapy patients. Median total actuarial survival was nearly 51 months for the first-line chemotherapy group and 30 months for the second-line line group, with a statistically significant difference between the two groups (P<0.01).

**Keywords:** Neuroblastoma; Chemotherapy; Treatment.

## 70. Synchronous Chemoradiotherapy in Patients with Stage Iii and iv Head and Neck Cancer: Comparing Cisplatin with Capecitabine

Sherif A. Raafat, Emmad E. Habib and Ashraf M. Maurice

*Journal of Cancer Therapy*, 3: 1045-1051 (2012)

To evaluate the efficacy of concurrent intravenous cisplatin versus oral capecitabine with radical radiotherapy in locally advanced squamous cell carcinoma of the head and neck.

**Materials and methods:** Between January 2007 and December 2009, 60 patients with stage III/IV head and neck squamous cell carcinoma (0 to 1 performance status) were enrolled into this study. Thirty cases are given cisplatin 30 mg/m<sup>2</sup> IV infusion weekly for 6 weeks with conventional radiotherapy. the remaining thirty cases are given oral capecitabine 500 mg/m<sup>2</sup> twice daily, continuously for 28 - 35 days with conventional radiotherapy also. the radiotherapy dose was 4600 cGy in 20 fractions over 4 weeks to primary and neck nodes followed by boost to primary site and any residual disease 1500 - 2000 cGy in 6 to 8 fractions.

**Results:** the median age was 53 (range 25 - 71) years; 10 cases had stage III disease, 36 cases IVa disease and 14 cases IVb disease. Seventy-three percent of patients completed the course of capecitabine and 80% completed prescribed cisplatin. There were no treatment-related deaths, grade 4 haematological toxicity or grade 3 renal toxicity in either arm. the complete response rate at 3 months was 77% (23/30 patients) in the capecitabine group and 60% (18/30) in the cisplatin group. Relapse occurred in 10/30 (33%) patients by 2 years in the capecitabine group and in 12/30 (40%) in the cisplatin group. on analysis of survival data, the median follow-up period was 35 ± 15 months for overall survival and 33 ± 10 months for disease free survival. the overall survival, and disease-free survival rates at 2 years were 67%, and 85%, respectively for the capecitabine group versus 60% and 73% for the cisplatin group.

**Conclusion:** Synchronous chemo-radiotherapy with capecitabine was found to be very effective, with excellent response, local control and 3-year cancer-specific survival rates.

**Keywords:** Capecitabine; Cisplatin; Advanced Squamous Cell Carcinoma of the Head and Neck; Synchronous Chemoradiotherapy.

## 71. Representation of Expatriates Among Cancer Patients in Kuwait and the Need for Culturally-Competent Care

Salem H. Alshemmari, Samar M. Refaat, Amani A. Elbasmi and Samy A. Alsirafy

*Journal of Psychosocial Oncology*, 30 ( 3 ): 380-385 (2012)

From 2000 to 2007, 11,793 cancer patients received treatment in Kuwait. Non-Kuwaitis accounted for 6,016 (51%) patients. They came from 68 countries, mainly from the World Health Organization Eastern Mediterranean (59%) and South-East Asian (20%) regions. the majority (69%) was from low- and low-middle income countries. Thirty-seven percent were from non-Arabic speaking countries. to provide culturally-competent care for expatriate patients, there is a need to explore the impact of their ethnic, sociocultural, economic, language diversity, and expatriation-related stressors on different aspects of cancer care.

**Keywords:** Expatriates; Cancer care; Cultural competency; Needs assessment; Kuwait.

## Dept. of Clinical Pathology

## 72. CD 200 Expression in B-Cell Chronic Lymphoproliferative Disorders

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*J Invest Med*, 60 (1): 56-61 (2012) IF: 1.964

Flowcytometry immunophenotyping (FCIP) is used for rapid, specific diagnosis of B-chronic lymphoproliferative disorders (BCLPDs). However; cases may deviate from the typical immunophenotype, therefore, there is a need for adding new marker(s) for differentiating BCLPDs. Lately, few researches highlighted CD200 expression in some BCLPDs. Our aim was to evaluate CD200 expression in different BCLPDs, and whether adding CD200 to BCLPDs-FCIP routine panels, could improve the ability of their differential diagnosis.

**Methods:** We evaluated CD200 expression in 49 BCLPDs patients and 26 age and sex matched controls. FCIP first panel included CD5, CD19, sIg, CD23, CD22, CD79b and FMC7, for BCLPDs other than chronic lymphocytic leukemia (CLL) and mantle cell lymphoma (MCL), CD11c, CD103, CD25 and CD10 were evaluated.

**Results:** Using tricolor FCIP, CD200 showed high bright expression on CD5/19 positive clone in all B-CLL patients (100%), with a mean of 94 ± 11%, in the 2 cases of HCL, CD200 was brightly expressed on 96 and 99% of cells. in all other BCLPDs including MCL, CD200 expression (on CD19/22 positive cells) was less than 20% with a mean of 10 ± 8% and a dim pattern. CD200 expression was significantly higher in CLL compared to NHL groups (P value < 0.001).

**Conclusion:** Evaluating CD200 expression has a great impact on accurate BCLPDs diagnosis and could be added to the BCLPDs routine panels. the high expression of CD200 in B-CLL and HCL could open the option for targeted immune (Anti CD200) therapy.

**Keywords:** Cd200; Bclpds; Flowcytometry.

## 73. Frequency of Vkorc1 (C1173t) and Cyp2c9 Genetic Polymorphisms in Egyptians and their Influence on Warfarin Maintenance Dose: Proposal for A New Dosing Regimen

M. S. El Din, D. G. Amin, S. B. Ragab, E. E. Ashour, M. H. Mohamed and A. M. Mohamed

*Int J Lab Hematol*, (2012) IF: 1.176

Warfarin is one of the most widely used anticoagulants, yet interindividual differences in drug response, a narrow therapeutic range and a high risk of bleeding or stroke complicate its use. We aimed to determine the allele and genotype frequency of VKORC1 1173 C>T, CYP2C9\*2 and CYP2C9\*3 variant polymorphisms in the Egyptian population and to evaluate their influence on the interindividual differences in warfarin dosage.

**Methods:** A total of 154 unrelated healthy adult patients and 46 warfarin-treated patients were included. SYBR Green-based real-time polymerase chain reaction (PCR) assay was used for studying VKORC1 (C1173T) and CYP2C9\*3 polymorphisms.

Mutagenically separated PCR assay was used to detect the CYP2C9\*2 allele.

**Results:** VKORC1 genotype frequencies were 11%, 24% and 65% for CC, CT and TT, respectively. the prevalence of CYP2C9 haplotypes was 81% (\*1\*1), 3.3% (\*1\*2), 9.7% (\*1\*3), 4.5% (\*2\*2) and 0.65% (2\*3 and \*3\*3). VKORC1 TT and CYP2C9\*2\*2 were associated with a significantly lower warfarin dose. VKORC1 and CYP2C9 accounted for 31.7% and 15.6% of warfarin dose variability, respectively, and together with clinical factors explained 61.3% of total variability.

**Conclusion:** VKORC1-TT and CYP2C9 \*1/\*1 are the most prevalent genotypes among Egyptians. Patients with VKORC1-TT genotype required a lower warfarin dose.

**Keywords:** Vkorc1; Cyp2c9; Warfarin; Realtime Pcr.

#### 74. Genetic Polymorphism of Microsomal Epoxide Hydrolase Enzyme Gene in Preeclamptic Females

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*Am J Med Sci*, 343 (4): 291-294 (2012) IF: 1.391

**Introduction:** Microsomal epoxide hydrolase enzyme is involved in xenobiotics detoxification. It catalyzes the phase I hydrolysis of epoxides and plays a role in the detoxification processes and in the metabolism of endogenous and exogenous compounds. Preeclampsia, which is one of the most serious complications of pregnancy, may be due to an imbalance between these compounds, such as lipid peroxides and oxygen-free radicals and detoxifying and scavenging substances.

Two variants of human epoxide hydrolase enzyme with different enzyme activity have been described; exon 3 polymorphism is associated with lower enzyme activity whereas exon 4 polymorphism is associated with higher activity. the authors tried to investigate the association between these genetic polymorphisms and preeclampsia.

**Method:** Thirty preeclamptic females together with 30 normal pregnant females as controls were included in the study. Genotyping for exons 3 and 4 of microsomal epoxide hydrolase enzyme was done by polymerase chain reaction–restriction fragment length polymorphism.

**Results:** There was no statistical significant difference in the distribution of exon 3 genotype between cases and controls (P= 0.4); on the other hand, a highly statistical significant difference was found between cases and controls as regard exon 4 genotype (P= 0.002).

**Conclusion:** There may be an association between epoxide hydrolase enzyme polymorphism and the risk of preeclampsia. Key Indexing Terms: EPHX; Preeclampsia; PCR-RFLP; Genetic polymorphism.

**Keywords:** Ephx; Preeclampsia; Pcr-Rflp; Genetic Polymorphism.

#### Dept. of Dermatology

#### 75. Artemin Causes Hypersensitivity to Warm Sensation, Mimicking Warmth-Provoked Pruritus in Atopic Dermatitis

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*J. Allergy Clin Immunol*, 130 (3): 671-682 (2012) IF: 11.003

Itch impairs the quality of life for many patients with dermatoses, especially atopic dermatitis (AD), and is frequently induced by a warm environment. Objective: to determine the mechanism underlying itch induction by warmth, we focused on artemin, a member of glial cell line–derived neurotrophic factors (GDNFs).

**Methods:** A gene array assay revealed that artemin was expressed in substance P–treated dermal fibroblasts. the expression of artemin in healthy and AD-lesional skin was evaluated with immunohistochemistry and in situ hybridization. the impact of fibroblast-derived artemin on the proliferation and morphology of neural cell was investigated in vitro. to confirm the involvement of artemin in skin sensibility, wild-type and GDNF family receptor  $\alpha 3$  knockout mice were employed for sensory examination.

**Results:** Artemin-expressing fibroblasts accumulated in skin lesions of patients with AD. Artemin induced cell proliferation of a neuroblastoma cell line in vitro, and intradermal injection of artemin in mice resulted in peripheral nerve sprouting and thermal hyperalgesia. Artemin-treated mice demonstrated scratching behavior in a warm environment, but mice deficient for GDNF family receptor  $\alpha 3$ , a potent artemin receptor, did not show this behavior. Furthermore, the escaping response to heat stimulus was attenuated in GDNF family receptor  $\alpha 3$  knockout mice, suggesting that artemin may contribute to sensitivity to heat.

**Conclusion:** These data suggest that dermal fibroblasts secrete artemin in response to substance P, leading to abnormal peripheral innervation and thermal hyperalgesia. We hypothesize that artemin lowers the threshold of temperaturedependent itch sensation and might therefore be a novel therapeutic target for treating pruritic skin disorders, including AD.

**Keywords:** Artemin; Fibroblast; Substance P; Atopic Dermatitis; Itch; Nerve Fiber; Warmth.

#### 76. Pathogenic Anti-Desmoglein 3 MAbs Cloned from A Paraneoplastic Pemphigus Patient by Phage Display

Marwah A. Saleh, Ken Ishii, Jun Yamagami, Yuji Shirakata, Koji Hashimoto and Masayuki Amagai

*Invest Dermatol*, 132: 1141–1148 (2012) IF: 6.314

Paraneoplastic pemphigus (PNP) is an autoimmune blistering disease associated with lymphoproliferative neoplasms and characterized by antibodies against plakins and desmoglein 3 (Dsg3). Anti-Dsg3 antibodies have a primary role in blister formation in PNP. in this study, we used phage display to clone monoclonal anti-Dsg3 antibodies from a PNP patient to further characterize their pathogenicity. We isolated 20 unique Dsg3-reactive mAbs, which we classified into four groups according to the heavy-chain complementarity-determining region 3 (CDR3) region. Genetic analyses demonstrated that three antibody groups

used the VH1-46 gene (18 clones) and one group used the VH1-02 gene (2 clones). the results of an in vitro keratinocyte dissociation assay and a human skin organ culture injection assay showed that three antibodies displayed pathogenic activity in blister formation with different potencies. Epitope mapping using domain-swapped Dsg3/Dsg2 showed that these pathogenic mAbs bound Ca<sup>2+</sup>-dependent conformational epitopes in the middle portion of the extracellular region of Dsg3 (EC2 and EC3 domains), in contrast to most previously characterized pathogenic pemphigus vulgaris antibodies, which bound to the EC1 domain of Dsg3. These mAbs reflect the unique polyclonal nature of anti-Dsg3 antibodies in PNP and represent an important tool for detailing the pathophysiological mechanisms of blister formation in PNP.

**Keywords:** Pemphigus, Desmoglein, Autoimmune bullous Diseases, Autoantibodies.

### 77. Live Attenuated Varicella Vaccine: A New Effective Adjuvant Weapon in the Battlefield Against Severe Resistant Psoriasis, A Pilot Randomized Controlled Trial

Mohammad A. El-Darouti, Rehab A. Hegazy, Rania M. Abdel Hay and Dalia M. Abdel Halim

*J Am Acad Dermatol*, 66: 511-513 (2012) IF: 3.991

This study included 35 patients with severe resistant psoriasis randomly divided into two groups: group A (18 patients) and group B (17 patients). They all received low-dose cyclosporine (2.5 mg/kg/d). in addition, group A received 4 doses of Varilrix once every 3 weeks; the first dose was administered 2 weeks before cyclosporine. Simultaneously group B received placebo in the form of 4 doses of subcutaneous saline once every 3 weeks. Before each vaccination we checked that all patients were not immunocompromised (normal IgG and IgM, T/B lymphocytes, and CD4 T cells  $\geq 25\%$ ).

**Keywords:** Cyclosporine; Live Attenuated Varicella Vaccine; Pasi; Psoriasis.

### 78. Hair Loss In Pityriasis Versicolor Lesions: A Descriptive Clinicopathological Study

Wedad Z. Mostafa, Magda I. Assaf, Iman A. Ameen, Omar S. El Safoury and Shatha A. Al Sulh

*Journal of the American Academy of Dermatology*, (2012) IF: 3.991

**Background:** We have observed that hair thinning and/or loss occur at times as a presenting symptom or sign in patients with pityriasisversicolor (PV).

**Objective:** Our objective was to verify and explore this clinical observation and depict its underlying pathology.

**Methods:** A total of 39 patients with PV were examined during a period of 11 months and skin biopsy specimens were taken from lesional and nonlesional skin. Hematoxylin-eosine and periodic acideSchiffstained sections were examined and described. Results were statistically analyzed.

**Results:** Hair loss and/or thinning within PV lesions was shown in 61.5% of patients (P value  $\leq .0005$ ), appearing most commonly on forearms, abdomen, and neck as well as the beard area (only in male participants). Histopathologically, in addition to the classically described features of PV, basal hydropic degeneration,

follicular degeneration, miniaturization, atrophy, plugging, and/or hair shaft absence occurred in 46% of lesional versus 20.5% of nonlesional biopsy specimens (P value $\leq .05$ ); these changes appeared to be directly or indirectly related to the presence of Malassezia organisms in hair follicles and/or stratumcorneum.

**Limitations:** Some patients with PV lesions on the face did not approve facial biopsy.

**Conclusion:** This study provides clinical and histopathological evidence that PV lesions may be associated.

**Keywords:** Hair Loss; Hair Shaft; Histopathology; Hydropic Degeneration; Hyphae; Malassezia; Pityriasis Versicolor.

### 79. Hypopigmented Parapsoriasis En Plaque, A New Overlooked Member of the Parapsoriasis Family: A Report of Thirty-Four Patients and A Seven Year Experience

Mohammad A. El-Darouti, Marwa M. Fawzy, Rehab A. Hegazy, and Rania M. Abdel Hay

*J. Am Acad Dermatol*, (2012) IF: 3.991

In the past 7 years we have extensively studied an uncommon hypopigmented disorder that, apart from hypopigmentation, showed many common features with parapsoriasis en plaque (PSEP), both clinically and histopathologically.

**Objective:** We sought to verify whether this disorder should be considered a hypopigmented variant of PSEP and thus be referred to as hypopigmented PSEP.

**Methods:** A total of 34 patients presenting with this peculiar hypopigmented disorder were included (2003-2010). Patients were subjected to a predesigned algorithm excluding all possible differential diagnoses of hypopigmented lesions.

**Results:** Our findings indicated that this disorder can be diagnosed as hypopigmented PSEP. These findings included: (1) exclusion of all other disorders causing similar hypopigmented lesions; (2) shape and size of the lesions being very similar to those of classic small PSEP (small-plaque parapsoriasis [SPP]); (3) similar distribution of the lesions (trunk, proximal upper and lower limbs) to the classic PSEP; (4) digitiform extensions of most the lesions (70.5% of our patients) as in SPP; (5) absence of itching as in PSEP (SPP type); (6) good response to narrowband ultraviolet B in 76.4% of the patients (n = 26); and (7) during follow-up 5 patients (14.7%) converted into hypopigmented mycosis fungoides.

**Limitations:** A limitation in our study is that we did not perform clonal T-cell receptor gene rearrangement because of limited resources.

**Conclusion:** Based on our findings we believe that this hypopigmented disorder is a well-defined new variant of the PSEP family that shows, apart from the hypopigmentation, all the features of PSEP, particularly the SPP variant, and accordingly could be referred to as hypopigmented PSEP.

**Keywords:** Igitiform Extensions; Follow-Up; Hypopigmented; Mycosis Fungoides; Parapsoriasis En Plaque; Phototherapy.

### 80. DNA Polymorphisms and Tissue Cyclooxygenase-2 Expression in Oral Lichen Planus: A Case-Control Study

R.M. Abdel Hay, M.M. Fawzy, Metwally, Kadry, M. Ezzat, W. Rashwan and L.A. Rashed

*J Eur Acad Dermatol*, 26: 1122-1126 (2012) IF: 2.98

Oral lichen planus (OLP) is a chronic inflammatory disorder defined as a precancerous condition. Special attention has been paid to the expression of cyclooxygenase-2 (COX-2) and its potential role in development of oral squamous cell carcinoma. The identification of single nucleotide polymorphisms that affect gene function or expression and contribute to disease predisposition has become a major area of investigation toward understanding the mechanisms for cancer.

**Objective:** the objective of this study is to investigate the association between the COX-2 765G>C gene polymorphism, tissue COX-2 expression and the development of OLP as a chronic inflammatory condition.

**Methods:** This study was done on 50 patients with OLP and 50 healthy controls. COX-2 activity was assessed by measuring tissue prostaglandin E (PGE)<sub>2</sub> levels by enzyme immunometric assay kit. COX-2 765G>C gene polymorphism was assessed by reverse transcriptase-polymerase chain reaction (RT-PCR) followed by restricted fragment length polymorphism (RFLP).

**Results:** OLP patients showed statistically significant higher mean PGE<sub>2</sub> than the control group. We did not observe any statistically significant differences in genotype distribution or allele frequency between the patients and the control group (P > 0.05). Odds ratio showed no statistically significant association between COX-2 765G>C polymorphism and lichen planus.

**Conclusion:** the present evidence thus indicates that variation in the COX-2 gene is unlikely to be of relevance to the aetiology of OLP. As this is the first report concerning the COX-2 -765G>C gene polymorphism and the risk of OLP, additional studies with larger sample size will be required to confirm these findings.

**Keywords:** Cyclooxygenase-2; Oral lichen planus; Prostaglandin E<sub>2</sub>.

### 81. Plasma and Tissue Osteopontin in Relation to Plasma Selenium in Patients with Psoriasis

D. Kadry and L. Rashed

*J. Eur Acad Dermatol*, 26 (1): 66-70 (2012) IF: 2.98

The association between psoriasis and cardiovascular diseases (CVD) is well documented yet the underlying mechanisms remain unknown. Over-expression of osteopontin (OPN) was reported in plasma of patients with psoriasis; with increased cardiovascular risk factors in these patients. Selenium (Se) compounds are effective in down-regulation of OPN expression.

**Objective:** We investigated the levels of OPN and Se in psoriasis, and their relation to metabolic status in patients to identify a possible link between these markers and co-morbidities observed.

**Methods:** Plasma and tissue samples from 20 patients with psoriasis and 10 control subjects were collected for enzyme-linked immunosorbent assays. The clinical significance of plasma, tissue OPN and plasma Se levels in patients vs. control subjects was analysed in relation to metabolic disorders.

**Results:** Plasma and tissue OPN were significantly higher in patients than in controls (P < 0.001). Plasma Se levels were

significantly lower in patients than in controls (P < 0.001). Elevated plasma OPN levels ( $\geq 51.10$  ng / mL) and depressed plasma Se ( $\leq 5.19$   $\mu$ g /dL) were significantly associated with the occurrence of psoriasis. Plasma OPN negatively correlated with plasma Se in patients (P = 0.003), but not in controls (P = 0.183).

**Conclusions:** High plasma OPN and low plasma Se levels are predictable factors for occurrence of psoriasis. Further studies examining the effects of Se supplementations on the levels of plasma OPN, together with their effects on psoriasis outcome and cardiovascular risk factors in these patients, are needed.

**Keywords:** Psoriasis; Osteopontin; Selenium.

### 82. Acral Lesions of Vitiligo: Why are they Resistant to Photochemotherapy?

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*J Eur Acad Dermatol*, 26 ( 9 ): 1097-1104 (2012) IF: 2.98

Acral lesions of vitiligo are usually resistant to conventional lines of treatment as well as surgical interventions.

**Objective:** to clarify causes underlying resistance of acral lesions to pigmentation in vitiligo by studying some of the factors associated with mechanisms of repigmentation following photochemotherapy.

**Methods:** the study included twenty patients with active vitiligo. Skin biopsies were taken from lesional and perilesional skin of areas expected to respond (trunk and proximal limb) and skin of acral areas, before and after PUVA therapy. Sections were stained with H and E, Melan-A, MHCII, CD1a, SCF and c-kit protein.

**Results:** Before treatment acral areas showed significantly lower hair follicle density, melanocyte density, Langerhans cell (LC) density, epidermal MHCII expression, lesional SCF expression and perilesional c-kit expression. Following treatment with PUVA in both non-responsive acral and repigmenting non-acral lesions identical immunohistochemical changes in the form of significant decrease in LC density, epidermal MHC-II and SCF expression were observed.

**Conclusion:** the surprisingly similar histochemical changes in response to PUVA in acral and non-acral lesions did not manifest with clinical repigmentation except in non-acral ones. Factors such as inherent lower melanocyte density, lower melanocyte stem cell reservoirs and/or lower baseline epidermal stem cell factor may be considered as possible play makers in this respect.

**Keywords:** Acral Vitiligo; Melan-A; Mhcii.

### 83. The Efficacy of Laser Assisted Hair Removal in the Treatment of Acne Keloidalis Nuchae; A Pilot Study

Samia M. Esmat, Rania M. Abdel Hay, Ola M. Abu Zeid and Hala N. Hosni

*Eur J Dermatol*, 22 (5): 645-650 (2012) IF: 2.526

Laser-assisted hair removal causes miniaturization of hair shafts which are the principal contributors to inflammation in acne keloidalis nuchae (AKN). **Objective:** to assess the efficacy of hair reduction by long pulsed Nd-YAG laser as a therapeutic modality for AKN.

**Methods:** This interventional pilot trial included 16 patients with AKN who received 5 sessions of long pulsed Nd-YAG laser. Lesions were objectively and subjectively assessed at the third



and fifth laser sessions, and 1 year after. Global response to treatment was rated using a quartile grading scale regarding the percentage improvement in the count of papules and the size of the plaques. Biopsies were taken before and 2 weeks after the fifth session to evaluate the pathological changes associated with improvement of the treated lesions.

**Results:** All patients showed a significant improvement. The percentage of improvement in the early cases was significantly higher when compared to late cases. Two weeks after the fifth session, all biopsies showed a significant decrease in the inflammatory infiltrate except one case. Sclerosis was markedly decreased. Complete absence of hair follicles and adenexa was observed, apart from in 2 cases.

**Conclusion:** Laser hair depilation can significantly improve this disfiguring chronic disorder. Starting treatment as early as possible achieves the best results and can stop the disease process if followed by maintenance sessions.

**Keywords:** Acne keloidalis nuchae; Hair reduction; Nd-Yag laser.

#### 84. Reduction of Rantes Expression in Lesional Psoriatic Skin after Narrow Band Ultraviolet Therapy: A Possible Marker of Therapeutic Efficacy

Amr A. Rateb, Marwa M.T. Fawzi, Rania M. Abdel Hay, Faissal N. Mohammed and Khalda S. Amr

*Eur J Dermatol*, 22 ( 4): 482-487 (2012) IF: 2.526

The regulated upon activation, normal T cell expressed and secreted (RANTES) production in psoriatic lesions may amplify the inflammation in these lesions. Narrow band ultraviolet B (NB-UVB), a therapeutic modality for psoriasis, affects the expression of inflammatory cytokines and chemokines.

**Objective:** Our aim was to evaluate RANTES mRNA expression in skin lesions of psoriasis before and after NB-UVB phototherapy.

**Methods:** This study included 25 psoriatic patients who received 24 sessions of NB-UVB. Skin biopsies were taken before and after phototherapy for real time PCR evaluation of RANTES mRNA.

**Results:** the relative quantitation values (RQ) of RANTES mRNA expression was significantly reduced after treatment. A significant negative correlation was found between pre-treatment RQ RANTES mRNA expression and post-treatment PASI score. We found a significant negative correlation between dRQ RANTES mRNA expression (difference between RQRANTES mRNA expression before and after phototherapy) and PASI score after phototherapy. We found significant negative correlations between pre-treatment RQ RANTES mRNA expression and both initial response session number and total NB-UVB dose at the end of phototherapy.

**Conclusion:** NB-UVB reduces RANTES mRNA expression in psoriatic lesions. Pre-treatment RQ RANTES mRNA expression could be considered as a marker for clinical improvement and NB-UVB phototherapy efficacy.

**Keywords:** Chemokines; Nb-Uvb; Psoriasis; Rantes.

#### 85. Psoriasis and Metabolic Syndrome: is Peroxisome Proliferator-Activated Receptor- $\gamma$ Part of the Missing Link?

Rehab A. Hegazy, Rania M. Abdel Hay, Olfat Shaker, Safinaz S. Sayed and Dalia A. Abdel Halim

*Eur J Dermatol*, 22 (5): 622-628 (2012) IF: 2.526

Growing evidence points to a causative relationship between altered activity of peroxisome proliferator-activated receptor (PPAR) and psoriasis on the one hand, and its relationship with metabolic syndrome (MS) on the other.

**Objective:** Could altered PPAR levels be one of the culprits responsible for translating the metabolic state among psoriatic patients?

**Materials and Methods:** This investigational cross-sectional study included 60 psoriatics and 60 controls. Subjects were subgrouped according to the presence or absence of MS. Biopsies were taken from all subjects for immunohistochemical staining for PPAR and western blot technique was carried out.

**Results:** PPAR immunostaining in psoriatics was significantly lower than in controls with the lowest levels documented in patients with MS ( $P < 0.001$ ). PPAR immunostaining level was significantly lower in diabetics, hypertensive and insulin resistance patients ( $P < 0.05$ ). It also showed a significant positive correlation with high density lipoprotein (HDL) levels and significant negative correlation with age, psoriasis area and severity index (PASI), body mass index, and blood glucose levels. Similar results were obtained by western blot technique.

**Conclusion:** Reduced PPAR could be added to the factors responsible for translating the metabolic state among psoriatic patients. PPAR agonists can present an adjuvant therapeutic tool in treatment of psoriatics with MS.

**Keywords:** Immunohistochemistry; Metabolic Syndrome; Ppar.

#### 86. Intralesional Cryosurgery and Intralesional Steroid Injection: A Good Combination Therapy for Treatment of Keloids and Hypertrophic Scars

Ahmed Hany Weshahy and Rania Abdel Hay

*Dermatol Ther*, 25: 273-276 (2012) IF: 1.687

Hypertrophic scars and keloids exhibit high recurrence rates following surgical excision. Intralesional cryosurgery (ILC) can achieve a higher degree of effectiveness than the surface cryotherapy.

The aim of this study is to assess the clinical efficacy of ILC using Weshahy cryoneedles followed by IL steroid in a trial of getting rid of the fibrous mass by destruction, not by surgery to avoid being under tension of the new scar.

This study included 22 patients. Evaluation of the volume reduction of the lesions was done after a single ILC session followed by IL steroid injections. There was a significant decrease in the volume of the lesions after 4 months ( $P < 0.01$ ), with a volume reduction of 93.5%. by using ILC at the base of keloids or hypertrophic scars, we can change the old fibrous tissue into a recent scar or granulation tissue which will respond more successfully to IL steroid injection.

**Keywords:** Hypertrophic Scars; Intralesional Steroid; Keloids.

### 87. Broad Band Uva: A Possible Reliable Alternative to Puva in the Treatment of Early-Stage Mycosis Fungoides

Medhat El Mofty, Shahira Ramadan, Marwa M. Fawzy, Rehab A. Hegazy and Safinaz Sayed

*Photodermatol Photo*, 28: 274-277 (2012) IF: 1.305

UVA1 phototherapy was found to induce marked improvement in skin lesions of patients with stages IA and IB mycosis fungoides (MF). Broad band UVA (BB-UVA) is composed of 80.1% UVA1, with similar mechanisms of action. Our aim was to evaluate the efficacy of BB-UVA in the treatment of early-stage MF. Thirty patients with early stage MF were included. They were divided into two equal groups receiving either BB-UVA at 20 J/cm<sup>2</sup>/ session or PUVA three times/week for 40 sessions. Clinical and histopathological evaluations were performed before and after therapy in addition to immunohistochemical measurement of CD4+ cells and Bcl-2. Patients were followed up for an average duration of 36 months. Comparable clinical and histopathological improvement was noted in MF patients in both groups. Clinical improvement graded 'Excellent' was achieved in 33% of patients in the BB-UVA versus 13.3% in the psoralen and UVA (PUVA) group. Long-term follow-up indicated superiority of BB-UVA over PUVA. BB-UVA group showed a more rapid clearance rate, shorter time to achieve complete clearance, a longer disease-free interval and lower relapse rate. The use of BB-UVA in the treatment of early-stage MF is comparable or even superior to PUVA regarding efficacy and remission periods.

**Keywords:** Bcl2; Broad Band-Uva; Mycosis Fungoides; Puva; Uva1.

### 88. A Comparative Study on Efficacy of Uva1 Vs. Narrow-Band Uvb Phototherapy in the Treatment of Vitiligo

Bakr Mohamed El-Zawahry, Dalia Ahmed Bassiouny, Rehab Mohamed Sobhi, Eman Abdel-Aziz, Naglaa Sameh Zaki, Dawoud Fakhry Habib and Dalia Mamdouh Shahin

*Photodermatol Photo*, 28: 84-90 (2012) IF: 1.305

**Background/Purpose:** Narrow-band ultraviolet B (NB-UVB) is considered the most effective and safe initial treatment for moderate-to-severe vitiligo but phototoxicity and possible carcinogenicity are the reported side effects. Ultraviolet A1 (UVA1) phototherapy has overlapping biological effects to NB-UVB and is relatively free of side effects associated with other phototherapy regimens.

**Methods:** Forty patients with vitiligo were included in this prospective, randomized controlled comparative clinical trial. Twenty patients received NB-UVB and 20 received UVA1 three times weekly for 12 weeks. The UVA1 group was divided into two subgroups. Ten patients received moderate and 10 received low dose of UVA1. Serum samples were collected before and after 36 sessions to assess soluble interleukin 2 receptor level. Patients were clinically evaluated before therapy then monthly according to Vitiligo Area Scoring Index (VASI) and Vitiligo European Task Force (VETF) scores. In addition, extent of response was determined by a blinded dermatologist comparing before and after therapy photographs. Pattern of response and side effects were recorded.

**Results:** NB-UVB was superior to UVA1 with a significant difference in blinded dermatological assessment ( $P < 0.001$ ), percentage change in VASI score ( $P < 0.001$ ) and percentage change in VETF area score ( $P = 0.001$ ). No significant difference in side effects was observed between both groups. Comparing UVA1 subgroups, better response in moderate-dose group was found as regard to percentage change in VASI ( $P < 0.001$ ) and percentage change in VETF area score ( $P = 0.001$ ), while no significant difference was found in blinded dermatological assessment ( $P = 0.121$ ).

**Conclusion:** NB-UVB phototherapy remains to be an effective and safe therapeutic option in vitiligo. Response to UVA1 in vitiligo seems to be dose dependent and seems to be of limited value in treatment of vitiligo as a monotherapy. Further studies combining it with other lines of therapy such as systemic steroids may prove beneficial.

**Keywords:** Nb-Uvb; Serum Ii2 R; Uva; Vitiligo.

### 89. Comparative Study of the Effect of A Daily Steroid Regimen Versus A Weekly Oral Pulse Steroid Regimen on Morphological Changes, Blood Sugar, Bone Mineral Density and Suprarenal Gland Activity

Mohammad A. El-Darouti, Heba M. Mashaly, Eman El-Nabarawy, Amira M. El-Tawdy, Marwa M. Fawzy, Dorreya S. E. Salem, Khaled M. H. El-Kaffas and Dalia A. M. El Sayed.

*J Dermatol Treat*, 1-7 (2012) IF: 1.234

the most serious side effects of systemic steroids include osteoporosis and suprarenal suppression. Many steroid regimens have been suggested to minimize these side effects; one of them is oral steroid pulse therapy.

**Objective:** to compare the side effects of a daily oral steroid regimen versus a weekly oral steroid pulse regimen on bone mineral density and suprarenal suppression.

**Methods:** Thirty patients with different skin diseases were divided into two groups: 15 for oral daily steroids (ODS) (group 1) and 15 for weekly oral pulse steroids (WOPS) (group 2). They were evaluated for bone mineral density (measured by DEXA) and suprarenal suppression (measured by serum cortisol level), morphological changes and blood sugar. Treatment was continued for 6 months to 3 years.

**Results:** Cushingoid features in group 1 were observed in 73%, yet they were not detectable in group 2. Disturbed blood sugar in group 1 was 33% and 0% in group 2. The serum cortisol level was lower in patients on ODS than those on WOPS. The effect of WOPS on bone mineral density was very limited in comparison with the ODS.

**Conclusion:** Weekly oral steroid pulse therapy induces no significant bone loss and no suprarenal suppression and can be an alternative option in the treatment of chronic disorders requiring long-term oral steroid therapy.

**Keywords:** Cushingoid Features; Dexa; Osteopenia; Osteoporosis; Steroid Pulse Therapy; Suprarenal Suppression.

## 90. Glutathione S-Transferase M1 and T1 Genetic Polymorphism in Egyptian Patients with Nonsegmental Vitiligo

D. A. Bassiouny and M. M. Khorshied

*Clinical and Experimental Dermatology*, 38: 160-163 (2012)

IF: 1.198

Oxidative stress and accumulation of free radicals might play a role in the pathogenesis of vitiligo. Glutathione S-transferase (GST) is a multigene family of enzymes that detoxify oxidative stress products. In this study, genotyping by multiplex PCR of GSTM1 and GSTT1 in 101 women with nonsegmental vitiligo vulgaris and 101 age-matched healthy female volunteers showed that only the GSTM1 null genotype ( $P = 0.04$ ) was significantly overexpressed in patients with vitiligo. Analysis of the combined effect of GSTM1 and GSTT1 genotyping identified a significant association of risk for vitiligo with the GSTT1 / GSTM1 double-null type only ( $P = 0.01$ ; OR = 2.69; 95% CI 1.12–6.46). Age of onset of vitiligo was significantly earlier in patients with the T1 null genotype ( $P < 0.01$ ) and those with the T1- / M1+ and T1- / M1 combined genotypes ( $P < 0.01$  and  $P = 0.01$ , respectively). In conclusion, the GSTM1 gene and the GSTM1 / GSTT1 double-null genotype may be a risk factor for vitiligo in Egyptian patients. Inability to cope with oxidative stresses because of GST deficiency may cause early disease onset.

**Keywords:** Glutathione S-Transferase; Genetic polymorphism; Nonsegmental vitiligo.

## 91. Downregulation of TLR-7 receptor in hepatic and non-hepatic patients with lichen planus

Amira El Tawdy and L. Rashed

*International Journal Of Dermatology*, (2012) IF: 1.142

**Background:** Lichen planus (LP) is an inflammatory disease of the skin and oral mucosa. The association of LP and chronic hepatitis C virus (HCV) is well established, with variable prevalence rates among different populations. TLRs are key regulators of both the innate response and the adaptive response. However, TLRs also interact with endogenous ligands released by necrotic cells, and this process can intensify autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus.

**Objective:** To investigate the role of Toll-like receptor-7 (TLR-7) in LP through the detection of TLR-7 protein, and to compare between the expression of TLR-7 protein in HCV-positive and HCV-negative patients with LP.

**Materials and methods:** The study included 20 skin biopsies from patients with LP and 10 control biopsies. TLR-7 protein was detected by Western blot analysis. Detection of HCV-specific antibodies in the patient serum was done using ELISA technique.

**Results:** Our analysis revealed a significantly lower level of TLR-7 protein in all the LP skin biopsies compared with controls. The expression showed no difference between HCV-positive and HCV-negative patients.

**Conclusion:** We concluded that TLR-7 abnormal expression in LP may have an impact on the pathogenesis of the disease. TLR-7 receptor and HCV relationship in patients with LP could not be confirmed by this study.

**Keywords:** Glutathione S-transferase; Genetic polymorphism; Nonsegmental vitiligo.

## 92. Detection of Plasma and Urinary Monoamines and their Metabolites Levels in Non Segmental Vitiligo

Zeinab Shahin, Tahra M. Leheta, Rania M. Abdel Hay, Hanaa M. Abdel Aal and Laila A. Rashed

*Acta Dermatovener Cr*, 20 (1): 14-20 (2012) IF: 0.36

Vitiligo is one of the most troubling diseases to both patient and physician. Monoamines are chemical compounds derived from the hydroxyderivative of amino acids. They have been implicated in many dermatoses, but their role in the etiopathogenesis of vitiligo remains obscure.

The aim of the study was to evaluate the role of the neural factor in the pathogenesis of nonsegmental vitiligo (NSV) by measuring catecholamines and their metabolites in plasma and urine of patients suffering from NSV, and to correlate these factors with the onset and activity of the disease. The study included 20 patients with NSV and 20 healthy individuals.

All subjects were subjected to plasma and urine detection of catecholamines and 5-hydroxyindoleacetic acid (5-HIAA) using high-performance liquid chromatography and electrochemical detection. Comparison of plasma and urinary catecholamines and 5-HIAA between the patient and control groups revealed a statistically significant increase in the group of NSV patients ( $P < 0.05$ ). There was no statistically significant difference ( $P > 0.05$ ) between the patients with recent and old onset of NSV. In conclusion, the increase in the level of monoamines may be the initiating event in the pathogenesis of NSV.

**Keywords:** Catecholamines; Monoamines; Vitiligo.

## Dept. of Diagnostic Radiology

## 93. Revisiting the Harem Conspiracy and Death of Ramesses III: Anthropological, Forensic, Radiological and Genetic Study

Zahi Hawass, Somaia Ismail, Ashraf Selim, Sahar N Saleem, Dina Fathalla, Sally Wasef, Ahmed Z Gad, Rama Saad, Suzan Fares, Hany Amer, Paul Gostner, Yehia Z Gad, Carsten M Pusch and Albert R Zink

*British Medical Journal*, 1-9 (2012) IF: 14.093

to investigate the true character of the harem conspiracy described in the Judicial Papyrus of Turin and determine whether Ramesses III was indeed killed.

**Design** Anthropological, forensic, radiological, and genetic study of the mummies of Ramesses III and unknown man E, found together and taken from the 20th dynasty of ancient Egypt (circa 1190-1070 BC).

**Results** Computed tomography scans revealed a deep cut in Ramesses III's throat, probably made by a sharp knife. During the mummification process, a Horus eye amulet was inserted in the wound for healing purposes, and the neck was covered by a collar of thick linen layers. Forensic examination of unknown man E showed compressed skin folds around his neck and a thoracic inflation. Unknown man E also had an unusual mummification procedure. According to genetic analyses, both mummies had identical haplotypes of the Y chromosome and a common male lineage.

**Conclusions** This study suggests that Ramesses III was murdered during the harem conspiracy by the cutting of his throat.

Unknown man E is a possible candidate as Ramesses III's son Pentawere.

**Keywords:** Paleopathology; Paleoradiology; Forensic; Genetics; anthropology; Ramesses Iii; Unknown man E; Egypt; Ct; Dna; Ancient.

#### 94. Diencephalic-Mesencephalic Junction Dysplasia: A Novel Recessive Brain Malformation

Maha S. Zaki, Sahar N. Saleem, William B. Dobyns, A. James Barkovich, Hauke Bartsch, Anders M. Dale, Manzar Ashtari, Naiara Akizu, Joseph G. Gleeson and Ana Maria Grijalvo-Perez

*Brain*, : 1-12 (2012) IF: 9.457

We describe six cases from three unrelated consanguineous Egyptian families with a novel characteristic brain malformation at the level of the diencephalic-mesencephalic junction. Brain magnetic resonance imaging demonstrated a dysplasia of the diencephalic-mesencephalic junction with a characteristic 'butterfly'-like contour of the midbrain on axial sections. Additional imaging features included variable degrees of supratentorial ventricular dilatation and hypoplasia to complete agenesis of the corpus callosum. Diffusion tensor imaging showed diffuse hypomyelination and lack of an identifiable corticospinal tract. All patients displayed severe cognitive impairment, post-natal progressive microcephaly, axial hypotonia, spastic quadriparesis and seizures. Autistic features were noted in older cases. Talipes equinovarus, non-obstructive cardiomyopathy and persistent hyperplastic primary vitreous were additional findings in two families. One of the patients required shunting for hydrocephalus; however, this yielded no change in ventricular size suggestive of dysplasia rather than obstruction. We propose the term 'diencephalic-mesencephalic junction dysplasia' to characterize this autosomal recessive malformation.

**Keywords:** Diencephalon; Mesencephalon; Brainstem malformation; Mental retardation; Brain wiring.

#### 95. Endovascular Management of Early Hepatic Artery Thrombosis after Living Donor Liver Transplantation

Omar Abdelaziz, Karim Hosny, Ayman Amin, Sally Emadeldin, Shinji Uemoto and Mohamed Mostafa

*Transplant International*, 25: 847-856 (2012) IF: 2.921

to study the feasibility of endovascular management of early hepatic artery thrombosis (HAT) after living-donor liver transplantation (LDLT) and to clarify its role as a less invasive alternative to open surgery. A retrospective review of 360 recipients who underwent LDLT. Early HAT developed in 13 cases (3.6%). Diagnosis was performed using Doppler, CT angiography, and digital subtraction angiography. Intra-arterial thrombolysis (IAT) was performed using streptokinase or tPA. In case of underlying stricture, PTA was attempted. If the artery did not recanalize, continuous infusion was performed and monitored using Doppler US. Initial surgical revascularization was successful in 2/13 cases.

IAT was performed in 11/13 cases. The initial success rate was 81.8% (9/11), the failure rate was 18.2% (2/11). Rebound thrombosis developed in 33.3% (3/9). Hemorrhage developed after IAT in 2/11 cases (18.2%). Definite endovascular treatment of HAT was achieved in 6/11 cases (54.5%) and definite

treatment (surgical, endovascular or combined) in 9/13 cases (69%). (Follow-up 4 months–4 years). Endovascular management of early HAT after LDLT is a feasible and reliable alternative to open surgery. It plays a role as a less invasive approach with definite endovascular treatment rate of 54.5%.

**Keywords:** Endovascular; Hepatic Artery Thrombosis; Living; Donor Liver Transplantation.

#### 96. Elastography Ultrasound and Questionable Breast Lesions: Does It Count?

Sahar M. Mansour and Omar S. Omar

*Eur J Radiol*, 81: 3234-3244 (2012) IF: 2.606

**Objective:** to check possible additional value of using elastography ultrasound in the specification of questionable breast lesions.

**Subjects and Methods:** Questionable breast lesions on gray scale ultrasound examination had been further evaluated by elastography ultrasound in 97 cases with median age of 42 years. The studied lesions were pathologically proven (58 benign and 39 malignant) using true cut tissue / surgical excision biopsy that was considered the gold standard of reference.

**Results:** Conventional ultrasound categorization before biopsy included: category 3 (probably benign) in 42.3% (n=41), category 4a (low suspicion of malignancy) in 13.4% (n=13), category 4b (intermediate suspicion of malignancy) in 16.5% (n=16) and category 4c (moderate suspicion of malignancy) in 27.8% (n=27). We had evaluated elastography ultrasound regarding elastography strain scoring and quantitative strain ratio. Sensitivity, specificity and accuracy was 89.7%, 86.2% and 87.6% for conventional ultrasound, 92.3 %, 74.1% and 81.4% for elastogram 5-point scoring method and 87.1%, 89.6% and 88.6% for the calculated strain ratios respectively in the assessment of the examined breast lesions.

**Conclusion:** Ultrasound elastography, using both qualitative and quantitative methods can improve the performance of conventional B-mode ultrasound and enhance its specificity and accuracy in the diagnosis of questionable (BI-RADS category 3 &4) breast lesions.

**Keywords:** Breast; Ultrasound; Elastography; Strain Index.

#### 97. Does Mri Add to Ultrasound in the Assessment of Disorders of Sex Development?

S.M. Mansoura, S.T. Hamed, L. Adel, R.M. Kamal and D.M. Ahmed.

*Eur J Radiol*, 81: 2403-2410 (2012) IF: 2.606

The objective of the study was to evaluate the need of magnetic resonance imaging and using different approaches (transabdominal, endoluminal and transperineal) in the proper assessment of disorders of sex development regarding gonadal detection and gender differentiation.

**Subjects and Methods:** Twenty five patients with abnormalities of sex disorders were included. They were classified into two groups according to the time of clinical presentation: Group 1 (early onset) included eight cases. Their age ranged from one month to 12 years (mean age = 3.0). They presented with overt genital ambiguity of clitoral hypertrophy in a phenotypic female, non palpable testes or micropenis in a phenotypic male. Group 2 (late onset) included 17 cases. Their age ranged from 16 to 33

years (mean age 18.1). This group presented by distressing puberty symptoms of primary amenorrhea in a female phenotype or undescended testis and behaving as a male. Cases were subjected to Ultrasound and MR imaging examinations. Imaging results were correlated results of chromosomal and hormonal assays as well as laparoscopy findings.

**Results:** the study included: 10/25 cases (40 %) of Female pseudo-hermaphroditism, 13/25 cases (52%) of male pseudo-hermaphroditism, one case (4%) of true hermaphroditism and one case (4%) of pure gonadal dysgenesis. the accuracy of multi approach ultrasound was 89.8% compared to 85.7% in MR imaging.

**Conclusion:** Ultrasound should be considered the initial screening modality in the assessment of developmental sex disorders. MRI examination could be reserved for gonad identification when ultrasound examination fails to do so and for corrective surgery guidance.

**Keywords:** Mri; Ultrasound; Disorder of sex development.

### 98. Treatment with High Intensity Focused Ultrasound: Secrets Revealed

Islam Ahmed Shehata

*Eur J. Radiol*, 81: 534-541 (2012) IF: 2.606

for many decades open surgery remained the only way available for local control of body tumors. in order to decrease the patients' morbidity and mortality several image guided minimally invasive procedures have been adopted. High intensity focused ultrasound (HIFU) is an extracorporeal non invasive method for tumor ablation. High intensity ultrasonic waves can be focused to a focal point resulting in lethal elevation of the temperature at the target site with consequent damage of the tumoral cells. the advances in HIFU technology during the past two decades expanded the HIFU applications to include ablation of both benign and malignant tumors with different treatment strategies being implemented for each type. the aim of this review is to introduce the reader to the details of the treatment process including pretreatment preparation, treatment planning, different ablation strategies, patients' after care as well as the follow up regimens for the most common HIFU applications.

**Keywords:** Hifu; Therapeutic ultrasound; Thermal ablation.

### 99. Profound Microcephaly, Primordial Dwarfism with Developmental Brain Malformations: A New Syndrome

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*Am J. Med Genet A*, : 0-0 (2012) IF: 2.391

We describe two sibs with a lethal form of profound congenital microcephaly, intrauterine and postnatal growth retardation, subtle skeletal changes, and poorly developed brain. the sibs had striking absent cranial vault with sloping of the forehead, large beaked nose, relatively large ears, and mandibular micro-retrognathia. Brain magnetic resonance imaging (MRI) revealed extremely simplified gyral pattern, large interhemispheric cyst and agenesis of corpus callosum, abnormally shaped hippocampus, and proportionately affected cerebellum and brainstem. in addition, fundus examination showed foveal

hypoplasia with optic nerve atrophy. No abnormalities of the internal organs were found. This profound form of microcephaly was identified at 17 weeks gestation by ultrasound and fetal brain MRI helped in characterizing the developmental brain malformations in the second sib. Molecular analysis excluded mutations in potentially related genes such as RNU4ATAC, SLC25A19, and ASPM. These clinical and imaging findings are unlike that of any recognized severe forms of microcephaly which is believed to be a new microcephalic primordial dwarfism (MPD) with developmental brain malformations with most probably autosomal recessive inheritance based on consanguinity and similarly affected male and female sibs.

**Keywords:** Microcephaly; Mri; Mental retardation; Dwarfism.

### 100. Fetal Cardiac Magnetic Resonance (Cmr)

Saleem S.N.

*Echocardiography - New Techniques*, (2012)

Congenital heart disease (CHD) is present in 0.8% of all live births and is therefore one of the most common congenital malformations (Fyler et al., 1980). the spectrum of congenital heart defects is significantly higher in fetuses than in live born infants because of their reduced viability (Tennstedt et al., 1999). the prognosis of congenital heart disease can be poor; almost one third to one half of congenital heart defects are severe and lethal unless an intervention is done early (Hoffman & Kaplan, 2002). Prenatal diagnosis of congenital heart disease results in referral of mothers with affected fetuses to equipped centers where all facilities for neonatal cardiac care are available. the diagnosis of a congenital heart disease in a fetus should also prompt evaluation for genetic syndromes and associated non cardiac malformations (Cohen, 2001). Improvements in diagnosis and treatment have lead to more patients surviving to adulthood (Carvalho et al., 2002). Echocardiography is the gold standard diagnostic imaging tool for prenatal detection of cardiac malformations (Kleinman et al., 1980). Fetal echocardiography combines the benefit of accurate assessment of cardiac anatomy and function probability (Carvalho et al., 2002). However, Ultrasonography (US) is occasionally limited by acoustic window, poor images of the distal vasculature, fetal position, maternal adipose tissue, abdominal wall scar form previous abdominal or pelvic surgery, and is user dependent (Forbus et al., 2004). as a consequence, there remains room for other modalities in studying the fetal cardiovascular system. the intent of this chapter is to serve as a primer for fetal Cardiac Magnetic Resonance (CMR) based on our clinical cases of normal and abnormal fetal hearts. the chapter will include discussion of fetal Magnetic Resonance Imaging (MRI); fetal CMR technical aspects; MRI anatomy of the fetal heart; in-utero diagnosis of CHD and associated fetal syndromes; and future of fetal CMR.

### 101. Measuring Competence of Radiology Education Programs and Residents: the Egyptian Experience

Saleem S.N. and Sabry Y.Y.

*Radiology Education: The Evaluation And Assessment of Clinical Competence*, (2012)

the Ancient Egypt had an advanced elaborate medical education and practice ruled by a competent bureaucracy that apprenticed physicians to be practicing healers. in modern history, the Faculty of Medicine at Cairo University (Kasr Al-Ainy), established in

1827, continues the glory of Egypt in medical education as one of the biggest and oldest medical schools in Africa and the Middle East. Its central Radiology Department, with its total 77 radiologists, is responsible for clinical services as well as for providing multiple calibre radiology education programs for about 100 trainees annually from Egypt and neighbouring countries. Radiology education programs are planned for radiology residents to obtain master's degree (M.Sc.), for assistant lecturers to obtain medical doctorate (M.D.) and for visitor trainees. Objectives of radiology education programs include knowledge, practical skills, intellectual capabilities and communications with medical societies and communities. Trainees are assessed to determine if learning objectives have been fulfilled on a daily, weekly and biannual basis. Radiology education programs are measured for professional performance through the university's self-assessment studies; national assessment is measured through the National Authority for Quality Assurance and Accreditation in Education (NAQAAE), Egypt, and international assessment is measured through the World Federation for Medical Education (WFME).

#### Dept. of Ear Nose & Throat

### 102. Hypertrophied Tonsils Impair Velopharyngeal Function after Palatoplasty

Mosaad Abdel-Aziz

*Laryngoscope*, 122: 528-532 (2012) IF: 2.018

When tonsillar hypertrophy obstructing the airway is encountered in a child with a repaired cleft palate and velopharyngeal insufficiency, the surgeon may opt for tonsillectomy to relieve the airway obstruction, with possible effects on velopharyngeal closure. The aim of this study was to assess the impact of hypertrophied tonsils on velopharyngeal function in children with repaired cleft palate and to measure the effect of tonsillectomy on velopharyngeal closure and speech resonance.

**Study Design:** Case series.

**Methods:** Twelve children with repaired cleft palate and tonsillar hypertrophy underwent tonsillectomy to relieve airway obstruction. Preoperative and postoperative evaluation of velopharyngeal function was performed. Auditory perceptual assessment of speech and nasalance scores were measured, and velopharyngeal closure was evaluated by flexible nasopharyngoscopy.

**Results:** Preoperative impairment of velopharyngeal function was detected. However, significant postoperative improvement of speech parameters (hypernasality, nasal emission of air, and weak pressure consonants measured with auditory perceptual assessment) was achieved, and the overall postoperative nasalance score was improved significantly for nasal and oral sentences. Reduction of velopharyngeal gap size was detected after removal of hypertrophied tonsils. Although the improvement of velopharyngeal closure was not significant, three cases demonstrated complete postoperative closure with no gap.

**Conclusions:** Hypertrophied tonsils may impair velopharyngeal function in children with repaired cleft palate, and tonsillectomy is beneficial for such patients as it can improve the velopharyngeal closure and speech resonance. Secondary corrective surgery may be avoided in some cases after tonsillectomy.

**Keywords:** Tonsillectomy; Hypertrophied tonsils; Cleft palate; Velopharyngeal insufficiency.

### 103. The Effectiveness of Tonsillectomy and Partial Adenoidectomy on Obstructive Sleep Apnea in Cleft Palate Patients

Mosaad Abdel-Aziz

*Laryngoscope*, 122: 2563-2567 (2012) IF: 2.018

The most common cause of pediatric obstructive sleep apnea (OSA) is adenotonsillar hypertrophy (ATH). In cleft palate patients, however, the obstructive effects of ATH are more severe due to narrow airways. The aim of this study was to assess the effectiveness of tonsillectomy and/or partial adenoidectomy on OSA in cleft palate patients.

**Study design:** Case series.

**Methods:** Tonsillectomy and/or partial adenoidectomy was performed in 17 repaired cleft palate patients with tonsillar and/or adenoid hypertrophy and OSA. Apnea/hypopnea (A/H) index and minimum O<sub>2</sub> saturation were measured before and after surgery. In addition, because these patients are vulnerable to speech impairment after pharyngeal surgery, auditory perceptual assessment (APA) and nasometric assessment of speech were performed.

**Results:** The mean preoperative A/H index was 17.6 ± 6.3, and the mean preoperative minimum O<sub>2</sub> saturation was 88.7 ± 6.1%. Both parameters improved postoperatively, to 1.9 ± 6.2 and 93.7 ± 6.1% respectively, and the changes were significant ( $P < 0.001$ ). In 12 cases (70.6%), A/H indexes were normalized following surgery. Associated comorbidities such as retrognathia and narrow pharyngeal airways may underlie incomplete recovery in some cases. There were no significant postoperative changes in APA and nasalance scores.

**Conclusions:** In most cases, tonsillectomy and/or partial adenoidectomy is an effective method for treatment of OSA in repaired cleft palate patients presenting with tonsillar and/or adenoid hypertrophy. However, some cases may need further procedures to relieve airway obstruction due to associated comorbidities.

**Keywords:** Obstructive sleep apnea; Cleft palate; Polysomnography; Tonsillectomy; Adenoidectomy.

### 104. The Effect of Steroid Injection of the Tongue Base on Reducing Postoperative Airway Obstruction in Cleft Palate Repair

M. Abdel-Aziz, A. Ahmed, N. Naguib and M. I. Abdel-Khalik

*Int. J. Oral Max Surg*, 41: 612-615 (2012) IF: 1.506

Upper airway obstruction (UAO) is a well known complication of cleft palate repair. The aim of this study was to evaluate the efficacy of local tongue base steroid injection in preventing or reducing the lingual oedema that can cause UAO following palatoplasty. Thirty children with unilateral complete cleft palate were included. They were randomly divided into two equal groups. Children in group I received intravenous dexamethasone whilst children in group II received both intravenous dexamethasone and local betamethasone injected at the tongue base. Both groups underwent the same technique of palatoplasty, postoperative breathing was assessed and UAO was rated as mild, moderate or severe. Postoperative UAO developed in six cases (40%) in group I and in two cases (13%) in group II. In group I, it was mild in three cases, moderate in one case, and severe in two cases. In group II, it was mild in one case and moderate in another

case. Despite the differences in the number and severity of the condition in both groups, comparison was statistically insignificant. Local steroid injection of the tongue base during cleft palate surgery reduced the incidence and severity of post-palatoplasty UAO.

**Keywords:** Local steroid injection; Tongue base; Airway obstruction; Cleft palate; Postoperative oedema.

### 105. Origin Oriented Management of Inverted Papilloma of the Frontal Sinus

Reda H. Kamel, Ahmed F. Abdel Fattah and Ayman G. Awad

*Rhinology*, 262-268 (2012) IF: 1.321

Despite the great progress in endoscopic management of inverted papilloma (IP), involvement of the frontal sinus (FS) remains a challenge.

**Methodology:** Six cases of FS IP were assessed. Extent of surgery included simple frontal recess clearance, extended frontal sinu-sotomy, and modified Lothrop approach. There was no need for adjuvant frontal trephination or an external osteoplastic flap.

**Results:** FS involvement was observed in 6 out of 119 cases of IP (5%). in one case, IP was originating from the FS and in four it was extending to the FS. the sixth case had a wide origin from the anterior ethmoid and FS. Complete resection of FS IP was achieved in all cases with a single incidence of CSF leak. No recurrence was identified after a follow-up period of an average of 27 months.

**Conclusions:** FS IP originating outside FS can be delivered transnasally with or without frontal ostium widening and preserving FS mucosa and bone. Inverted papillomata originating from FS proper and those with origin from inside and outside the FS can also be resected transnasally after widening of the frontal ostium with removal of surrounding mucosa and drilling or curettage of underlying bone at attachment sites.

**Keywords:** Inverted papilloma; Frontal sinus; Origin; Endoscopic surgery; Transnasal.

### 106. Furlow Technique for Treatment of Soft Palate Fistula

Mosaad Abdel-Aziz, Hassan El-Hoshy, Nader Naguib and Ramez Reda

*Int. J. Pediatr Otorhi*, 76: 52-56 (2012) IF: 1.167

Fistula of the palate is a common complication of palatoplasty, it leads to nasal regurgitation of fluids and hypernasality of speech. Its treatment is technically difficult due to paucity and fibrosis of palatal tissues. the aim of this study was to evaluate the efficacy of closure of soft palate fistula by using Furlow double opposing Z-palatoplasty.

**Methods:** Nineteen patients were subjected for repair of their soft palate fistulas using Furlow Z-plasty. Pre and postoperative speech analysis using auditory perceptual assessment, measurement of nasalance score using nasometric assessment, and measurement of velar movement using flexible nasopharyngoscopy were done.

**Results:** All cases showed complete closure of their fistulas at first attempt, with no operative or postoperative complications. Recurrence was not recorded in any case after a follow up period of at least 12 months. Significant improvement of speech quality and nasalance score was achieved. Flexible nasopharyngoscopy

showed postoperative increase in velar movement which was not significant relative to the preoperative records.

**Conclusions:** Treatment of soft palate fistula by using Furlow technique is an effective method as a primary treatment with a high success rate and a good functional outcome.

**Keywords:** Palatoplasty; Z-Plasty; Palatal fistula; Hypernasal speech nasometry.

### 107. Repair of Submucous Cleft Palate with Furlow Palatoplasty

Mosaad Abdel-Aziz, Hassan El-Hoshy, Nader Naguib and Nassim Talaat

*Int. J. Pediatr Otorhi*, 76: 1012-1016 (2012) IF: 1.167

Submucous cleft palate is a congenital anomaly caused by abnormal insertion of the levator veli palatini muscles to the posterior border of the hard palate, normally these muscles unite together to form the levator sling. Velopharyngeal insufficiency (VPI) may occur in about 10% of cases, our previous treatment protocol was pharyngeal flap that may result in obstructive breathing. Furlow technique seems to be a more physiologic solution as it reconstructs the levator sling. the aim of this study was to determine the efficacy of Furlow palatoplasty in treatment of submucous cleft palate cases presented with VPI.

**Methods:** This prospective study was conducted on 15 children with symptomatic submucous cleft palate. All cases were treated by Furlow double opposing Z-plasty technique for repositioning of levator muscles, preoperative and postoperative speech evaluation was done using auditory perceptual assessment and nasometry, while velopharyngeal closure was assessed with flexible nasopharyngoscopy.

**Results:** Significant improvement of speech and overall nasalance score were achieved. Flexible nasopharyngoscopy showed complete velopharyngeal closure of 13 cases (86.7%), while one case needed secondary pharyngoplasty for correction of residual VPI and the parents of the other case refused secondary surgery as the speech improvement of their child was satisfactory.

**Conclusions:** Furlow palatoplasty technique is an effective method in treatment of VPI in cases of submucous cleft palate as it has high success rate with no morbidity.

**Keywords:** Submucous cleft palate; Furlow palatoplasty; Velopharyngeal insufficiency; Hypernasal speech.

### 108. Lack of Significant Estrogen and Progesterone Receptor Expression in Nasal Telangiectasias in Hereditary Hemorrhagic Telangiectasia: an Immunohistochemical Analysis

Behfar Eivazi, Jochen A. Werner, Marion Roessler, Hesham Negm and Afshin Teymoortash

*Acta Oto-Laryngologica*, 132: 86-89 (2012) IF: 1.084

This immunohistochemical study of estrogen and progesterone receptors could not confirm a significant expression in nasal telangiectasias. Thus, a specific effect of these hormones or anti-hormone therapy on malformed nasal vessels has to be questioned and only offered under strict clinical control.

**Objective:** the efforts to control recurrent epistaxis in hereditary hemorrhagic telangiectasia (HHT) using alternative methods are very intense. Hormone or anti-hormone therapy has frequently been postulated and the reported results are controversial.

Therefore it was important to find an explanation regarding a possible impact of hormonal therapies by immunohistochemical evaluation of progesterone and estrogen receptor expression on nasal telangiectasias of affected patients.

**Methods:** Tissue samples of nasal mucosa with evidence of telangiectasias from 14 patients with HHT were analyzed for the expression of progesterone and estrogen receptors on the nuclei of endothelial cells of the malformed vessels using immunohistochemistry.

**Results:** Progesterone receptors were not detected in any of the cases and only two cases showed a weak expression of estrogen receptors with an immunoreactive score of 2/12.

**Keywords:** Osler'S disease; Hht; Hormone receptors; Epistaxis; Estrogen; Progesterone.

### 109. Congenital Cholesteatoma of the Infratemporal Fossa with Congenital Aural Atresia and Mastoiditis: A Case Report

Mosaad Abdel-Aziz

*Bmc Ear, Nose and Throat Disorders*, 12 ( 6): 2- 4 (2012)

Congenital cholesteatoma may be expected in abnormally developed ear, it may cause bony erosion of the middle ear cleft and extend to the infratemporal fossa. We present the first case of congenital cholesteatoma of the infratemporal fossa in a patient with congenital aural atresia that has been complicated with acute mastoiditis.

**Case presentation:** A sixteen year old Egyptian male patient presented with congenital cholesteatoma of the infratemporal fossa with congenital aural atresia complicated with acute mastoiditis. Two weeks earlier, the patient suffered pain necessitating hospital admission, magnetic resonance imaging revealed a soft tissue mass in the right infratemporal fossa. on presentation to our institute, Computerized tomography was done as a routine, it proved the diagnosis of mastoiditis, pure tone audiometry showed an air-bone gap of 60 dB. Cortical mastoidectomy was done for treatment of mastoiditis, removal of congenital cholesteatoma was carried out with reconstruction of external auditory canal. Follow-up of the patient for 2 years and 3 months showed a patent, infection free external auditory canal with an air-bone gap has been reduced to 35db. One year after the operation; MRI was done and it showed no residual or recurrent cholesteatoma.

**Conclusions:** Congenital cholesteatoma of the infratemporal fossa in cases of congenital aural atresia can be managed safely even if it was associated with mastoiditis. It is an original case report of interest to the speciality of otolaryngology.

**Keywords:** Congenital Cholesteatoma; Congenital Aural Atresia; Mastoiditis; Infratemporal Fossa.

### 110. Characteristics of Auditory Brainstem Response Latencies in Children with Autism Spectrum Disorders

Abeir Osman Dabbous

*Audiological Medicine, Uk.*, 122-131 (2012)

Hypersensitivity to loud sounds is commonly noticed in children with autism spectrum disorders.

**Objective and methods:** This was a cross-sectional study that included 50 children, ages ranging from 1.5 to 3.33 years, divided

into a study group of 25 autistic children with normal hearing and a control group of 25 normal hearing healthy children. the aim of this research was to the assess any abnormality in the loudness growth function objectively using auditory brainstem response (ABR), as well as to detect any ABR abnormalities in normal hearing autistic children with delayed language development.

**Results:** Forty-four percent of normal hearing autistic children showed a lower threshold compared to healthy controls.

They also showed significantly delayed wave III, but within-normal wave V, and consequently a longer inter-peak interval (IPI): I III and shorter IPI: III V, reflecting retro-cochlear dysfunction that may be related to their difficulty in communication. the mean slope of wave V latency intensity curve did not differ between autism and their controls, reflecting normal loudness growth. Male autistic children showed statistically significant longer latencies of wave V than females except at high intensities, but there was no statistically significant difference between them with regard to the mean slope of wave V latency intensity curve.

**Conclusion:** Autistic children with normal hearing showed a within-normal loudness growth indicating that their abnormal reactions to sounds may either be phonophobia, an efferent system affection or a more central pathology that needs further evaluation. They also showed a retro-cochlear dysfunction that may be related to their difficulty in communication.

**Keywords:** Auditory brainstem response; Autism; Hypersensitivity; Latency-intensity function; Loudness.

### 111. Does Reduced Frequency Selectivity in Children with Mild to Moderate Sensorineural Hearing Loss Affect Frequency Discrimination in Mismatch Negativity and Pitch Pattern Sequence Tests?

Mohamed Ibrahim Shabana, Amani Ahmed Shalaby, Abeir Osman Dabbous and Abir Abd-El-Meneim Emara

*Hearing, Balance and Communication*, 10 (1): 40-49 (2012)

Sensorineural hearing loss (SNHL) results in reduced sensitivity, abnormal growth of loudness, reduced frequency selectivity and reduced temporal resolution (Edwards,2003). Our aim was to study frequency discrimination abilities in children with SNHL using the psychophysical Pitch Pattern Sequence Test (PPST) and an electrophysiological measure, the Mismatch Negativity Test (MMN).

**Methods:** This is a cross-sectional study that included 90 children, ages ranging from 6 - 12 years, divided into a study group of 60 children with mild to moderate SNHL and a control group of 30 normal hearing children. Both groups were subdivided into 3 subgroups according to age.

**Results:** Subgroups of children with SNHL showed statistically significant poorer scores on the PPST than their well-matched controls. Although MMN can be elicited in children with mild to moderate degree of SNHL, its latency was prolonged. the older control subgroups did not show any statistically significant better scores on the PPST; MMN latencies were longer with increased duration of hearing loss. Degree of hearing loss, gender and side had no effect on PPST or MMN. There was no statistically significant correlation between the results of the PPST and MMN.

**Conclusion:** SNHL affects frequency discrimination abilities demonstrated in poor scores on the PPST and prolonged MMN latency.



**Keywords:** Mismatch negativity; Pitch pattern test; Frequency discrimination; Sensorineural hearing loss.

### 112. Mucoepidermoid Carcinoma of the Tongue in a Child

Mosaad Abdel-Aziz

*Int. J. of Pediatric Otorhinolaryngology Extra*, 7: 6-8 (2012)

Tongue base tumors are not common, they are mostly malignant and although the rarity of mucoepidermoid carcinoma of tongue base, it constitutes more than 50% of malignant lesions of salivary glands in this region. In this report, we present a 15-year old girl with mucoepidermoid carcinoma of tongue base with discussion of histopathological types of the tumor and its management.

**Keywords:** Tongue base; Mucoepidermoid carcinoma; Minor salivary gland tumors; Pediatric malignancy.

### 113. Medicine and Otorhinolaryngology in Ancient Egypt

Hesham Negm

*Xi Apo Manual Of Pediatric Otorhinolaryngology*, (2012)

Medicine has always been one of the most honorable professions throughout history. It took different forms and types according to the needs in each time. (Magic, Religion...) Medicine was advanced and physicians acquired a highly respectable position in ancient Egypt. Because the Egyptians believed in the after life, they did every effort to preserve the human body in a good condition, by medical and surgical measures during life, and by mummification after death. This medical knowledge continued to grow and develop till the Hellenistic era when Alexandria with its famous library became the center of science and education in the ancient world. Imhotep, Hesi-Re, and Ny Ankh Re were among the most famous Ancient Egyptian physicians. The medical papyri are the first medical texts, date from late 12th to 20th Dynasty (1993-1090B.C). The Ebers, and Edwin Smith are the most important. Edwin Smith papyrus describes many Otorhinolaryngological conditions among other surgical cases. The 1st convincing evidence of successful intentional mummification occurs in the 4th dynasty, in the Giza tomb of Queen Hetep Heres (the mother of Khufu). The 2 crucial steps to arrest the decomposition of the body were evisceration and dehydration of the tissues. Recent studies using multi slice CT scanner with 3D reformatting, and volume rendering technique, proved that in most of the mummies of the 18th dynasty the brain was not taken out, except the mummy of Tutankhamun, where broken bones and a hole were found in the base of the skull.

*Dept. of Emergency Medicine*

### 114. Molecular Imaging of Early $\alpha_v\beta_3$ Integrin Expression Predicts Long-Term Lv Remodeling after Myocardial Infarction in Rats

Hossam M. Sherif, Antti Saraste, Stephan G. Nekolla, Eliane Weidl, Sybille Reder, Arne Tapfer, Martina Rudelius, Takahiro Higuchi, Rene M. Botnar, Hans-Jürgen Wester and Markus Schwaiger

*J. Nucl Med*, 53 (2): 318-323 (2012) IF: 6.381

$^{18}\text{F}$ -galacto-RGD ( $^{18}\text{F}$ -RGD) is a PET tracer binding to  $\alpha_v\beta_3$  integrin receptors that are upregulated after myocardial infarction

(MI) as part of the healing process. We studied whether myocardial  $^{18}\text{F}$ -RGD uptake early after MI is associated with long-term left-ventricle (LV) remodeling in a rat model.

**Methods:** Wistar rats underwent sham operation (n = 9) or permanent coronary ligation (n = 25). One week after MI, rats were injected with  $^{18}\text{F}$ -RGD to evaluate  $\alpha_v\beta_3$  integrin expression using a preclinical PET system. In the same rats, LV volumes and defect size were measured 1 and 12 wk after MI by  $^{13}\text{N}$ -ammonia PET and MRI, respectively.

**Results:** One week after MI,  $^{18}\text{F}$ -RGD uptake was increased in the defect area as compared with the remote myocardium of MI rats or sham-operated controls (percentage injected dose per cubic centimeter,  $0.20 \pm 0.05$  vs.  $0.06 \pm 0.03$  and  $0.07 \pm 0.04$ ,  $P < 0.001$ ). At this time,  $^{18}\text{F}$ -RGD uptake was associated with capillary density in histologic sections.

Average  $^{18}\text{F}$ -RGD uptake in the defect area was lowest in the rats demonstrating greater than 20% relative increase in the LV end-diastolic volume from 1 to 12 wk (percentage injected dose per centimeter cubed,  $0.15 \pm 0.07$  vs.  $0.21 \pm 0.05$ ,  $P < 0.05$ ). In a multivariable logistic regression analysis, low  $^{18}\text{F}$ -RGD uptake was a significant predictor of increase in end-diastolic volume ( $r = 0.51$ ,  $P < 0.05$ ).

**Conclusion:** High levels of  $^{18}\text{F}$ -RGD uptake in the perfusion defect area early after MI were associated with the absence of significant LV remodeling after 12 wk of follow-up. These results suggest that  $\alpha_v\beta_3$  integrin expression is a potential biomarker of myocardial repair processes after MI and enables the monitoring of these processes by molecular imaging to derive possible prognostic information.

**Keywords:**  $^{18}\text{F}$ ; Galacto-Rgd; Pet; Lv Remodeling; Mri; Myocardial Infarction.

### 115. Diastolic Dysfunction in Septic Patients in Correlation with Renal Function

Sabry A. Omar, Mohamed Elshafey, Khalid Toema and Rania El-Hoseiny

*Life Science Journal*, 9 (1): 572-579 (2012) IF: 0.073

Septic shock remains one of the most challenging medical conditions, with increasing incidence over the last years. One of the most important features of sepsis is myocardial dysfunction and renal impairment.

**Objective:** is to evaluate diastolic dysfunction in patient with septicemia and detect its relation to renal impairment in this subset of patients.

**Methods:** the study was conducted on 40 patients diagnosed to have various degrees of systemic sepsis admitted to Intensive Care Unit of Mansoura International Specialized Hospital. After exclusion of patients with structural heart diseases and renal impairment, each patient was subjected to the following: Full clinical evaluation, complete laboratory investigation -including serum troponin I & creatinine levels- and echocardiographic evaluation with measuring of left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), calculation of LVEF & assessment of diastolic function measuring mitral annulus E/A ratio, E deceleration time (DT) & isovolumic relaxation time (IVRT) Results A non-randomized non-controlled prospective study done between July 2009 to August 2010. The study included 40 patients, 24 males & 16 females, with mean age of  $62 \pm 12$ . Renal impairment (defined as serum creatinine  $> 1.4$  mg/dl following a normal creatinine level on admission associated with oliguria  $< 0.5$  ml/kg/6hours) was

present in 78% (31 pts). These pts had significantly shorter IVRT & shorter DT than those with normal renal function. LVEDD and LVESD were significantly larger & LVEF was significantly lower in pts with renal impairment. Renal impairment was associated with significantly lower hemoglobin, higher liver enzymes, higher bilirubin and higher troponin levels. Eighteen patients had SIRS & sepsis (group A, 45%) & 22 had septic shock (group B, 55%). Patients with septic shock showed significantly higher creatinine & significantly higher troponin level than pts with sepsis. Regarding ventricular functions, LVEDD and LVESD were significantly larger & LVEF was significantly lower in septic shock pts than pts with SIRS & sepsis. In group B, both DT and IVRT were significantly shorter than group A. Overall mortality was 55% (100% in septic shock versus 0% in pts with SIRS & sepsis).

**Conclusion:** the presence of renal impairment was associated with a more severe form of diastolic & systolic dysfunction in septic patients. Septic shock patients, showed larger ventricular dimensions and significant systolic and diastolic dysfunctions than patients with sepsis. Higher evidence of myocardial injury in septic shock.

**Keywords:** Diastolic Dysfunction; Septic Patients; Renal Function.

#### Dept. of Endemic

### 116. Ns5a Sequence Heterogeneity of Hepatitis C Virus Genotype 4A Predicts Clinical Outcome of Pegylated-Interferon-Ribavirin Therapy in Egyptian Patients

Ahmed El-Shamy, Ikuo Shoji, Wafaa El-Akel, Shymaa E. Bilasy, Lin Deng, Maissa El-Raziky, Da-peng Jiang, Gamal Esmat and Hak Hotta

*J Clin Microbiol*, 50 (12): 3886-3892 (2012) IF: 4.153

Hepatitis C virus genotype 4 (HCV-4) is the cause of approximately 20% of the 180 million cases of chronic hepatitis C in the world. HCV-4 infection is common in the Middle East and Africa, with an extraordinarily high prevalence in Egypt. Viral genetic polymorphisms, especially within core and NS5A regions, have been implicated in influencing the response to pegylated-interferon and ribavirin (PEG-IFN/RBV) combination therapy in HCV-1 infection. However, this has not been confirmed in HCV-4 infection. Here, we investigated the impact of heterogeneity of NS5A and core proteins of HCV-4, mostly subtype HCV-4a, on the clinical outcomes of 43 Egyptian patients treated with PEG-IFN/RBV. Sliding window analysis over the carboxy terminus of NS5A protein identified the IFN/RBV resistance-determining region (IRRDR) as the most prominent region associated with sustained virological response (SVR). Indeed, 21 (84%) of 25 patients with SVR, but only 5 (28%) of 18 patients with non-SVR, were infected with HCV having IRRDR with 4 or more mutations (IRRDR $\geq$ 4) (P=.0004). Multivariate analysis identified IRRDR $\geq$ 4 as an independent SVR predictor. The positive predictive value of IRRDR $\geq$ 4 for SVR was 81% (21/26; P=.002), while its negative predictive value for non-SVR was 76% (13/17; P=.02). On the other hand, there was no significant correlation between core protein polymorphisms, either at residue 70 or at residue 91, and treatment outcome. In conclusion, the present results demonstrate for the first time that IRRDR $\geq$ 4, a viral genetic heterogeneity, would be a useful predictive marker for SVR in HCV-4 infection when treated with PEG-IFN/RBV.

**Keywords:** Ns5a Sequence; Hcv; Pegylated Interferon; Ribavirin; Hcv4a.

### 117. Tamoxifen Alleviates Hepatitis C Virus-Induced Inhibition of Both Toll-Like Receptor 7 and Jak-Stat Signalling Pathways in Pbmcs of Infected Egyptian Females

I. O. Fawzy, M. Negm, R. Ahmed, G. Esmat, N. Hamdi and A. I. Abdelaziz

*J Viral Hepatitis*, (2012) IF: 4.088

Hepatitis C virus (HCV) is a major health concern in Egypt being highly prevalent among Egyptians. The two genders experience different responses to HCV infection and show variations in response to interferon (IFN)-based therapy that may be attributed to sex hormones. We previously demonstrated the suppressive effect of 17 $\beta$ -estradiol (E2) on the expression of the IFN-stimulated gene MxA in HCV-infected peripheral blood mononuclear cells (PBMCs). The selective oestrogen receptor (ER) modulator Tamoxifen has been shown to have an antiviral effect against HCV, but its effect on the host immune response is unknown. We investigated the effect of Tamoxifen on the IFN signaling pathways in PBMCs of HCV-infected Egyptian females. We pooled PBMCs and treated them with exogenous interferon alpha (IFN $\alpha$ ) or the TLR7 ligand, Imiquimod, and quantified the relative expressions of MxA using RTqPCR. Studies were performed with and without Tamoxifen pretreatment. Pretreatment with Tamoxifen reversed the suppressive effect of E2 on the JAK-STAT pathway in IFN $\alpha$ -treated PBMCs as indicated by a significant increase in MxA expression (P = 0.05\*). Tamoxifen pretreatment also significantly upregulated MxA expression in Imiquimod-treated PBMCs (P = 0.0011\*\*), an effect not ascribed to ER blocking nor to an upregulation in TLR7 expression because Tamoxifen showed no potentiating effect on the expression of the receptor. In conclusion, our findings reveal that Tamoxifen has immunomodulatory effects whereby it enhances the host IFN signalling pathways during HCV infection.

**Keywords:** Females; Hepatitis C virus; Interferon; Jak-stat.

### 118. The Future for the Treatment of Genotype 4 Chronic Hepatitis C

G. Esmat, M. El Raziky, M. El Kassas, M. Hassany and M.E. Gamil

*Liver International*, 146-150 (2012) IF: 3.824

Hepatitis C virus genotype 4 (HCV-4) is the most common type of hepatitis C virus (HCV) in the Middle East and Africa, in particular Egypt. Since the development of new protease inhibitors, the response of HCV-4 to the standard regimen of treatment (pegylated interferon/ribavirin) lags behind other genotypes and has become the most resistant type to treat. The development of therapeutic strategies for all patients with HCV-4 whether they are naïve, have experienced a virological breakthrough, are relapsers or non-responders is still a considerable challenge. New types of interferon (Consensus Interferon, Y-shaped, Albinterferon...) and new direct action antiviral drugs (Nitazoxanide, Vit.D, other) may improve the treatment of patients with HCV-4. The IL28B CC polymorphism may be associated with sustained virological response.

Introduction Hepatitis C virus (HCV) is the cause of a significant proportion of cases of chronic liver disease, hepatocellular carcinoma (HCC) and deaths from liver disease, and is the most common indication for liver transplantation (LTx). Projections based on the current prevalence of infection and anticipated rates of progression suggest that morbidity and mortality as well as the costs of medical care for HCV infection will increase alarmingly in the next two decades (1). Six major genotypes (1–6) and more than 50 subtypes of HCV have been described (2). In general, HCV genotype 4 (HCV4) is predominant in Africa and the Middle East (3). In Egypt, where hepatitis C is highly endemic (up to 15% of the population), 91% of the patients are infected with HCV (4). Numerous studies have confirmed that HCV4 is the predominant HCV.

**Keywords:** Genotype 4; Hcv; IL28b polymorphism.

### 119. Non-Invasive Prediction of Hepatic Fibrosis in Patients with Chronic Hcv Based on the Routine Pre-Treatment Workup

Marwa Khairy, Mahassen Abdel-Rahman, Maissa El-Raziky, Wafaa El-Akel, Naglaa Zayed, Hany Khatib and Gamal Esmat

*Hepatitis Monthly*, 12 (11): 1-6 (2012) IF: 2.19

**Background:** Hepatic fibrosis is an inclusion indicator for treatment and a major independent predictor of treatment response in patients with chronic hepatitis C. Liver biopsy, considered as the 'gold standard' for evaluating liver fibrosis, has carried some drawbacks. Currently used noninvasive predictors of fibrosis are considered less accurate than liver biopsy.

**Objectives:** Our aim was to assess noninvasive predictors of fibrosis in patients with chronic hepatitis C using the routine laboratory pre-treatment workup. Patients and Methods: Cross sectional study including 4289 Egyptian patients with chronic hepatitis C were assessed for the need to interferon and ribavirin therapy. Routine pre-treatment workup and reference needle liver biopsy were performed. FIB-4 index, APRI and modified APRI scores were validated. Patients were divided into two groups, first with no or minimal fibrosis, and second with moderate and marked fibrosis using the Metavir score.

**Results:** Multivariate logistic regression analysis showed that age, body mass index, aspartate aminotransferase, alpha fetoprotein, platelets count, FIB-4 index, APRI and modified APRI score were significant independent predictors of fibrosis. Age >43 years, aspartate aminotransferase >47U/L, platelets <205~103/mm<sup>3</sup>, and alpha fetoprotein >2.6 ng/ml had the highest cutoff points in receiver operator characteristic curves. Taking into account the four variables together; the presence of 2 variables is associated with moderate and advanced fibrosis with a sensitivity of 0.81, specificity of 0.5, positive predictive value of 0.53 and negative predictive value of 0.79. FIB-4 index represented the best performing receiver operator characteristic curve for diagnosing moderate and marked fibrosis among other independent factors with a sensitivity of 0.74, specificity of 0.6, positive predictive value of 0.56 and negative predictive value of 0.76.

**Conclusions:** Chronic HCV pre-treatment routine work up and composite fibrosis scores are good noninvasive predictor of liver fibrosis and can be used as an alternative method to invasive liver biopsy without adding more financial expenses to the treatment.

**Keywords:** Hepatitis C; Liver Cirrhosis; Fibrosis.

### 120. Association of IL 28B Snp with Progression of Egyptian Hcv Genotype 4 Patients to End Stage Liver Disease

Mostafa K. El-Awady, Lotiaf Mostafa, Ashraf A. Tabll, Tawfeek H. Abdelhafez, Noha G Bader El Din, Naglaa Zayed, Reem El Shenawy, Yasmin El Abd, Reham M. Hasan, Hosam Zaghlol, Hesham El Khayat and Ashraf O. Abdel Aziz

*Hepatitis Monthly*, 12(4): 272-277 (2012) IF: 2.19

IL28B single nucleotide polymorphisms (SNPs) play important roles in the management of hepatitis C virus (HCV) infections and are strongly associated with spontaneous and treatment-induced HCV clearance.

**Objectives:** in the present study, the association between IL28B variants and the progression of HCV infection in Egyptian patients infected with type 4a virus will be examined. Patients and Methods: Frequencies of the protective genotype C/C of SNP, rs12979860 were determined in healthy subjects, spontaneous resolvers, and chronic HCV type 4 patients with low F scores and in patients with end stage liver disease (ESLD). This study included a total of 404 subjects. Patients infected with HCV type 4a (n = 304) were divided into; chronic hepatitis C (CHC) with low F scores (CHC, n = 110), end stage liver disease (n = 110), liver cirrhosis (LC) (n = 35) and hepatocellular carcinoma (HCC) patients (n = 75), spontaneous resolvers of HCV infection (n = 84) were also included. A healthy group representing the Egyptian population (n = 100) was also included in the genotyping of IL28B. The later was typed via a polymerase chain reaction based restriction fragment length polymorphism (PCR-RFLP) assay analysis on purified genomic DNA extracted from all individuals.

**Results:** A significant increase (P < 0.0005) was observed in frequencies of IL-28B rs12979860 C/C genotypes in the healthy population, than in the CHC, LC and HCC groups (C/C = 48%, 13%, 0% and 0% respectively). On the other hand the C/C genotype was significantly higher (P < 0.0005) in spontaneous resolvers than in healthy subjects. A comparable significant increase in the frequency of C/T allele accompanied by mild elevation of T/T allele frequency, were detected along the progression towards ESLD.

**Conclusions:** Genotype C/C is associated with viral clearance during acute infection. The sharp decline in the C/C genotype from healthy to CHC subjects and the total absence of the C/C genotype in ESLD suggests a central role of this genotype against HCV disease progression.

**Keywords:** Hepatitis C; Interleukin 28B polymorphism; Genetic liver; Cirrhosis carcinoma; Hepatocellular.

### 121. Serum Mannan-Binding Lectin in Egyptian Patients with Chronic Hepatitis C: its Relation to Disease Progression and Response to Treatment

Serag Esmat, Dalia Omran, Gihan A. Sleem and Laila Rashed

*Hepatitis Monthly*, 12 (4): 259-264 (2012) IF: 2.19

Chronic hepatitis C virus (HCV) infection is a major worldwide public health problem. Egypt has the highest prevalence of adult HCV infection in the world, averaging 15%–25% in rural communities. Mannan-binding lectin (MBL) is a liver-derived pluripotent serum lectin that plays a role in the innate immune system of the host. It is an acute-phase protein that is involved in the activation of the classical complement pathway. MBL may play a defensive role in HCV infection.

**Objectives:** to investigate the relationship between MBL concentration and HCV infection in Egyptian patients suffering chronic hepatitis C.

**Patients and Methods:** Serum samples obtained from 35 Egyptian hepatitis C patients and 30 normal controls were assayed for MBL. MBL concentrations were correlated to disease characteristics and treatment response.

**Results:** Serum MBL was significantly higher in HCV patients than in controls, but no relationship was found between MBL concentration and disease progression in terms of hepatic fibrosis and inflammation.

Responders to interferon (INF)-based therapy had significantly higher serum MBL than non-responders.

**Conclusions:** We found no association between serum MBL concentration and progression of HCV related liver disease. Responders to INF-based therapy had significantly higher serum MBL than non-responders.

**Keywords:** Hepatitis C; Interferon; Mannan; Egypt.

### 122. Health-Related Quality of Life in Egyptian Patients after Liver Transplantation

Mahasen Mabrouk, Gamal Esmat, Ayman Yosry, Magdy El-Serafy, Wahid Doss, Naglaa Zayed, Medhat El-Zahhar, Sally Awny and Ashraf Omar

*Annals of Hepatology*, 11 (6): 882-890 (2012) IF: 1.811

**Introduction-Aim:** Health-Related Quality of Life (HRQOL) has become an important focus of patient care and clinical outcomes research with the improvement in patient and graft survival after liver transplantation (LT). The current study was designed to evaluate the post-transplant HRQOL profiles using the Liver Disease Quality of Life 1.0 (LDQOL 1.0) Questionnaire and demonstrate the possible effect of peri-transplant clinical covariates on these profiles.

**Material and methods:** Participants included pre-transplant group (waiting-list patients n = 50) and post-transplant group (mean 5 ± 4 years after deceased or living donor LT n = 103) who were recruited from 3 specialized centers in Egypt. We applied the LDQOL 1.0 questionnaire; a 111-item containing the Short Form-36 version 2.0 (SF-36v2) as a generic component supplemented by 75 disease-specific items. The etiology of cirrhosis, co-morbidities, model for end-stage liver disease (MELD), Child-Pugh class and post-operative complications were analyzed.

**Results:** All recipients had significant higher HRQOL scores than patients in waiting-list using both questionnaire components. Recipients with pre-LT MELD ≥ 15, Child-Pugh class C, history of hepatocellular carcinoma (HCC) demonstrated low HRQOL scores. Recipients without post-operative surgical complications had a statistically better HRQOL using the disease-specific, but not the SF-36v2 component. On the other hand, both components demonstrated non-significant lower scores in recipients with rejection episodes, cytomegalovirus (CMV) infection and hepatitis C recurrence had compared to those without medical complications.

**Conclusion:** Generally HRQOL improves dramatically after LT as assessed by LDQOL questionnaire. Moreover, combined questionnaires can provide accurate information about the possible impaired HRQOL post-LT due to pre-transplant disease severity and post-operative complications.

**Keywords:** Ldqol 1.0 questionnaire; Liver transplant recipients; Ldlt-Sf-36-Egypt.

### 123. Hla Tissue Typing Has no Effect on the Outcome of Patients Undergoing A Living-Donor Liver Transplant: A Single-Center Experience in Egypt

Ayman Yosry, Mohamed Said, Gamal Esmat, Magdy Al-Serafy, Ashraf Omar, Wahid Doss, Dalia Omran, Yasmin Saad, Sanna Kamel, Akram Abdel-Bary, Yaser Hatata and Adel Hosny

*Exp Clin Transplant*, 2: 136-140: 136-140 (2012) IF: 0.813

To analyze the effect of human leukocyte antigen tissue typing on outcome of livedonor liver transplant.

**Materials and Methods:** Fifty recipients underwent live-donor liver transplant in the Dar Al-Fouad Hospital in Egypt and were retrospectively evaluated. Patients were classified into 2 groups: those with human leukocyte antigen +ve, and those with human leukocyte antigen -ve and donors. Hepatitis C virus-related end-stage liver disease was the main indication for transplant. Demographic data, preoperative laboratory data, results of human leukocyte antigen tissue typing, Child score, model for end-stage liver disease score, graft/recipient weight-ratio, ischemia times, surgical complications, postoperative laboratory data, liver biopsy, immunosuppression, and pulse steroids were collected. Graft and patient survivals were studied using Kaplan-Meier curves.

**Results:** the mean model end-stage liver disease score was 18 ± 3.61 in group 1 and 17.73 ± 3.72 in group 2, with no significant difference. Graft/recipient weight ratio, ischemia times, and postoperative complications showed P = NS. Cyclosporine and tacrolimus were used in 5/9, 8/41, and 4/9 in group 1, and 32/41 in group 2 (P = NS). Rejection and pulse steroids were reported in 3/9 and 12/41 of group 1, and 3/12 and 11/41 of group 2 (P = NS). Hepatitis C virus-recurrence was diagnosed in 5/9 of patients (55%) and 8/41 of patients (29.5%) in groups 1 and 2 (P < .05). No statistical difference was found regarding mortality; 5-year patient and graft survival was 35/50 (70% in group 1 [human leukocyte antigen +ve]), 7/9 (77.8%), and 28/41 in group 2 (68.3%) (human leukocyte antigen -ve).

**Conclusions:** Positive human leukocyte antigen typing before live-donor liver transplant has no effect on the incidence of postoperative complications, rejection episodes, and patient or graft survival. Recipients with positive human leukocyte antigen typing may have increased risk of hepatitis C virus-recurrence after live-donor liver transplant.

**Keywords:** Hla; Liver transplantation; Outcome.

### 124. The Initial Experience of Safety and Efficacy of Argon Plasma Coagulation (APC) in the Primary Prevention of Variceal Bleeding

I. Hamza, M. Mahmoud and S. Labib

*Arab Journal of Gastroenterology*, 13: 125-129 (2012)

The well-known complications of variceal bleeding together with the high mortality rate mandate effective prophylaxis. Because of the intolerance, failure of response and lack of compliance related to B blockers and because of the high incidence of variceal recurrence after endoscopic variceal ligation (EVL), other alternatives should be investigated. As APC provides coagulation at a shallow depth, it has been considered an ideal procedure to promote mucosal fibrosis for oesophageal varices. This study aims to investigate the safety and effectiveness of APC

application to the oesophagus post-variceal obliteration in an attempt to decrease variceal recurrence and bleeding, as compared to EVL.

**Patients and methods:** This study included 60 patients with chronic liver disease and portal hypertension referred to the Gastrointestinal Endoscopy Unit, Kasr Al-Aini Hospital, Cairo University, during the period from August 2008 till January 2010. Patients had to have large-sized varices (F3), without history of bleeding, portal hypotensive drugs or intervention. Patients were allocated into either group I that included 30 patients for whom EVL was performed and sequentially followed by one session of APC or group II that included 30 patients for whom EVL alone was done. Patients underwent surveillance endoscopy at 3 and 6 months to evaluate variceal recurrence (F1 or more).

**Results:** Both groups were comparable in terms of the demographic features, hepatic functional reserve and endoscopic findings. Post-APC, fever was reported in 6.7%, dysphagia in 3.3%, procedure-related bleeding in 0% and stricture in 3.3%. at 3 and 6 months follow-up, both groups were comparable in terms of variceal recurrence and none of the patients in both groups developed variceal bleeding.

**Conclusion:** Although, APC application to the oesophageal mucosa is a safe technique, its additive benefit in terms of variceal recurrence and re-bleeding is comparable to EVL alone. This is encountered when only a single session of APC is applied. A more beneficial effect of multiple sessions of APC awaits further studies.

**Keywords:** Argon Plasma Coagulation; Oesophageal Varices; Band Ligation.

### 125. Potent Inhibitory Effects of P7 Inhibitors on Genotype 4 Hcv-Infected Peripheral Blood Mononuclear Cells

Maged A. Saleh, Radwa Y. Mekky, Nada El-Ekiaby, Nabila Hamdi, Rasha Ahmed, Abdel Rahman Zekri, Gamal Esmat and Ahmed I. Abdelaziz

*Recent Patents on Biomarkers*, 2: 227-233 (2012)

Several patents were published for HCV p7 protein including a synthetic p7 model for drug design and screening of experimental compounds. Additionally, patents were published for identification and use of compounds as p7 inhibitors.

HCV p7 protein is a viral ion channel (viroporin) that was found to be crucial for viral production through facilitating assembly and release. Accordingly, targeting the protein is expected to inhibit these stages in the HCV lifecycle. p7 inhibitors displayed effectiveness against recombinant replicons of different HCV genotypes with genotype-dependant responses, but they were never tested on genotype 4 (GT-4). Our study focused on examining the effects of four p7 inhibitors; amantadine, rimantadine, N-nonyl-deoxyojirimycin (NN-DNJ) and hexamethylene amiloride (HMA) on HCV GT-4 for the first time which involves the majority of cases in Egypt and the Middle East-North Africa (MENA) region. HCV viral load was assessed after stimulation by p7 inhibitors for HCV-positive Peripheral Blood Mononuclear Cells (PBMCs) which are known to be extra-hepatic reservoirs for the virus. The compounds showed strong reduction of viral load without affecting cell viability in congruency with previous experimental work that alternatively used other HCV genotypes and cell lines.

**Keywords:** Amantadine; Genotype 4; Hepatitis C virus (Hcv); Hexamethylene amiloride (Hma); N-Nonyl-Deoxyojirimycin.

### 126. Repressed Induction of Interferon-Related Micrnas Mir-146a and miR-155 in Peripheral Blood Mononuclear Cells Infected with HCV Genotype 4

Nada El-Ekiaby, Nabila Hamdi, Mohamed Negm, Rasha Ahmed, Abdel Rahman Zekri, Gamal Esmat and Ahmed Ihab Abdelaziz

*Febs Open Bio* 2, 2: 179-186 (2012)

MicroRNAs regulate the expression of many genes and subsequently control various cellular processes, such as the immune response to viral infections mediated by type I interferon (IFN). In this study, the expression pattern of two interferon-related microRNAs, miR-146a and miR-155, was examined in healthy and HCV-genotype-4-infected peripheral blood mononuclear cells (PBMCs) using qRT-PCR. In contrast to other viral infections, the expression pattern was similar in both healthy and infected PBMCs.

This could be attributed to attenuation of IFN pathway by HCV, which was assessed by investigating the expression of MxA, an interferon-stimulated gene, that showed lower expression in HCV-infected PBMCs. To determine the site of interference of HCV in the IFN pathway, expression of both microRNAs was examined following stimulation of PBMCs with IFN- $\gamma$ 2a, an activator of the JAK/STAT pathway as well as with imiquimod, a toll-like receptor-7 (TLR-7) agonist that promotes interferon release. IFN stimulation induced the expression of miR-146a and miR-155 in HCV-infected and healthy PBMCs.

Stimulation with imiquimod led to a down-regulation of both microRNAs in infected PBMCs, while it increased their expression in healthy PBMCs, indicating that HCV might interfere with miR-146a and miR-155 expression at sites upstream of interferon release, specifically in the TLR-7 pathway. The pattern of expression of both miR-146a and miR-155 was very similar with a strong positive correlation, but showed no correlation to the patients' clinical or histopathological parameters or response to treatment.

In conclusion, HCV infection might repress the induction of miR-146a and miR-155 by interfering with TLR-7 signaling.

**Keywords:** Hcv; Pbmcs; Mir-146A ; Mir-155; Interferon; Tlr-7.

### 127. Treatment of Chronic HCV Genotype 4 Infection

G. Esmat, M. El Raziky, M. El-Kassas, M. Hassany and M. E. Gamil

*Current Hepatitis Reports*, (2012)

Hepatitis C virus genotype 4 (HCV4) is the most common type of hepatitis C virus (HCV) in the Middle East and Africa, in particular Egypt. Treatment with pegylated interferon and Ribavirin is still the standard regimen of care with overall response ranging between 50 and 60 %. New types of interferon (Y-shaped, Reiferon Retard,...), new DAAD (protease inhibitors, polymerase inhibitors, NS5A inhibitors....), and many off label drugs (Nitazoxanide, Vit.D...) may improve the treatment outcome of patients with HCV-4.

**Keywords:** Hcv4; Pegylated interferon; New interferon Molecule; Daat; Middle east.

**Dept. of Forensic & Toxicology**

**128. Abusing Female Children by Circumcision is Continued in Egypt**

Abeer Ahmed Zayed and Abla Abdelrahman Ali

*Journal of Forensic and Legal Medicine*, 19 (2012): 196-200 (2012) IF: 1.098

Female circumcision is a frank picture of female child abuse that is practised widely in many countries especially in Africa. This procedure is considered a fundamental violation of human rights. the procedure is expected to be declining in Egypt in response to the recent medicolegal litigation in 2007. the aim of this study is to record the prevalence of female circumcision in 2010, in the region of Cairo and Giza, seeking to show if there is difference in the practice after the change in the law and banning of the procedure. A formatted questionnaire for 244 female volunteers was conducted. Statistical analysis revealed that 63.9% of the sample had been victimised by circumcision. the mean age of circumcision was 10.846 1.98 years. Circumcision took place at victim's home in 56.5%, private clinics in 38.5% or at hospitals in 5%. the procedure was performed by medical personnel in the majority of cases. the motivation behind the practice was primarily traditional beliefs (64.1%) followed by religious considerations (35.9%). Experienced complications were emotional trauma in 94.9%, haemorrhage in 33.3% and dysuria in 7.7%. Sexual problems were exclusively reported by the victimised subjects in 72.7% of sexually experienced subjects.

**Keywords:** Female circumcision; Egypt; Child abuse; Human rights.

**Dept. of Histology**

**129. Tissue Regeneration and Stem Cell Distribution in Adriamycin Induced Glomerulopathy**

Maha Baligh Zickri, Marwa Mohamed Abdel Fattah and Hala Gabr Metwally

*International Journal of Stem Cells*, 5 (2): 115-124 (2012)

Glomerulosclerosis develops secondary to various kidney diseases. It was postulated that adriamycin (ADR) induce chronic glomerulopathy. Treatment combinations for one year did not significantly modify renal function in resistant focal segmental glomerulosclerosis (FSGS). Recurrence of FSGS after renal transplantation impacts long-term graft survival and limits access to transplantation. the present study aimed at investigating the relation between the possible therapeutic effect of human mesenchymal stem cells (HMSCs), isolated from cord blood on glomerular damage and their distribution by using ADR induced nephrotoxicity as a model in albino rat.

**Methods and Results:** Thirty three male albino rats were divided into control group, ADR group where rats were given single intraperitoneal (IP) injection of 5 mg/kg adriamycin. the rats were sacrificed 10, 20 and 30 days following confirmation of glomerular injury. in stem cell therapy group, rats were injected with HMSCs following confirmation of renal injury and sacrificed 10, 20 and 30 days after HMSCs therapy. Kidney sections were exposed to histological, histochemical, immunohistochemical, morphometric and serological studies. in response to SC therapy multiple Malpighian corpuscles (MC) appeared with patent Bowman's space (Bs) 10 and 20 days following therapy. One month following therapy no remarkable

shrunken glomeruli were evident. Glomerular area and serum creatinine were significantly different in ADR group in comparison to control and SC therapy groups.

**Conclusions:** ADR induced glomerulosclerosis regressed in response to cord blood HMSC therapy. A reciprocal relation was recorded between the extent of renal regeneration and the distribution of undifferentiated mesenchymal stem cells.

**Keywords:** Mesenchymal stem cells; Cord blood; Glomerulosclerosis; Adriamycin.

**130. Effect of Stem Cell Therapy on Adriamycin Induced Tubulointerstitial Injury**

Maha Baligh Zickri, Somaya Zaghoul, Mira Farouk and Marwa Mohamed Abdel Fattah

*International Journal of Stem Cells*, 5 (2): 130-139 (2012)

It was postulated that adriamycin (ADR) induce renal tubulointerstitial injury. Clinicians are faced with a challenge in producing response in renal patients and slowing or halting the evolution towards kidney failure. the present study aimed at investigating the relation between the possible therapeutic effect of human mesenchymal stem cells (HMSCs), isolated from cord blood on tubular renal damage and their distribution by using ADR induced nephrotoxicity as a model in albino rat.

**Methods and Results:** Thirty three male albino rats were divided into control group, ADR group where rats were given single intraperitoneal (IP) injection of 5 mg/kg adriamycin. the rats were sacrificed 10, 20 and 30 days following confirmation of tubular injury. in stem cell therapy group, rats were injected with HMSCs following confirmation of renal injury and sacrificed 10, 20 and 30 days after HMSCs therapy. Kidney sections were exposed to histological, histochemical, immunohistochemical, morphometric and serological studies. in response to SC therapy, vacuolated cytoplasm, dark nuclei, detached epithelial lining and desquamated nuclei were noticed in few collecting tubules (CT). 10, 20 and 30 days following therapy. the mean count of CT showing desquamated nuclei and mean value of serum creatinine revealed significant difference in ADR group. the mean area% of Prussian blue+ve cells and that of CD105+ve cells measured in subgroup S1 denoted a significant increase compared to subgroups S2 and S3.

**Conclusions:** ADR induced tubulointerstitial damage that regressed in response to cord blood HMSC therapy.

**Keywords:** Mesenchymal stem cells; Cord blood; Tubular damage; Adriamycin.

**131. Effect of Stem Cell Therapy on Induced Diabetic Keratopathy in Albino Rat**

Maha Baligh Zickri, Nagwa Abdel Wahab Ahmad, Zeinab Mohamad El Maadawi, Yasmin Kamal Mohamady and Hala Gabr Metwally

*International Journal of Stem Cells*, 5 (1): 0-0 (2012)

Type 2 diabetes mellitus (DM) is a prevalent disorder. Diabetic keratopathy is a well-known ocular complication secondary to type 2 DM. Topical insulin application did not affect apoptosis and necrosis levels in corneal epithelium. Autologous cell transplantation is not a viable option for diabetic patients with bilateral limbal stem cell deficiency. the present study aimed at

assessing the possible effect of hemopoietic stem cell (HSC) therapy on induced diabetic keratopathy in albino rat.

**Methods and Results:** Fifteen male albino rats were divided into control group of 2 rats, diabetic group of 8 rats receiving single intraperitoneal (IP) injection of 50 mg/kg streptozotocin (STZ). 3 animals were sacrificed 6 weeks following confirmation of diabetes to confirm keratopathy and 5 rats were sacrificed 4 weeks following confirmation of keratopathy. SC therapy group included 5 rats injected with HSCs 6 weeks following confirmation of diabetes and sacrificed 4 weeks following SC therapy. Cord blood collection, stem cells isolation and labeling were performed. Eye specimens were subjected to histological, histochemical, immunohistochemical, morphometric and statistical studies. In diabetic group, the central cornea showed multiple cells with vacuolated cytoplasm and dark nuclei, focal epithelial discontinuity, reduced corneal thickness and less number of layers of corneal and conjunctival epithelia. In stem cell therapy group, few cells with vacuolated cytoplasm and dark nuclei were found in the corneal and conjunctival epithelia with more number of epithelial layers.

**Conclusions:** A definite ameliorating effect of HSC therapy was detected on diabetic keratopathy. The therapeutic cells were effective in limiting corneal epithelial changes.

**Keywords:** Hemopoietic stem cells; Diabetes; Cord blood; Keratopathy.

#### Dept. of Internal Medicine

### 132. Noninvasive Assessment of Hepatic Fibrosis in Egyptian Patients with Chronic Hepatitis C Virus Infection

Shawky Abdelhamid Fouad, Serag Esmat, Dalia Omran, Laila Rashid and Mohamed H Kobaisi

*World Journal of Gastroenterology*, 18 (23): 2988-2994 (2012)  
IF: 2.471

**Aim:** to evaluate the accuracy of specific biochemical markers for the assessment of hepatic fibrosis in patients with chronic hepatitis C virus (HCV) infection.

**Methods:** One hundred and fifty-four patients with chronic HCV infection were included in this study; 124 patients were non-cirrhotic, and 30 were cirrhotic. The following measurements were obtained in all patients: serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, total bilirubin, prothrombin time and concentration, complete blood count, hepatitis B surface antigen (HBsAg), HCVAb, HCV-RNA by quantitative polymerase chain reaction, abdominal ultrasound and ultrasonic-guided liver biopsy. The following ratios, scores and indices were calculated and compared with the results of the histopathological examination: AST/ALT ratio (AAR), age platelet index (API), AST to platelet ratio index (APRI), cirrhosis discriminating score (CDS), Pohl score, G?teborg University Cirrhosis Index (GUCI).

**Results:** AAR, APRI, API and GUCI demonstrated good diagnostic accuracy of liver cirrhosis (80.5%, 79.2%, 76.6% and 80.5%, respectively); P values were: < 0.01, < 0.05, < 0.001 and < 0.001, respectively. Among the studied parameters, AAR and GUCI gave the highest diagnostic accuracy (80.5%) with cutoff values of 1.2 and 1.5, respectively. APRI, API and GUCI were significantly correlated with the stage of fibrosis (P < 0.001) and the grade of activity (P < 0.001, < 0.001 and < 0.005, respectively), while CDS only correlated significantly with the

stage of fibrosis (P < 0.001) and not with the degree of activity (P > 0.05). In addition, we found significant correlations for the AAR, APRI, API, GUCI and Pohl score between the non-cirrhotic (F0, F1, F2, F3) and cirrhotic (F4) groups (P values: < 0.001, < 0.05, < 0.001, < 0.001 and < 0.005, respectively; CDS did not demonstrate significant correlation (P > 0.05).

**Keywords:** Age platelet index; Aspartate aminotransferase Platelet ratio index.

### 133. Can We Consider the Right Hepatic Lobe Size/Albumin Ratio A Noninvasive Predictor of Oesophageal Varices in Hepatitis C Virus-Related Liver Cirrhotic Egyptian Patients

Serag Esmat, Dalia Omarn and Laila Rashid

*Eur J Intern Med*, 23: 267-272 (2012) IF: 2

The current guidelines recommend the screening of all cirrhotic patients by endoscopy, but repeated endoscopic examinations are unpleasant for patients and have a high cost impact and burden on endoscopic units. The aim of this study is to evaluate the optimal liver lobe size/albumin ratio and to compare this ratio with spleen size, platelet count and platelet count/spleen diameter ratio as potential noninvasive predictors of oesophageal varices in hepatitis C virus (HCV)-related liver cirrhosis in Egyptian patients.

**Methods:** This prospective study included one hundred patients with HCV-related liver cirrhosis. All studied subjects underwent a detailed clinical examination, biochemical workup, upper gastrointestinal endoscopy and abdominal ultrasound. The platelet count/spleen diameter ratio and the right liver lobe/albumin concentration ratio for all patients were calculated.

**Results:** The 4 predictors demonstrated a high statistically significant correlation with the presence and grade of oesophageal varices (P values < 0.001). The platelet count/spleen diameter ratio had the highest accuracy, followed by the right liver lobe/albumin concentration ratio, spleen size and then platelet count.

**Conclusion:** The use of the studied noninvasive predictors, especially the platelet count/spleen diameter ratio and the right liver lobe/albumin concentration ratio, can help physicians by restricting the use of endoscopic screening only to patients presenting a high probability of oesophageal varices. This is especially useful in clinical settings where resources are limited and endoscopic facilities are not present in all areas. Such is the case in Egypt, where there is a large number of patients who require oesophageal screening for oesophageal varices.

**Keywords:** Noninvasive diagnosis of oesophageal varices; Right liver lobe size/albumin ratio; Platelet count/spleen diameter ratio; Oesophageal varices; Hcv related liver cirrhosis.

### 134. Outcome and Relapse Risks of Thrombotic Thrombocytopenic Purpura: an Egyptian Experience

Noha M. El-Husseiny, Hady Goubran, Hala M Fahmy, Nehad M. Tawfik, Heba Moustafa, Sherif N. Amin and Magdy El-kiaby

*Post Graduate Medical Journal*, 88: 433-436 (2012) IF: 1.939

**Background:** Thrombotic thrombocytopenic purpura (TTP) is a rare life-threatening disease. Plasma exchange has significantly decreased the mortality from this disease, which still tends to recur in a substantial proportion of patients. This study describes

the clinical spectrum and response to treatment and explores the risks of relapse in a cohort of patients.

**Methods:** Patients treated for TTP at the Clinical Haematology Unit, Cairo University, Egypt, between 2000 and 2008 were identified. Complete demographic, clinical history and full clinical examination, laboratory, treatment modalities and duration, and outcome data were collected and analysed. the follow-up duration was 24 months.

**Results:** 30 patients; 13 men (43%) and 17 women (57%) with a median age of 42 years were treated for 46 episodes of TTP. the median duration of disease onset to diagnosis for the first episode was 7 days. Twenty-three patients (76.66%) were diagnosed as idiopathic primary and seven patients (23.33%) were secondary TTP. Four patients died during the first 24 h. of the 26 patients, 22 (85.6%) achieved remission with an average of 7.55 plasma exchange sessions, Another nine patients had 25 relapses (mean 2.7). Splenectomy was performed in three patients (11.5%). the 24-month overall survival was 80%. the initial low platelet count and high LDH were the only two statistically significant relapse predictors.

**Conclusions:** the current results conform to the reported literature on the outcome of TTP. the very early mortality due to late referral highlights the need of education about the disease among primary healthcare providers.

**Keywords:** Thrombotic thrombocytopenic purpura.

### 135. Endogenous Soluble Receptor of Advanced Glycation End- Products (esRAGE) is Negatively Associated with Vascular Calcification in Non-Diabetic Hemodialysis Patients

Mohamed M. NasrAllah, Amal R. El- Shehaby, Noha A. Osman, Mona M. Salem, Amr Nassef and Usama A. A. Sharaf El Din

*Int Urol Nephrol*, 44 (4): 1193-1199 (2012) IF: 1.471

Advanced glycation end products (AGE) accumulate in CKD and may predispose to cardiovascular diseases by inducing inflammatory and oxidant stress in the vascular endothelium. soluble forms of the receptor for AGE (RAGE) may be protective against these effects by binding AGE in the soluble phase. accumulating evidence suggests a protective role of soluble RAGE against vascular calcification. this study investigates the association between endogenous soluble receptor RAGE and vascular calcification in hemodialysis patients.

**Methods:** we studied 65 non- diabetic hemodialysis patients on 3x4 h dialysis schedule and 19 normal controls. serum levels of esRAGE, hsCRP, parathormone, lipids, calcium and phosphorous were measured. Aortic calcification index ACI was measured using non- contrast CT of the abdominal aorta.

**Results:** aortic calcification was detected in 64 out of 65 hemodialysis patients. levels of esRAGE were lower among hemodialysis patients (278pg/ml,SD101.1) than in controls (443pg/ml, SD109) Pvalue= 0.001. ACI correlated negatively in stepwise multivariate analysis with esRAGE P= 0.002 and positively with hsCRP P= 0.0001

**Conclusion:** levels of esRAGE were low among hemodialysis patients and correlated negatively with ACI

**Keywords:** Vascular Calcification; RAGE; Inflammation; Ckd-Mbd; HsCRP; Advanced Glycation End Products.

### 136. Sleep-Related Breathing Disorders in Cerebrovascular Stroke and Transient Ischemic Attacks: A Comparative Study

ElKholy, Saly H.Amer, Hanan A. Nada, Mona M. Nada, Mona A. F. and Labib Amira

*J Clin Neurophysiol*, 29 (2): 194-198 (2012) IF: 1.451

Sleep-related breathing disorders are said to be common in patients with established cerebrovascular accidents. the aim of this study was to assess the frequency and characteristics of sleep-related breathing disorders in ischemic stroke and transient ischemic attacks. All patients were subjected to neurologic assessment, Berlin questionnaire (Arabic version), brain computed tomographic scan, and polysomnography along 6 to 8 hours overnight with special emphasis to apnea/hypopnea indices. All assessments were done for 30 patients who had stroke and transient ischemic attacks as well as 20 age- and sex-matched controls. Overall, 13.3% of patients had mild sleep apnea (apnea/hypopnea index, .5), 13.3% had moderate sleep apnea (apnea/hypopnea index, .15), and 34% had severe sleep apnea (apnea/hypopnea index, .30). the sensitivity and specificity of Berlin questionnaire for obstructive sleep apnea diagnosis were 55% and 100%, respectively, for mild sleep apnea, 56.3% and 85.7% for moderate sleep apnea, 66.7% and 83.3% for severe condition. Berlin questionnaire is a moderate sensitive but highly specific screening test for sleep apnea in cerebrovascular diseases. Those who scored high risk should consider polysomnography to specify the type and severity of apnea.

**Keywords:** Stroke; Tias; Berlin questionnaire; Polysomnogram; Apnea hypopnea index.

### 137. Role of Ultrasound Elastography in Prediction of Malignancy in Thyroid Nodules

Mona Mansor, Hussein Okasha, Serag Esmat, Ahmed Murad Hashem, Khaled A. Attia and Hossam El-din Hussein

*Endocr Res*, 37 (2): 67-77 (2012) IF: 0.969

Ultrasonography is considered useful to distinguish between solid and cystic thyroid nodules and to stratify a nodule's risk of cancer as low, medium, or high. Ultrasound (US) elastography has been applied to study the hardness/elasticity of nodules to differentiate malignant from benign lesions. Elastography possibly can solve the dilemma in reaching an accurate diagnosis for the cytologically known as indeterminate nodules.

**Aim:** to evaluate the sensitivity and specificity of US elastography in the diagnosis of thyroid cancer. Patients and methods. This prospective study included 40 patients. the total number of nodules was 46, they were all euthyroid. Laboratory investigations were done including FT3, FT4, and TSH to exclude hot nodules. Neck US, US elastography, and fine-needle aspiration were done to all patients, and US elastography scoring system from 1 to 4 was used.

**Results:** Four out of the 46 studied nodules were malignant. the ROC curve for elastography score (E-score) showed high sensitivity, specificity for the diagnosis of malignant thyroid nodules with a cut-off value of E-score 4 and high significance (p < 0.001), the area under curve was 0.92. the sensitivity was 75.0% and specificity was 100%. for E-score more than 2, the sensitivity was 100% and specificity was 85.37%.

**Conclusion:** US elastography can be used to increase both the sensitivity and the specificity of US for the detection of malignant



thyroid nodules, and so it seems to have great potential as a new tool for the diagnosis of thyroid cancer.

**Keywords:** Thyroid nodules; Thyroid cancer; Elastography.

### 138. A Comparative Study between Virtual Colonoscopy (Ct Colonoscopy) and Conventional Colonoscopy in Different Presentations of Suspected Colonic Disorders

Wael M. Aref; Ahmed El-Mazny and Farid G. Amin

*Life Science Journal*, 9 (3): 561-567 (2012) IF: 0.073

Virtual colonoscopy is a promising new modality for investigating suspected colonic disorders, it is relatively safe, can be done without sedation and in less time compared to conventional colonoscopy.

**Aim of this work:** to evaluate the application of virtual colonoscopy in different indications of conventional colonoscopy and compare between both procedures as regards sensitivity and specificity of both methods, putting the hypothesis that virtual colonoscopy can replace the conventional colonoscopy.

**Subjects and Methods:** a group of eighty two patients having different indications for colonoscopy were included; all patients underwent full medical history, examination and any needed investigations. Patients were scheduled to undergo both conventional and virtual colonoscopy on the same week, both endoscopist and radiologist were unaware of the other report.

**Results:** Both conventional and virtual colonoscopy detected colonic masses in 18 patients, colonic diverticulae in 5 patients and colonic strictures in 2 patients with no missed or false positive results with 100% sensitivity and specificity; and 100% positive and negative predictive values. Meaning that virtual colonoscopy was accurate in detection of masses, diverticulae and strictures. However detection of polyps by virtual colonoscopy was 88% sensitive and 77% specific with 3 missed polyps (small polyps) and 13 false positive polyps detected by virtual colonoscopy. Virtual Colonoscopy Could not detect any of the following.

**lesions:** angiodysplasia (2 patients), ulcerative colitis (without pseudo polyps) (3 patients), flat ulcers and non-specific colitis (11 patients), with a Sensitivity 0%.

**Conclusion:** Virtual Colonoscopy can be used in evaluation of patients presenting with constipation, weight loss or abdominal pain in whom colonoscopic examination was indicated (in these patients colonic lesions were masses, strictures and diverticulae, so virtual colonoscopy is sensitive in detecting these lesions).

But the use of virtual colonoscopy is limited in patients presenting with anemia and positive occult blood in stools, bleeding per rectum and chronic diarrhea (in these patients the colonic lesions were angiodysplasia, flat ulcers and non specific colitis, so virtual colonoscopy is not sensitive in detecting these lesions). Also, virtual colonoscopy is a good diagnostic tool for screening for colorectal carcinoma, however using the recent technology in virtual colonoscopy as new faster CT multi-slice machines with the least possible slice thickness in order not to miss a small lesion is recommended.

**Keywords:** Virtual colonoscopy; Conventional colonoscopy; Lower git symptoms; Colorectal carcinoma.

### 139. Insulin Versus Oral Hypoglycemic Drug Combination in Controlling Hyperglycemia in Hcv Patients During Interferon Therapy

M.A. Gawad Shaheen, Sahar M. Abdel-Wahab, Emad A. Hassan and Adel M.R.A. AbdelAziz

*Life Science Journal*, 4 (3): 260-266 (2012) IF: 0.073

Hepatitis-C virus is common in many areas of the world particularly in Egypt and interferon therapy helps around 40 % of the patients to eradicate the virus and good glycemic control is needed to get better results of interferon therapy This work aimed to study the efficacy of insulin therapy compared to oral hypoglycemic drugs in HCV patients receiving interferon therapy. Ninety six patients were included in the study divided into three groups (A) TREATED WITH INSULIN (B) treated with oral hypoglycemic drugs and (C) treated with two oral hypoglycemic drugs plus a bed time basal insulin. HbA1c,AST, ALT and the weight of the patients were measured at the start before intervention and 3 months after intervention. Results this study showed that insulin therapy – group-A- is more effective than oral hypoglycemic drug combination group-B and also more effective than group-C – treated with oral drugs and basal insulin – in reducing HbA1c ( $p = 0.001$ ) and in improving weight and reducing AST AND ALT ( $P < 0.05$ ). Also oral drugs plus a basal insulin at bed time - group – C was more effective than oral drug combination alone (group-B) in reducing HbA1c and the difference was statistically significant  $p < 0.05$  and improving weight  $p < 0.05$  and improving AST AND ALT but the results are statistically non significant ( $p=0.09$  and  $0.07$ ). Conclusion insulin therapy is more effective than oral hypoglycemic drug combination in controlling blood glucose, improving liver enzymes and prevention of weight loss with some weight gain.

**Keywords:** T2dm; Hba1c; Hcv; Interferon; Insulin; Resistant; Oral hypoglycemic drugs.

### 140. Prevalence of Vitamin - D Deficiency Among Premenopausal Women Working in Fayoum University

Mohamed Mashahit, Haidy Michel, Emad El Moatasem, Mohamed El Basel and Nagwa k. Roshdy

*Life Science Journal*, 9 (4): 3332-3337 (2012) IF: 0.073

Vitamin - D deficiency is a worldwide problem and the prevalence of deficiency reaches more than 50% of the population in most of the studies and causes of deficiency are either inadequate intake of food containing vitamin - D or inadequate exposure to sun light which plays an important role of biosynthesis of vitamin- D from the skin, vitamin -D deficiency is linked to many diseases like cancer, diabetes, bone disorders, hypertension, obesity, dyslipidemia and many other disorders and correction of 25 -vitamin - D deficiency which is very simple and available and not expensive improves those disorders significantly. This work aimed to screening for vitamin 25- D deficiency among premenopausal women working in Fayoum University.

**Subjects and methods:** two hundred healthy premenopausal non pregnant non lactating females aged 40-50 years old working at Fayoum University, subjected to thorough medical history and clinical examination, stressing on color of the skin BMI and style of clothing and all patients are screened for 25- vitamin D using ELISA.

**Results:** Our results showed that 45 females of 200 were sufficient (22.5%), 91 females were insufficient (45.5%), 64 females were deficient (32%). Vitamin D deficient females subdivided into deficient (82.8%) and severely deficient (17.2%). there was significant difference between the mean of vitamin -D in the different BMI, in normal body weight subjects the mean of vitamin D level was  $77.9 \pm 21.7$  in overweight was  $51.4 \pm 15.5$  in obese ( $40 \pm 22.4$ ) and the difference is highly statistically significant ( $p < 0.001$ ). the mean vitamin -D level for western wearing clothes was  $66.8 \pm 16.4$ , for ladies wearing Higab was  $62 \pm 23.2$ , and for ladies wearing Niqab  $28.3 \pm 16.3$  and the difference is highly statistically significant ( $p < 0.001$ ). the mean of vitamin D level in dark skinned subjects was  $57.2 \pm 21.2$  while in white skinned subjects was  $96.2 \pm 33.8$  and the difference is highly statistically significant ( $p < 0.001$ ).

**Conclusion:** More than 75 % of the premenopausal women working in Fayoum University had either vitamin -D deficiency or insufficiency. obesity, darker skin and insufficient sun exposure are the main factors leading to or associated with 25 – vitamin – D deficiency

**Keywords:** Vitamin D; Deficiency; Skin color; Bmi; Diet; Sun exposure.

#### 141. Left Ventricular Hypertrophy and Plasma Nitric Oxide in Hemodialysis Patients

Ragai, M.F.R. Fouda, Yasser M. Abdelehamid and Hamdy.A. Ahmed

*Life Science*, 9 (4): 3280-3284 (2012) IF: 0.073

Development of Left ventricular hypertrophy (LVH) in hemodialysis (HD) patients is reported in different clinical studies. the mechanisms responsible for LVH in these patients are complex and multifactorial. Experimental studies have shown that Nitric oxide (NO) is a possible anti-hypertrophic molecule. the aim of this study was to assess prevalence of LVH and its pattern in these patients and plasma NO in these patients.

**Methods:** Twenty six HD patients participated in the study. Measurement of plasma NO, and trans-thoracic echocardiographic assessment of left ventricular mass index (LVMI) and relative wall thickness (RWT) were done. LVH was diagnosed in men with  $LVMI > 115g/m^2$  and women with  $LVMI > 95g/m^2$ . LVH was concentric when  $RWT > 0.42$  and eccentric when  $RWT < 0.42$ .

**Results:** Twenty one out of twenty six (80.8%) HD patients suffered of LVH with a mean LVMI of  $191 \pm 78.14g/m^2$ . 73% of them suffered of concentric LVH, while only 7.8% of them suffered of eccentric LVH and only one patient had normal left ventricle geometry. Mean plasma NO of HD patients was significantly less than mean plasma level of healthy control subjects ( $6.46 \pm 1.0$  microgram/dl vs  $11.18 \pm 1.22$  microgram/dl) and LVMI showed a significant negative correlation to plasma NO.

**Conclusion:** Nearly 80% of our studied HD patients suffer of LVH, most of them suffer of concentric LVH. Mean plasma NO was significantly lower in HD patients compared to healthy control subjects. Plasma NO level was significantly negatively correlated with LVMI. Possible role of NO in the development of LVH in HD patients requires further study.

**Keywords:** Left ventricle; Hypertrophy; Nitric oxide; Hemodialysis.

#### 142. Study of Cognitive Functions and Cerebral Blood Flow in Elderly

Afaf A. Hemeda, Dalia R. Abdel-Rahman, Mohamed Naguib Abdalla, Ahmed A. El-Naggar and Dina M. Riad

*Science Life Journal*, 9 (4): 1704-1707 (2012) IF: 0.073

Little information is available about cognitive functions and changes in cerebral blood flow in elderly people with or without cognitive dysfunction, despite the great influence of this problem on patient, family and society. Our study aimed at evaluating the cerebral blood flow (CBF) in elderly patient with cognitive dysfunction, either primary (Alzheimer Dementia), or secondary (vascular Dementia).

**Methods:** assessment of the cognitive function and CBF of a group of 20 patients aged  $> 65$  years old, 10 patients with vascular dementia while the other 10 patients with Alzheimer dementia and the results compared to a group of healthy volunteers. Results: all patients had significantly decreased Mini Mental State Examination (MMSE), Set test scores compared to that of healthy volunteers while there is significant difference regarding the Geriatric Depression Scale (GDS). Patients with vascular dementia had significantly diminished CBF compared to the healthy volunteers which doesn't go for those with Alzheimer dementia. There is significant positive relationship between MMSE scores and CBF in patients with vascular dementia ( $r=0.77$ ,  $p$ -value=0.009). Patients with vascular dementia had significantly high percent of hypertension and diabetes than do Alzheimer group.

**Conclusion:** Brain ischemia was suggested to be the main factor responsible for decline of cognitive functions. the role of cerebral ischemia in Alzheimer dementia was insignificant. Cardiovascular risk factors are more related to vascular dementia.

**Keywords:** Mmse; Cbf; Set Test; Vascular dementia; Alzheimer dementia.

#### 143. Plasma Concentration of Platelet Factor 4 as an Evidence of Platelet Activation in Parasitic Infections

Aisha A. El-Awady, Mayssa M. Zaki, Manal Kamal, Ahmed Nabil, El-Sayed Abdallah and Walid El-Nabawy.

*Research Journal of Parasitology*, 7 (1) : 25-31 (2012)

Platelets number in the circulation largely exceeds that needed for haemostasis. There is increasing evidences that platelets have an immunological role against parasites. Assessment of platelet factor 4 concentrations in patients with parasitic infections can be used as an indicator for platelet activation. This study aims to evaluate the in vivo platelet activation in parasitic infections through measuring the plasma level of platelet factor 4 in a protozoal and a helminthic infection both before and after treatment. Thus 30 patients, 22 diagnosed to have giardiasis and 8 diagnosed to have hydated disease, were subjected to serum samples collection before (Ag1 and Ah1) and after treatment (Ag2 and Ah2), respectively. the study also included 20 healthy adult as a control group. Both platelet counts and plasma levels of PF4 were measured. Platelet counts in both giardiasis and hydatid patients were significantly elevated after treatment compared to their counts before treatment. Plasma level of PF4 was reduced with a statistically significant difference in both diseases after treatment. Also there was a statistically significant difference between the mean values of PF4 of the control group (C-PF4) and in the tested groups of both diseases before and after treatment ( p

< 0.5 ). Thus parasitic infections lead to platelets activation with increase in platelet count although within normal range for platelets. Plasma level of platelet factor 4 is significantly increased in both infections and decreased after treatment, thus can be used as an indicator for parasitic infection and for prediction of success of recovery after treatment.

**Keywords:** Platelet factor 4, Hydatid disease, Giardia, Parasitic infections.

#### 144. Relationship between Vitamin D and IL-23, IL-17 and Macrophage Chemoattractant Protein-1 as Markers of Fibrosis in Hepatitis C Virus Egyptians

Noha M El Husseiny, Hala M Fahmy, Waleed A Mohamed and Hisham H Amin

*World Journal of Hepatology*, 4 (8): 242-247 (2012)

**Aim:** to assess vitamin D in hepatitis C patients and its relationship to interleukin (IL)-23, IL-17, and macrophage chemoattractant protein-1 (MCP-1).

**Methods:** the study was conducted on 50 Egyptian hepatitis C virus (HCV) genotype number IV-infected patients and 25 age- and gender-matched healthy subjects. Venous blood samples were obtained.

Samples were allowed to clot and sera were separated by centrifugation and stored at -20. A 25 hydroxy vitamin D assay was carried out using solid phase RIA. A 1,25dihydroxy vitamin D assay was carried out using a commercial kit purchased from Incstar Corporation. IL-17 and -23 and MCP-1 were assayed by an enzyme immunoassay.

Quantitative and qualitative polymerase chain reaction for HCV virus were done by TaqMan technology. Only HCV genotype IV-infected subjects were included in the study. the mean  $\pm$  SD were determined, a t-test for comparison of means of different parameters was used.

Correlation analysis was done using Pearson's correlation. Differences among different groups HZ were determined using the Kruskal-Wallis test.

**Results:** the mean vitamin D level in HCV patients (group I) was  $15 \pm 5.2$  ng/mL while in control (group II) was  $39.7 \pm 10.8$ . for active vitamin D in group I as  $16.6 \pm 4.8$  ng/mL while in group II was  $41.9 \pm 7.9$ . IL-23 was  $154 \pm 97.8$  in group I and  $6.7 \pm 2.17$  in group II. IL-17 was  $70.7 \pm 72.5$  in cases and  $1.2 \pm 0.4$  in control. MCP-1 was  $1582 \pm 794.4$  in group I and  $216.1 \pm 5.38$  in group II. Vitamin D deficiency affected 72% of HCV-infected patients and 0% of the control group.

Vitamin D insufficiency existed in 28% of HCV-infected patients and 12% of the control group. One hundred percent of the cirrhotic patients and 40% of non cirrhotic HCV-infected patients had vitamin D deficiency. IL-23, IL-17, and MCP-1 were markedly increased in HCV-infected patients in comparison to controls. A significant negative correlation between vitamin D and IL-17 and -23 and MCP-1 was detected. HCV-infected males and females showed no differences with respect to viral load, vitamin D levels, IL-17, IL-23 and MCP-1. the viral load was negatively correlated with vitamin D and active vitamin D ( $P = 0.0001$  and  $P = 0.001$ , respectively), while positively correlated with IL-23, IL-17, and MCP-1.

We classified the patients according to sonar findings into four groups. Group Ia with bright hepatomegaly and included 14 patients. Group Ib with perihepatic fibrosis and included 11 patients. Group Ic with liver cirrhosis and included 11 patients. Group Id with hepatocellular carcinoma (HCC) and included 14

patients. Vitamin D and active vitamin D were shown to be lower in cirrhotic patients and much lower in patients with HCC, and this difference was highly significant ( $P = 0.0001$ ). IL-17 and -23 and MCP-1 were higher in advanced liver disease) and the differences were highly significant ( $P = 0.0001$ ).

**Conclusion:** Whether the deficiency of vitamin D is related to HCV-induced chronic liver disease or predisposing factor for higher viral load is a matter of debate.

**Keywords:** Vitamin D; Macrophage chemoattractant Protein-1; Liver cirrhosis; Interleukin-23; Interleukin-17; Liver cirrhosis.

#### Dept. of Medical Biochemistry and Molecular Biology

#### 145. Pioglitazone Decreases Hepatitis C Viral Load in Overweight, Treatment Naïve, Genotype 4 Infected-V Patients: A Pilot Study

Mario Chojkier, Hisham Elkhayat, Dina Sabry, Michael Donohue and Martina Buck.

*Plos One*, 7 ( 3 ): 0-0 (2012) IF: 4.092

Insulin resistance (IR) is induced by chronic hepatitis C virus (HCV) genotypes 1 and 4 infections. It is not known whether drugs that affect IR such as Pioglitazone and Prednisone also affect serum HCV RNA titers independently of PEG-Interferon- $\alpha$ 2/ribavirin treatment. the primary aim was to assess whether Pioglitazone by improving IR and/or inflammation decreases HCV viral load independently of standard of care HCV treatment. A secondary aim was to assess whether Prednisone, a drug that induces insulin resistance and stimulates HCV viral entry and replication in replicon culture systems, increases HCV viral load in this population.

**Methodology/Principal Findings:** We designed a two-arm, parallel Pilot Study of overweight, treatment naïve genotype 4 HCV-infected patients at a public referral Liver Clinic in Giza, Egypt. the subjects received Pioglitazone (30 mg/day for 14 days) or Prednisone (40 mg/day for 4 days) in a randomized fashion, but the two arms can be considered independent pilot studies. Only changes from baseline within each arm were assessed and no contrasts of the interventions were made, as this was not an aim of the study.

Among 105 consecutive HCV genotype 4 patients, 39 were enrolled based on the optimal sample size and power analysis according to the CONSORT statement; 20 to the Pioglitazone group and 19 to the Prednisone group. Pioglitazone was effective in decreasing serum HCV RNA at day-14 ( $n = 10$ ; difference of means = 205,618 IU/ml; 95% CI 26,600 to 384,600;  $P, 0.001$ ). Although Prednisone did increase serum HCV RNA at day-4 ( $n = 10$ ; change from baseline = 242,786 IU/ml; 95% CI 285,500 to 215,700;  $P = 0.049$ ), the log<sub>10</sub> HCV RNA titers were statistically not different from baseline day-0.

**Conclusion/Significance:** This is the first documentation that Pioglitazone decreases the serum HCV RNA titers independently of PEG-Interferon- $\alpha$ 2/ribavirin treatment. the novel findings of our Study provide the foundation for basic and clinical investigations on the molecular mechanisms responsible for the Pioglitazone-induced decrease in HCV genotype 4 RNA titers.

#### 146. Effects of a Water Soluble Curcumin Protein Conjugate Versus Pure Curcumin in A Diabetic Model of Erectile Dysfunction

Mohamed Talaat Abdel Aziz, Tarek Motawi, Ameen Rezq, Taymour Mostafa, Hanan H. Fouad, Hanan H. Ahmed, Laila Rashed, Dina Sabry, Amira Senbel, A Al-Malki and Raghda El-Shafiey

*J Sex Med*, 9: 1815-1833 (2012) IF: 3.552

**Introduction:** Curcumin is involved in erectile signaling via elevation of cyclic guanosine monophosphate (cGMP).

**Aim:** Assessment of the effects of water-soluble curcumin in erectile dysfunction (ED).

**Methods:** One hundred twenty male white albino rats were divided into: 1st and 2nd control groups with or without administration of Zinc protoporphyrin (ZnPP), 3rd and 4th diabetic groups with or without ZnPP, 5th diabetic group on single oral dose of pure curcumin, 6th diabetic group on pure curcumin administered daily for 12 weeks, 7th and 8th diabetic groups on single dose of water-soluble curcumin administered with or without ZnPP, 9th and 10th diabetic groups on water-soluble curcumin administered daily for 12 weeks with or without ZnPP. All curcumin dosage schedules were administered after induction of diabetes.

**Main Outcome Measures:** Quantitative gene expression of endothelial nitric oxide synthase (eNOS), neuronal NOS (nNOS), inducible NOS (iNOS), heme oxygenase-1 (HO-1), nuclear transcription factor-erythroid2 (Nrf2), NF-Kb, and p38. Cavernous tissue levels of HO and NOS enzyme activities, cGMP and intracavernosal pressure (ICP).

**Results:** Twelve weeks after induction of diabetes, ED was confirmed by the significant decrease in ICP. There was a significant decrease in cGMP, NOS, HO enzymes, a significant decrease in eNOS, nNOS, HO-1 genes and a significant elevation of NF-Kb, p38, iNOS genes. Administration of pure curcumin or its water-soluble conjugate led to a significant elevation in ICP, cGMP levels, a significant increase in HO-1 and NOS enzymes, a significant increase in eNOS, nNOS, HO-1, and Nrf2 genes, and a significant decrease in NF-Kb, p38, and iNOS genes. Water-soluble curcumin showed significant superiority and more prolonged duration of action. Repeated doses regimens were superior to single dose regimen. Administration of ZnPP significantly reduced HO enzyme, cGMP, ICP/ mean arterial pressure (MAP), HO-1 genes in diabetic groups.

**Conclusion:** Water-soluble curcumin could enhance erectile function with more effectiveness and with more prolonged duration of action

**Keywords:** Curcumin; Heme oxygenase; Diabetes; Erectile dysfunction; Cgmp.

#### 147. IL-17 and IL-11 Gcf Levels in Aggressive and Chronic Periodontitis Patients: Relation to Pcr Bacterial Detection

Olfat G. Shaker and Noha A. Ghallab

*Mediators of Inflammation*, (2012) IF: 3.263

**Objectives:** This study evaluated IL-17 and IL-11 in gingival crevicular fluid (GCF) of generalized chronic periodontitis (GCP) and generalized aggressive periodontitis (GAgP) patients in relation to periodontopathic bacteria.

**Subjects and Methods:** GCF samples were collected from 65 subjects including 25 CP, 25 GAgP, and 15 controls (C) and analyzed for IL-17 and IL-11 by an enzymelinked immunosorbent assay. Molecular detection of bacteria in the dental plaque was determined by polymerase chain reaction.

**Results:** the total amount of IL-17 was significantly higher in GAgP group than in GCP and C groups ( $P < 0.001$ ). the IL-11 concentration was significantly higher in C and GCP groups than GAgP group ( $P < 0.001$ ). the IL-11/IL-17 ratio was significantly higher in the C group than in GCP and GAgP groups ( $P < 0.05$ ). Moreover, GAgP group showed lower ratios of IL-11/IL-17 when compared to GCP group. the high positivity of *P. gingivalis* in the dental plaque was associated with significantly increased GCF levels of IL-17 in GCP and GAgP patients. **Conclusions:** the increased IL-17 level in GCF of GAgP suggests a potential role in the aetiopathogenesis. Meanwhile, the decreased ratio of IL-11/IL-17 might reflect an imbalance between the proinflammatory and anti-inflammatory cytokines in different periodontal diseases.

**Keywords:** Il-17; Il-11.

#### 148. Polymorphisms in Interleukin-10 and Interleukin-28B Genes in Egyptian Patients with Chronic Hepatitis C Virus Genotype 4 and their Effect on the Response to Pegylated Interferon/ Ribavirin-Therapy

Olfat G Shaker and Nermin A H Sadik

*Journal of Gastroenterology and Hepatology*, 27: 1842-1849 (2012) IF: 2.865

Recently, it has been suggested that single nucleotide polymorphisms (SNPs) in some cytokine genes may influence the production of the associated cytokines that affect the host immune response to pegylated interferon-a (Peg-IFN-a) with ribavirin (RBV) in hepatitis C virus (HCV) patients. the aim of the present study was to investigate the possible role of the SNPs of IL-10 and IL-28B and their serum levels in predicting the response to treatment of HCV-4.

**Methods:** Egyptian patients were treated with Peg-IFN-a/RBV. A total of 100 HCV genotype 4-infected patients and 80 healthy control subjects were included in the present study. SNPs in the IL-10 (-592 A/C and -819 T/C) and IL-28B (rs8099917 T/G and rs12979860 C/T) genes and their serum levels were assessed. the IL-10-592-CC, IL-28- rs8099917-TT and IL-28-rs12979860-CC genotypes were significantly higher in responders than in non-responders.

**Results:** Interestingly, the serum levels of IL-10 were significantly increased; in contrast, the serum levels of IL-28B were significantly decreased in HCV patients compared with normal patients. Polymorphisms in IL-28B are more sensitive ( $P < 0.001$ ) than those in IL-10-592 ( $P = 0.03$ ). However, the serum level of IL-10 is higher than that of IL-28, and this difference can serve as a prognostic marker using a receiver operator characteristic (ROC) analysis.

**Conclusions:** It can be concluded that SNPs in IL-28B and the serum levels of IL-10 and IL-28 may be promising predictors for HCV therapy.

**Keywords:** Hepatitis C Patients; Interleukin-10; Interleukin-28; Single Nucleotide Polymorphisms.

#### 149. Single-Nucleotide Polymorphism in the Promoter Region of the Osteopontin Gene at Nucleotide -443 as A Marker Predicting the Efficacy of Pegylated Interferon/Ribavirin-Therapy in Egyptians Patients with Chronic Hepatitis

Olfat Gamil Shaker, Nermin A.H. Sadik and Abeer El-Dessouki

*Hum Immunol*, 73 (10 ): 1039-1045 (2012) IF: 2.837

Osteopontin (OPN) is an extracellular matrix glycoprophosphoprotein produced by several types of cells including the immune system. The present study examined the possibility that single-nucleotide polymorphisms (SNP) in the promoter region of the OPN at nt 443 is a marker predicting the therapeutic efficacy of pegylated interferon (peg-IFN- $\alpha$ 2b)-ribavirin combination therapy in Egyptian patients with chronic hepatitis C. Blood was collected from 95 patients with chronic hepatitis C who had received peg-IFN- $\alpha$ 2b-ribavirin combination therapy and 100 age and sex matched controls. SNP in OPN at nucleotide (nt) 443 and its serum protein level were analyzed. Sustained virological response (SVR) was higher in patients with T/T at nt 443 than in those with C/C or C/T. A univariate logistic regression analysis showed that fibrosis grade, serum OPN protein level and T/T homozygotes of SNP at 443 were significant predictors for response. Receiver operating characteristics (ROC) analysis revealed the diagnostic and prognostic efficacy of serum OPN. It can be concluded that SNP in the promoter region of OPN at nt 443 and serum OPN protein level are predictors of response to the efficacy of peg-IFN- $\alpha$ 2b-ribavirin therapy in Egyptian patients with chronic hepatitis C.

**Keywords:** Osteopontin; Hcv.

#### 150. Dietary Folate Suppresses Dmh-Induced Colon Carcinogenesis in A Rat Model and Affects Dmh-Induced Expression of Four Dna Repair Enzymes

Nermin A. H. Sadik and Olfat G. Shaker

*Nutrition and Cancer*, : 1-8 (2012) IF: 2.783

This study investigated the potential role of folate in the dimethylhydrazine (DMH) colon cancer model in male Wistar rats. For induction of colon cancer, group 1 rats were injected subcutaneously with 30 mg DMH/kg body weight weekly for 30 wk. Group 2 received DMH vehicle. Group 3 rats received DMH as in Group 1 but their diet was supplemented with 8 mg folate/kg diet. Group 4 was fed diet supplemented with 8 mg folate/kg diet. Upregulation of DNA damage repair genes Apurinic/apyrimidinic endonuclease 1, X-ray repair complementing defective repair in Chinese hamster cells 5, 8-oxoguanine-DNA glycosylase, and proliferating cell nuclear antigen, associated with a reduction of folic acid level was observed in colons of DMH group. Reductions of these gene upregulations and a significant increase of colonic folic acid level occurred in the DMH group supplemented with folic acid and this group also had significant inhibition of tumor incidence, normal survival rate and histologically nearly normal colonic architecture. It can be concluded that folate supplementation exerts a potent protective effect on rat colon carcinogenesis via significant modulation of DNA repair, providing a mechanism by which it plays a role in the etiology of human cancer.

**Keywords:** Folic Acid; Colon Cancer.

#### 151. Connexin 26 in Psoriatic Skin Before and After Two Conventional Therapeutic Modalities: Methotrexate and Puva

Olfat Shaker and Mona Abdel-Halim

*Eur J Dermatol*, 22 (2): 218-224 (2012) IF: 2.526

Direct intercellular signaling, which controls keratinocyte behavior, proliferation and differentiation, occurs through gap junctions.

Altered expression of connexins may play a role in the development of psoriatic lesions. Objectives: We estimated connexin 26 (Cx26) mRNA in psoriatic patients and investigated whether the standard therapeutic modalities (methotrexate and PUVA) exert their anti-psoriatic activity partially through altering Cx26 mRNA levels. We also detected Cx26 in skin biopsies by immunohistochemistry. RT-PCR measured Cx26 mRNA levels in 24 chronic plaque psoriasis patients.

Group A received intramuscular methotrexate and group B was treated by PUVA for ten weeks, each followed by measurement of Cx26 mRNA levels and immunohistochemistry. Twelve healthy volunteers served as controls. Results: Cx26 mRNA expression was significantly higher in the patients before treatment than in controls ( $P < 0.001$ ). Post treatment levels were significantly lower than pre-treatment levels ( $P < 0.001$ ), however, significantly higher than in controls ( $P < 0.001$ ). Methotrexate and PUVA caused significant reductions in Cx26 mRNA expression ( $P = 0.002$ ,  $P = 0.028$  respectively). Post treatment levels were slightly significantly lower in the methotrexate group than in the PUVA group ( $P = 0.046$ ). The reduction in Cx26 mRNA expression was significantly positively correlated with the clinical improvement of the psoriatic plaque ( $P = 0.002$ ).

Immunostaining of Cx26 decreased after treatment. Conclusion: Altered expression of the gap junction protein Cx26 may have a role in the development of the psoriatic phenotype. Both methotrexate and PUVA significantly lowered the expression of Cx26 mRNA and protein.

**Keywords:** Psoriasis; Gap junctions; Connexin 26; Methotrexate; Puva.

#### 152. Does Interferon and Ribavirin Combination Therapy Ameliorate Growth Hormone Deficiency in Hcv Genotype-4 Infected Patients?

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*Clin Biochem*, 45: 3-6 (2012) IF: 2.076

**Objectives:** to explore the impact of response to interferon and ribavirin antiviral therapy on human growth hormone (hGH) levels in Egyptian chronic hepatitis C genotype-4 infected patients.

**Design and methods:** We studied eighty Egyptian HCV infected patients visiting outpatient clinics of Tropical Medicine and Hepatology Department, El-Kasr El-Aini Hospital, Cairo University, Egypt. HCV patients received treatment of interferon and ribavirin combination therapy for 24 weeks. Clinical, virological, histological characteristics, and biochemical tests including; liver function tests (ALT and AST), prothrombin time (PT), alpha fetoprotein (AFP), complete blood picture (CBC), and hGH were monitored in hepatitis C genotype-4 infected patients before and after interferon therapy, and healthy controls.

**Results:** Chronic HCV genotype-4 infected patients have high significant decrease of hGH as compared to healthy control individuals. In addition to, there was high significant increase of hGH in responders as compared to non-responders after treatment.

**Conclusion:** We concluded that Egyptian HCV genotype-4 infected patients have growth hormone insufficiency. Besides, we found that response to interferon/ribavirin treatment has an impact on growth hormone levels.

**Keywords:** Growth hormone; Hcv genotype; 4 Ifn/Rbv combination therapy.

### 153. Rantes, Tnf- $\alpha$ , Oxidative Stress, and Hematological Abnormalities in Hepatitis C Virus

Gamil Amin Tawadrous, Amal A. Aziz, Dalia G. Amin, Ahmed Eldemery and Mostafa Abdel-Aziz Mostafa

*J. Invest Med*, 60: 878-882 (2012) IF: 1.964

**Background:** Chronic infection with hepatitis C virus (HCV) is associated with failures of T-cell-mediated immune clearance and with abnormal B-cell growth and activation. Hepatitis C virus infection is characterized by a systemic oxidative stress that is most likely caused by a combination of chronic inflammation, iron overload, liver damage, and proteins encoded by HCV. After a viral infection, multiple proinflammatory mediators contribute to recruitment of immune cells to the liver and to the generation of an antiviral immune response. Recent publications mark chemokines and their receptors as key players in leukocyte recirculation through the inflamed liver.

**Materials and Methods:** the present study involved 75 male subjects, divided into 2 groups: group 1 (n = 30), control group; group 2 (n = 45), patients with chronic HCV. For all subjects, the following investigations were performed: estimation of the levels of bilirubin, albumin, prothrombin concentration, glycosylated hemoglobin, creatinine,  $\gamma$ -fetoprotein, HCV RNA, and activities of alanine and aspartate transaminases as well as alkaline phosphatase. In addition, regulated on activation normal T cell expressed and secreted (RANTES), tumor necrosis factor alpha, malondialdehyde (MDA) and nitric oxide (NO) were assessed. Plasma HCV-RNA concentration (viral load) was determined by real-time polymerase chain reaction (PCR) StepOne system using Applied Biosystem. Complete blood picture was assayed using Abbott Cell-Dyn 3700 hematology analyzer.

**Results:** There were significant increases of the levels of RANTES, tumor necrosis factor alpha, MDA, and NO in HCV-infected patients compared with the control group (P < 0.05); and in these patients, these levels showed significant positive correlation with the HCV RNA viral load. Also, mild leukopenia, thrombocytopenia, neutropenia, and lymphocytosis, with consequent significant increase in the lymphocytes/ neutrophils ratio, were detected in these patients.

**Conclusion:** the data support the concept of chemokines (RANTES) as mediators of liver cell injury in HCV infection. In addition, MDA and NO levels might be used as monitoring markers for oxidative stress in hepatitis C infection.

**Keywords:** Chronic Liver Disease; Rantes; Tnf- $\alpha$ ; Nitric Oxide; Mda; Real-Time Pcr; Complete Blood Picture.

### 154. Changes in Adipocytokines and Insulin Sensitivity During and After Antiviral Therapy for Hepatitis C Genotype 4

Mahmoud A. Khattab, Mohammed Eslam, Mohammed Shatat, Hesham Abd-Aalhalim, Yousef I. Mousa, Fatma Samir, Hanan Aly, Olfat Shaker and Yehia Shaker

*J. Gastrointest Liver Dis*, 21 (1): 59-65 (2012) IF: 1.811

Hepatitis C virus (HCV) infection, especially genotypes 1 and 4, is associated with wide metabolic disarrangements.

**Aim:** to assess whether host metabolic factors influence sustained virological response (SVR) in patients with chronic hepatitis C genotype 4 (HCV- 4) treated with peginterferon / ribavirin and to evaluate the impact of antiviral therapy on insulin resistance (IR) and serum levels of adipocytokines.

**Methods:** Changes in levels of adiponectin, leptin, TNF- $\alpha$  and the homeostasis model assessment for insulin resistance (HOMA-IR) on antiviral combination in patients with HCV-4 were analyzed and effect on response was studied.

**Results:** 107 patients were included (M/F 86/21; mean age 41.4 $\pm$ 5.6 years). Neither serum adipocytokines nor HOMA-IR was correlated with viral load. SVR was achieved by 57% of patients and was associated with fibrosis score (odds ratio: 6.5; P = 0.001) and adiponectin level (odds ratio: 1.3; P = 0.01). At the end of follow-up, HOMA-IR, adiponectin, leptin and TNF- $\alpha$  were reduced, all these changes unrelated to predicting the outcome of treatment. At follow-up, HOMA-IR and adiponectin continued to decrease in patients with SVR, but remained unchanged significantly in patients who did not respond or relapse.

**Conclusions:** Serum adiponectin at baseline appears to be an independent predictor for the achievement of SVR and can be utilized as an additional predictive marker. Changes of IR and adipocytokines occur under treatment which is more evident with the resolution of HCV infection, suggesting that HCV could have a direct role in these metabolic changes.

**Keywords:** Hepatitis C; Insulin resistance; Homa; Adiponectin; interferon.

### 155. Epidermal Growth Factor Gene Polymorphism 61A/G in Patients with Chronic Liver Disease for Early Detection of Hepatocellular Carcinoma: A Pilot Study

Emad Abbas, Olfat Shaker, Ghada Abd El Aziz, Huda Ramadan and Gamal Esmat

*European Journal of Gastroenterology & Hepatology*, 24 (4): 458-463 (2012) IF: 1.757

Overexpression of epidermal growth factor (EGF) in the liver induces transformation into hepatocellular carcinoma (HCC) in animal models. Polymorphisms in the EGF gene modulate EGF levels.

**Objectives** to evaluate the effect of EGF gene single nucleotide polymorphism and to assess its correlation with the risk of HCC in patients with chronic liver diseases.

**Patients and methods** the present study included 80 participants divided into four groups: group 1 included 20 asymptomatic healthy control volunteers, group 2 included 20 patients with chronic hepatitis C viral (HCV) infection, group 3 included 20 patients with liver cirrhosis, and group 4 included 20 patients with HCC. For all participants, the following investigations were

performed: routine laboratory investigations including complete blood count, liver function tests, sero markers of hepatitis viruses HBsAg, HCV-RNA by quantitative polymerase chain reaction, and  $\alpha$ -fetoprotein. DNA was extracted from whole blood for detection of single nucleotide polymorphism of the EGF by polymerase chain reaction, followed by restriction fragment length polymorphism. Results We found a significant difference between both patients with HCC and HCV versus controls in terms of the G carrier (GG and GA; 80 vs. 40%,  $P < 0.05$ ). In addition, the cirrhotic and chronic hepatitis C patients with GG had three-fold and 2.3-fold odds ratio for developing HCC, respectively.

**Conclusion** the EGF 61GG genotype might be associated with a high risk for the development of HCC in Egyptian patients with chronic liver disease. Patients and methods the present study included 80 participants divided into four groups: group 1 included 20 asymptomatic healthy control volunteers, group 2 included 20 patients with chronic hepatitis C viral (HCV) infection, group 3 included 20 patients with liver cirrhosis, and group 4 included 20 patients with HCC.

For all participants, the following investigations were performed: routine laboratory investigations including complete blood count, liver function tests, sero markers of hepatitis viruses HBsAg, HCV-RNA by quantitative polymerase chain reaction, and  $\alpha$ -fetoprotein. DNA was extracted from whole blood for detection of single nucleotide polymorphism of the EGF by polymerase chain reaction, followed by restriction fragment length polymorphism.

**Keywords:** Chronic liver disease; Epidermal growth factor; Hepatocellular carcinoma; Polymorphism.

### 156. Is Human Papilloma Virus Associated with Salivary Gland Neoplasms? An in Situ-Hybridization Study

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*Arch Oral Biol*, 57: 1194-1199 (2012) IF: 1.603

HPV can infect cells of epithelial origin and is closely associated with carcinomas. Studies investigating its presence in salivary gland neoplasms are few and conflicting.

**Methods:** Detection of HPV types 16 & 18 was done on 34 formalin-fixed, paraffin-embedded archival material of different salivary gland neoplasms using Digene HPV types 16 & 18 probe using in situ hybridization technique.

**Results:** Eight of neoplastic salivary gland specimens were positively infected by HPV types 16 & 18. Seven of them were benign (4 Warthin's tumour, 2 pleomorphic adenoma and one myoepithelioma), in addition to one malignant specimen (lymphoma). Correlation was found between the incidence of HPV infection and histological differentiation of salivary gland neoplasms.

**Conclusions:** an association exists between HPV infections and salivary gland neoplasms. However, given the sparse pattern of reactive cells, it cannot be confirmed that this virus is implicated in the aetiology of this group of tumours.

**Keywords:** Hpv; Salivary Gland Neoplasms; in Situ Hybridization.

### 157. Effect of Novel Water Soluble Curcumin Derivative on Experimental Type- 1 Diabetes Mellitus (Short Term Study)

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*Diabetology & Metabolic Syndrome*, 4 (30): (2012) IF: 1.526

**Background:** Diabetes mellitus type 1 is an autoimmune disorder caused by lymphocytic infiltration and beta cells destruction. Curcumin has been identified as a potent inducer of heme-oxygenase-1 (HO-1), a redox-sensitive inducible protein that provides protection against various forms of stress. A novel water soluble curcumin derivative (NCD) has been developed to overcome low in vivo bioavailability of curcumin. The aim of the present work is to evaluate the anti-diabetic effects of the "NCD" and its effects on diabetes-induced ROS generation and lipid peroxidation in experimental type- 1 diabetes mellitus. We also examine whether the up-regulation of HO-1 accompanied by increased HO activity mediates these antidiabetic and anti-oxidant actions.

**Materials and methods:** Rats were divided into control group, control group receiving curcumin derivative, diabetic group, diabetic group receiving curcumin derivative and diabetic group receiving curcumin derivative and HO inhibitor ZnPP. Type-1 diabetes was induced by intraperitoneal injection of streptozotocin. Curcumin derivative was given orally for 45 days. At the planned sacrifice time (after 45 days), fasting blood samples were withdrawn for estimation of plasma glucose, plasma insulin and lipid profile. Animals were sacrificed; pancreas, aorta and liver were excised for the heme oxygenase - 1 expression, activity and malondialdehyde estimation.

**Results:** NCD supplementation to diabetic rats significantly lowered the plasma glucose by 27.5% and increased plasma insulin by 66.67%. On the other hand, the mean plasma glucose level in the control group showed no significant difference compared to the control group receiving the oral NCD whereas, NCD supplementation to the control rats significantly increased the plasma insulin by 47.13% compared to the control. NCD decreased total cholesterol, triglycerides, LDL cholesterol and increased HDL cholesterol levels. Also, it decreased lipid peroxides (malondialdehyde) in the pancreas, aorta and liver.

**Conclusion:** the (NCD) by its small dose possesses antidiabetic actions and that heme oxygenase induction seems to play an important role in its anti-diabetic effects. NCD also improves the lipid profile and oxidative status directly, proved by decreasing lipid peroxides (malondialdehyde) in pancreas, liver & aorta. The new water soluble curcumin derivative still retains the essential potencies of natural curcumin.

**Keywords:** Diabetes Type 1; Heme Oxygenase-1; Curcumin; Insulin Secretion; Oxidative Stress.

### 158. Occult Hepatitis B in Egyptian Thalassaemic Children

Olfat Shaker, Amal Ahmed, Inas Abdel Satar, Hamza El Ahl, Wafaa Shousha and Wahid Doss

*J. Infect Dev Ctries*, 6 (4): 340-346 (2012) IF: 1.191

Thalassemia is hereditary anemia which requires lifelong transfusion as treatment, and hepatitis viral infection is one of the

risks of repeated transfusions. Hepatitis B outbreaks in health-care settings are still a serious public health concern worldwide. Blood samples negative for HBsAg but positive for HBV-DNA, with or without the presence of HBV antibodies, are classified as "occult" HBV infection (OBI). This study investigated the prevalence of occult HBV infection in Egyptian thalassemic children.

**Methodology:** Eighty patients admitted to the Faculty of Medicine, Cairo University Hospital, were involved in this prospective study. Strict inclusion criteria were set to nullify the effect of confounding variables and further minimize selection bias. The following laboratory investigations were performed: complete blood count (CBC); serum AST and ALT; albumin; bilirubin; HBsAg; HBeAg; HBcAb; HCV-RNA; and HBV-DNA. Results: All our patients had no clinical manifestation suggestive of hepatitis. Molecular biology studies revealed positivity for HCV and HBV at 25% and 32.5% respectively.

**Conclusion:** the estimated risk of acquiring hepatitis B and C infection in children receiving multiple blood transfusions is surprisingly high. Moreover, occult hepatitis B infection is a considerably risk.

**Keywords:** Occult Hbv; Hepatitis C Virus; Dna; Thalassemia; Pediatrics.

### 159. Effect of Some Medicinal Plant Extracts on the Oxidative Stress Status in Alzheimer'S Disease Induced in Rats

K. Mahdy, O. Shaker, H. Wafay, Y. Nassar, H. Hassan and A. Hussein

*European Review for Medical and Pharmacological Sciences*, 16: 31-42 (2012) IF: 1.04

Alzheimer's disease (AD) is a progressive neurodegenerative disorder. Increased oxidative stress has been shown to be a prominent and early feature in AD. Medicinal plants with antioxidant activities have been used traditionally in the treatment of several human diseases. The present study aims to investigate the effect of *Salvia triloba* and *Piper nigrum* plant extracts on the oxidative stress status in Alzheimer's disease induced in rats.

**Materials and Methods:** 70 male rats were enrolled in this study and were classified into 7 groups (ten each). Group 1: control group, group 2: AD-induced rats by aluminum chloride, and served as positive control; group 3: AD group treated with Rivastigmine in a dose of 0.3 mg/kg b. wt. daily for three months; group 4 & 5: AD group treated with total extract of *Salvia triloba* in a dose of 750 or 375 mg/kg b. wt. respectively, daily for three months; group 6 & 7: AD group treated with total extract *Piper nigrum* in a dose of 187.5 or 93.75 mg/kg b. wt. respectively, daily for three months. After three months of treatment animals' sera and brain samples were collected. Malondialdehyde (MDA), nitric oxide (NO) and total antioxidant capacity (TAC) were determined in serum while superoxide dismutase (SOD) in erythrocyte. Brain samples were divided sagittally into two portions, the first portion was separated for determination of acetylcholine (ACh) and acetylcholinesterase (AChE). The second portion was used for histopathological investigation.

**Results:** the results indicated that extracts of *Salvia triloba* and *Piper nigrum* as well as Rivastigmine showed significant increase in brain ACh, serum TAC and SOD and significant decreases in brain AChE, MDA and NO in AD-induced rats. Moreover, histological investigation of brain sections showing nearly normal histological structure of hippocampus. Treatment with *Salvia*

*triloba* in a dose of 750 mg/kg b. wt. was more powerful in protection from Alzheimer's disease than *Piper nigrum*, as indicated by both biochemical and histopathological findings.

**Conclusion:** This study revealed that the treatment of AD-induced rats with *Salvia triloba* and *Piper nigrum*, total plant extracts significantly reduced the oxidative stress status and ameliorates the neurodegeneration characteristic of Alzheimer's diseases in rats. Noteworthy, *Salvia triloba* extract showed more interest in improvement Alzheimer's disease in rats.

**Keywords:** Alzheimer'S disease; Oxidative stress; *Salvia triloba*; *Piper nigrum*; Extract.

### 160. B-Cell Activating Factor (BAFF) in Systemic Lupus Erythematosus, Rheumatoid Arthritis, and Behçet'S Disease

Amina Badr Eldin, Safaa Sayed, Gehan Hegazy and Olfat Shaker

*Turk J Rheumatol*, 27(3): 185-194 (2012) IF: 0.191

**Objectives:** This study aims to determine B-cell activating factor (BAFF) serum levels in rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and Behçet's disease (BD) and correlate these levels with disease activity and severity.

**Patients and methods:** Between December 2010 and December 2011, 63 Egyptian patients with collagen diseases [RA (n=21), SLE (n=21); BD (n=21)] were recruited from Cairo and Ain Shams University Hospitals, along with 21 apparently healthy individuals as controls.

All participants underwent history taking, clinical examination, laboratory and radiological investigations, and disease activity score estimation. The serum BAFF level was measured by an enzyme-linked immunosorbent assay (ELISA) kit.

**Results:** the BAFF serum levels were significantly elevated in patients with SLE and BD versus the healthy controls ( $p < 0.011$ ,  $p < 0.023$ ) and in SLE versus RA and BD ( $p < 0.024$ ,  $p < 0.026$ ). A significant positive correlation was found between the BAFF and C-reactive protein (CRP) ( $r = 0.928$ ,  $p < 0.0001$ ), the Disease Activity Score 28 (DAS28) ( $r = 0.810$ ,  $p < 0.0001$ ), and disease control ( $r = 0.834$ ,  $p < 0.0001$ ) in RA. Also, a significant positive correlation was found between BAFF and SLE Disease Activity Index (SLEDAI) score classification ( $r = 0.894$ ,  $p < 0.0001$ ) and SLEDAI score ( $r = 0.748$ ,  $p < 0.0001$ ) in SLE as well as between the BAFF and disease duration ( $r = 0.578$ ,  $p < 0.006$ ) in BD.

**Conclusion:** the BAFF serum levels are increased in patients with SLE and BD versus the controls and in patients with SLE compared with those with RA and BD.

They also have a positive correlation with disease severity in SLE and RA, which suggests that BAFF may play a role in the pathogenesis and activity of these diseases. These results may pose the possibility that a human monoclonal antibody drug which selectively inhibits BAFF biological activity may be useful in the treatment of active resistant cases.

**Keywords:** Behçet's disease; Disease activity; Rheumatoid arthritis; Serum B-Cell activating factor; Systemic lupus erythematosus.



### 161. Association between CC16 Polymorphism and Bronchial Asthma

Nisreen M.El Abiad, Hisham Waheed, William M. Morcos, Samar M. Salem, Hala Ataa and Olfat G. Shaker

*Life Science Journal.*, 9 (1): 265-270 (2012) IF: 0.079

Asthma is one of the most common chronic pediatric diseases, and is responsible for a significant proportion of school day losses. Asthma is influenced by genetic and environmental factors. the inheritance pattern of asthma demonstrates that it is a complex genetic disorder. Clara cell secretory protein (CC16) is an ideal candidate for involvement in an inherited predisposition to asthma owing to its chromosomal location, nature and function. **Objective:** to screen exons of CC16 gene on chromosome 11 for detection of sequence variation in families to determine whether these allelic polymorphism are associated with clinical asthma or not and to detect the relation between type of genetic polymorphism and asthma severity.

**Patients and Methods:** This study included 20 stable asthmatic children with 21 of their atopic family members, also 11 healthy non atopic subjects were included as control group, all cases were subjected to genetic study methods including pedigree construction, PCR and detection of allelic polymorphism.

**Results:** Significant correlation (90%) between homozygous CC16, 38 (AA) (75%) and 38 (AG) (15%) allelic polymorphism and increased prevalence of asthma was detected in families but there was no correlation between CC16 allelic polymorphism and asthma severity.

**Conclusion:** There was a correlation between CC16 allelic polymorphism and increased prevalence of asthma and this gene is present also in normal subjects who are not triggered by environmental factors.

**Keywords:** Cc16; Gene Polymorphism; Pcr; Asthma.

### 162. Glutathione Peroxidase, Superoxide Dismutase and Catalase Activities in Children with Chronic Hepatitis

Nagwa Abdallah Ismail, Sawsan H. Okasha, Anil Dhawan, Azza M. O. Abdel Rahman, Nehal Abdel Hamid and Olfat Shaker

*Advances in Bioscience and Biotechnology*, 3: 972-977 (2012)

the advantages of measuring hepatic oxidative status in liver biopsy are that it helps in diagnosis of hepatic dysfunction, reflects the degree of deterioration in the liver tissues, and helps to determine the severity of hepatic injury. We aimed to study the oxidative stress state in children with chronic hepatitis by using indirect approach in which antioxidant enzymes such as glutathione peroxidase (GPX), superoxide dismutase (SOD) and catalase (CAT) are determined in the liver tissue. the present study included 21 children and adolescents (12 males, 9 females) suffering from chronic hepatitis. Patients were selected from the Hepatology Clinic, New Children's Hospital, Cairo University from November 2006 till 2009 and compared with a group of 7 children who happened to have incidental normal liver biopsy. Children with chronic hepatitis had mean age  $8.12 \pm 1.15$  years. It was further subdivided into 2 subgroups: chronic viral hepatitis (n = 13) and cryptogenic hepatitis (n = 8). GPX, SOD and CAT levels were measured in fresh liver tissue (cell free homogenates) using ELISA. in chronic hepatitis group; there was a significant increase in the hepatic GPX activity ( $38.59 \pm 35.82$  nmol/min/ml) as compared to the control group ( $10.62 \pm 6.68$  nmol/min/ml).

Also a significant correlation was observed between SOD and both ALT (r = 0.87, p < 0.05) and AST (r = 0.74, p < 0.05). GPX correlated with ALT (r = 0.80, p < 0.05) level in the chronic viral hepatitis subgroup. Our findings suggest that oxidative stress could play a role in the pathogenesis of chronic hepatitis. These preliminary results are encouraging to conduct more extensive clinical studies combining antioxidant therapy with various treatments.

**Keywords:** Glutathione Peroxidase; Superoxide Dismutase; Catalase; Chronic Hepatitis; Oxidative Stress.

### 163. Novel Anticancer Curcumin Derivative with Conserved Functional Groups

Mohamed T. Abdel Aziz, Mohamed F. El-Asmar, Ameen M. Rezaq, Hanan H. Fouad, Hanan H. Ahmed, Amira A. Hassouna, Fatma M. Taha and Hafez F. Hafez

*Journal of Cancer Therapeutics and Research*, (2012)

Curcumin, a polyphenol from turmeric, has potent anticancer properties in human cancer cell lines. Nevertheless, its multitargeting clinical application in cancer and other diseases is hampered by its poor systemic bioavailability. A novel curcumin derivative "NCD" was developed through covalent modification of the curcumin "CUR" molecule on sites remote from its natural functional groups.

**Methods:** the NCD was tested for its anticancer effect against six human cancer cell lines in comparison to CUR and the standard anticancer drug Doxorubicin "DOX". in vivo structure-action relationship to the dose-dependent inducible plasma Glutathione S-transferase (GST) was studied. Plasma GST activity was estimated one and half and 24 hours after oral administration of each of CUR and the NCD.

**Results:** the NCD showed significantly lower Half-maximal inhibitory concentrations (IC50s) as compared to the DOX with each of HELA, the human cervical, MCF7, the human breast and HCT116, the human colonic cancer cell lines. Significant improvements in terms of lower IC50 as compared to CUR with all tested human cancer cell lines were also found. in vivo, the NCD showed significant elevations in inducible plasma GST in the 1.5 hr and the 24 hr duration studies as compared to CUR.

**Conclusion:** the IC50 anticancer effect of the NCD significantly was improved against six human cancer cell lines in comparison to CUR. the NCD retained an improved potency in terms of in vivo structure-action relationship to dose-dependent induction of plasma GST. with GST as biomarker for cancer, it should not be taken as parameter in studies and/or clinical trial involving both cancer and CUR as GST is dose-dependently inducible by CUR and some of its derivatives.

**Keywords:** Curcumin derivative; Cell line.

### 164. Amelioration of Murine Schistosoma Mansoni Induced Liver Fibrosis by Mesenchymal Stem Cells

Abdel Aziz MT, Atta HM, Roshdy NK, Rashed LA1, Sabry D, Hassouna AA, Aboul Fotouh GI, Hasan NM, Younis RH and Chowdhury

*Journal of Stem Cells and Regenerative Medicine*, 8 (1) P28: 1-34 (2012)

Schistosomiasis is a common chronic helminthic infection of the liver that causes hepatic fibrosis and portal hypertension,

contributing to the death of over half a million people a year. Infusion of autologous bone marrow cells into patients with hepatic cirrhosis has been reported to ameliorate symptoms of portal hypertension and improve liver function, either by conversion of the infused mesenchymal stem cells (MSCs) to hepatocytes or by modulating of the hepatic fibrosis. Here, we have investigated the antifibrotic effect of mesenchymal stem cells (MSCs) using *S. mansoni*-induced liver fibrosis in mice, which causes an intense, stable fibrosis. MSCs derived from bone marrow of male mice were then infused intravenously into female mice that had received intraperitoneal injection of *S. mansoni* cercariae. Mice were divided into 4 groups: Untreated control; MSCs infusion only; Schistosomiasis only; and Schistosomiasis plus MSCs infusion. Serum alanine aminotransferase (ALT) and liver histopathology were evaluated. Expression of the collagen gene (type I), transforming growth factor (TGF- $\beta$ ), matrix metalloproteinase (MMP2), tissue inhibitor of metalloproteinase (TIMP-1), stromal cell-derived factor-1 (SDF-1) and its receptor (CXCR4) were analyzed. MSC infusion resulted in significant decrease in liver collagen and TGF- $\beta$  gene expression in the Schistosomiasis mice. the ratio of MMP-2 to TIMP-1 expression increased. SDF-1 and CXCR4 mRNA expression also increased. There was overall improvement of liver histology and a statistically significant reduction of serum ALT level. MSCs infusion ameliorated *S. mansoni*-induced liver fibrosis, probably by modulating the relative expression of MMP and TIMP. the findings support the hypothesis that MSCs participate in liver regeneration and functional improvement by reducing liver fibrosis.

**Keywords:** Schistosoma Mansoni; Liver Fibrosis; Stem Cells.

### 165. The Diagnostic and Prognostic Value of Salivary Scd44 Level Determination in Oral Malignant and Potentially Premalignant Lesions

Dalia M. Ghalwash, Khaled El Gaaly, Fat'heya M. Zahran, Olfat Shaker and Hossam A. El-Fol

*Advances in Environmental Biology*, 6 (1): 302-310 (2012)

A key factor in the lack of improvement in prognosis of oral squamous cell carcinoma (OSCC) lesions over the years is the fact that a significant proportion are not diagnosed or treated until they reach an advanced stage. A molecular marker for malignant transformation in innocent looking oral lesions and a monitor for the aggressiveness of malignant lesions might be of help. the present study included 40 subjects: 10 healthy control subjects, 10 patients with potentially premalignant oral lesions with dysplastic changes and 10 others without, in addition to 10 patients suffering from OSCC. Levels of soluble CD44 (sCD44) were measured in whole unstimulated saliva (WUS) using an enzyme linked immune- assay (ELISA). in patients suffering from malignant lesions the salivary sCD44 level was correlating well with the grading of the lesion. Also, most of the patients with the highest salivary sCD44 levels showed postoperative relapse. A highly significant difference was found in the mean value of salivary sCD44 level between the control group and the premalignant with dysplasia and the cancer groups, and on the other hand, a non significant difference was found between the control and the premalignant without dysplasia group. Also, a highly significant difference was found between salivary sCD44 level in cancer patients and those with premalignant lesions without dysplasia, and non significant difference between the cancer patients and those with premalignant lesions with dysplasia. A ROC Curve

was created to estimate salivary sCD44 level with the highest sensitivity and specificity which was 100% and 66.7% respectively. Results indicated that a level of salivary sCD44 lying within the range of 19.2 to 20.4 ng/ml could indicate malignant transformation within oral mucosal lesions.

**Keywords:** Salivary Scd44; Oral Malignant Lesions; Oral Potentially Premalignant Lesions.

### 166. Skin Tags and Acanthosis Nigricans in Patients with Hepatitis C Infection in Relation to Insulin Resistance and Insulin Like Growth Factor-1 Levels

Omar Soliman El Safoury, Olfat G Shaker, and May Mohsen Fawzy

*Indian Journal of Dermatology*, 57 (2): 102-106 (2012)

Skin tags (ST) are papillomas commonly found in the neck, axillae of middle-aged and elderly people Aim: Insulin and insulin-like growth factor (IGF-1) levels are affected by hepatitis C virus (HCV) infection and both of them may be implicated in the etiopathogenesis of ST and acanthosis nigricans (AN) through their proliferative and differentiating properties. So, the aim of this work was to evaluate the impact of HCV infection on ST and AN through the estimation of insulin resistance and IGF-1.

**Materials and Methods:** Participants were arranged into four groups: (ST +ve / HCV +ve) 23 subjects, (ST+ / HCV -ve) 19 subjects, (HCV -ve / STve) 20 subjects and (ST-ve /HCV +ve) 22 subjects. Age, ST size, color, number, AN, fasting glucose, fasting insulin, insulin resistance, IGF-1, HCV-antibodies (Ab) were recorded.

**Results:** the mean number of ST in Group 1 was half the number of ST in Group 2 (11.0 $\pm$ 9.3 / 22.3 $\pm$ 14.0) (P=0.005). the difference in insulin resistance between the same groups was non-significant (13.1 $\pm$ 10.6 / 9.0 $\pm$ 5.5) (P=0.441) while the difference in IGF-1 was statistically significant (218.6 $\pm$ 46.2 /285.4 $\pm$ 32.8) (P=0.002). the multivariate logistic regression for the variables revealed that insulin resistance is the only factor affecting the occurrence of ST (OR=1.096, P=0.023). Multivariate regression analysis for the variables showed that HCV was borderline but not a significant factor affecting the number of ST (Beta=-0.409, P=0.053). the number of patients with AN was doubled in Group 2 in comparison to Group 1 but this was non significant 3(13%) ? 6(32%) (P=0.2800).

**Conclusion:** HCV is associated with a significant decrease in the ST number and in the serum level of IGF-1 together with an obvious decrease in the occurrence of AN. Our results may point to the entrant effect of insulin resistance and IGF-1 in ST and AN development. the current study suggests the evaluation of IGF-1-lowering agents in the control of ST and AN especially in the females with polycystic ovary and in the prevention of the recurrence of ST after surgical removal.

**Keywords:** Acrochordons; Acanthosis Nigricans; Hepatitis C Virus; Insulin Resistance; Insulin-Like Growth Factor-1; Skin Tags.

### 167. Saving Big Toe of Diabetic Foot by Using Autologous Blood Injection: A Case Report

Mohammed Al Azrak and Olfat Shaker

*Journal of Wound Technology*, 17: 26-28 (2012)

Surgical caring of diabetic foot includes facing a diverse spectrum of foot diseases and is challenging to the surgeon in certain

circumstances. Amputation of foot in diabetic patients usually preceded by an ulcer in 85% of the cases. Many factors contribute to impaired healing in diabetic patients hence increase in the morbidity and mortality. Enhancing the ability of the diabetic ulcer to heal by local injection of autologous blood into the interstitium surrounding the ulcer, aiming at triggering and providing essential elements of the healing process cascade. Satisfactory results were achieved and in this case report amputation was avoided.

**Keywords:** Blood Injection; Diabetic Ulcers; Saving Toes.

### 168. Does HCV Patients Who Have BCL2 43Ala Genotype and Normal Gh1 Levels Can Achieve Response to Ifn Based Therapy?

Emad F. Eskander, Ahmed A. Abd- Rabou, Mervat S. Mohamed, Shaymaa M. M. Yahya and Olfat G. Shaker

*Ind. J. Clin. Biochem*, (2012)

The main objective of the current study is to examine the role of the statistical relation between BCL2 gene (Ala43Thr) single nucleotide polymorphism and growth hormone (GH1) levels in Egyptian HCV genotype- 4 patients before and after treatment with pegylated interferon plus ribavirin. Eighty patients with HCV genotype-4 and 40 healthy volunteers as controls were enrolled in the prospective study. Gene polymorphism of BCL2 (Ala43Thr) using PCR-RFLP technique and GH1 concentrations using ELISA procedure were measured for all patients and controls. The present study resulted that Responder HCV genotype-4 Patients, with BCL2 43Ala genotype, have high significant increase in pre-treatment GH1 levels ([1 ng/ml); which represent normal levels, as compared to non-responders pre-treatment GH1 levels (1 ng/ml); which represent low concentrations. We concluded that HCV genotype-4 patients who have normal GH1 concentrations and BCL-2 43Ala genotype can successfully achieve response to interferon based therapy.

**Keywords:** Bcl2; Snp; Gh1; Hcv; Peg-Ifn-A/Rbv.

### 169. Adipose Stem Cells as Alternatives for Bone Marrow Mesenchymal Stem Cells in Oral Ulcer Healing

Aly LA, El-Menoufy H, Ragae A and Rashed LA, Sabry

*International Journal of Stem Cells*, 5 (2): 104-114 (2012)

Adipose tissue is now recognized as an accessible, abundant, and reliable site for the isolation of adult stem cells suitable for tissue engineering and regenerative medicine applications.

**Methods and Results:** Oral ulcers were induced by topical application of formocresol in the oral cavity of dogs. Transplantation of undifferentiated GFP-labeled Autologous Bone Marrow Stem Cell (BMSCs), Adipose Derived Stem Cell (ADSCs) or vehicle (saline) was injected around the ulcer in each group. The healing process of the ulcer was monitored clinically and histopathologically. Gene expression of vascular endothelial growth factor (VEGF) was detected in MSCs by Reverse Transcription-Polymerase Chain Reaction (RT-PCR). Expression of VEGF and collagen genes was detected in biopsies from all ulcers.

**Results:** MSCs expressed mRNA for VEGF MSCs transplantation significantly accelerated oral ulcer healing compared with controls. There was increased expression of both

collagen and VEGF genes in MSCs-treated ulcers compared to controls.

**Conclusions:** MSCs transplantation may help to accelerate oral ulcer healing, possibly through the induction of angiogenesis by VEGF together with increased intracellular matrix formation as detected by increased collagen gene expression. This body of work has provided evidence supporting clinical applications of adipose-derived cells in safety and efficacy trials as an alternative for bone marrow mesenchymal stem cells in oral ulcer healing.

**Keywords:** Bone Marrow; Mesenchymal Stem Cells; Oral Ulcer.

### Dept. of Neuro Surgery

### 170. Long-Term Outcome of Surgical Management of Adult Chiari I Malformation

Nasser M. F. El-Ghandour

*Neurosurgical Review*, (2012) IF: 2.036

Chiari I malformation continues to inspire controversy. Debate still exists about surgical options. The aim of this study is to evaluate the long-term outcome of posterior fossa decompression procedure (PFD) in the treatment of adult Chiari I malformation, focusing on some factors or technical aspects which might influence the outcome.

**Methods:** Forty six adult patients with Chiari I malformation operated by PFD are the subject of this study. The group included 21 males and 25 females, with mean age of 37.4 years. Patients were divided into two groups: group I (32 cases) with syringomyelia and group II (14 cases) without syringomyelia. Group I was further subdivided into 3 subgroups according to the surgical procedure adopted: group Ia (12 cases) operated by PFD only, group Ib (14 cases) operated by PFD with fourth ventricular shunt, and group Ic (6 cases) operated by PFD and syringosubarachnoid shunt. All cases included in group II were operated by PFD only.

**Results:** in group I, symptoms improved in 14 cases (43.8%) and stabilized in 18 cases (56.2%), whereas in group II, symptoms resolved in 10 cases (71.4%) and improved in 4 cases (28.6%). Postoperative magnetic resonance imaging showed that the syrinx was resolved in 21 cases (65.6%), improved in 7 cases (21.9%), unchanged in 4 cases (12.5%). Among the mean follow-up period (5.8 years), recurrence of symptoms occurred in 5 cases (10.9%), all of them are included in group I, and were reoperated again.

**Conclusion:** Posterior fossa decompression is recommended as the treatment of choice in adult Chiari I malformation with or without syringomyelia. The presence of syringomyelia predicts a less favourable response to surgical intervention. Syringosubarachnoid shunting didn't improve the long-term outcome either clinically or radiologically. Implanting a fourth ventricular shunt in cases of syringomyelia associated with adhesions at the foramen of Magendie decreases the long-term incidence of recurrence significantly. For recurrent cases, re-exploration of the initial posterior fossa decompression is recommended before any consideration is given for direct management of the syrinx.

**Keywords:** Adult; Chiari; Decompression; Posterior Fossa; Syringomyelia.

### 171. Endoscopic Treatment of Middle Cranial Fossa Arachnoid Cysts in Children

Nasser M. F. El-Ghandour

*J Neurosurg Pediatrics*, 9: 231-238 (2012) IF: 1.533

Arachnoid cysts located in the middle cranial fossa are common, comprising about half of all intracranial arachnoid cysts. The management of these cysts is challenging, and the optimal surgical treatment is controversial. This study evaluates the role of endoscopy in the treatment of middle cranial fossa arachnoid cysts (MCFACs) in children, focusing on some factors or technical aspects that might influence the outcome.

**Methods:** Thirty-two children with symptomatic MCFACs were the subject of this study. The group included 23 boys and 9 girls, with a mean age of 3.6 years. All patients underwent operations using a purely endoscopic cystocisternostomy procedure through a transtemporal approach.

**Results:** Significant clinical improvement occurred in 28 cases (87.5%). Postoperative MR imaging showed a reduction in cyst size in 23 cases (71.9%), whereas in the remaining 9 cases (28.1%), the cyst size was unchanged. Minor intraoperative bleeding occurred in 3 cases (9.4%), which stopped spontaneously without any postoperative sequelae. Ipsilateral subdural hygroma occurred in 2 cases (6.3%) and resolved within a few weeks without surgery; transient oculomotor palsy occurred in 1 case (3.1%). During follow-up (mean 4.6 years), 3 patients (9.4%) experienced recurrence of symptoms and an increase in cyst size. Interestingly, all 3 patients who had recurrence had also experienced intraoperative bleeding at initial surgery. At a second endoscopic procedure, the fenestration was found to be closed in all 3 patients.

**Conclusions:** Endoscopic cystocisternostomy is recommended in the treatment of MCFACs in children because it is simple, minimally invasive, and effective. It maintains the basic strategy of cyst fenestration into the basal cisterns without the invasiveness of open craniotomy. This procedure reduces operative and recovery times and is associated with low morbidity and mortality rates.

**Keywords:** Arachnoid Cyst; Endoscopy; Middle Cranial Fossa; Cystocisternostomy.

### 172. Minimal Access Direct Spondylolysis Repair Using a Pedicle Screw-Rod System: A Case Series

Mohamed Mohi Eldin

*Journal of Medical Case Reports*, 1-8 (2012) IF: 0.35

**Introduction:** Symptomatic spondylolysis is always challenging to treat because the pars defect causing the instability needs to be stabilized while segmental fusion needs to be avoided. Direct repair of the pars defect is ideal in cases of spondylolysis in which posterior decompression is not necessary. We report clinical results using segmental pedicle-screw-rod fixation with bone grafting in patients with symptomatic spondylolysis, a modification of a technique first reported by Tokuhashi and Matsuzaki in 1996. We also describe the surgical technique, assess the fusion and analyze the outcomes of patients.

**Case presentation:** at Cairo University Hospital, eight out of twelve Egyptian patients' acute pars fractures healed after conservative management of those, two young male patients underwent an operative procedure for chronic low back pain secondary to pars defect. Case one was a 25-year-old Egyptian

man who presented with a one-year history of axial low back pain, not radiating to the lower limbs, after falling from height. Case two was a 29-year-old Egyptian man who presented with a one-year history of axial low back pain and a one-year history of mild claudication and infrequent radiation to the leg, never below the knee. Utilizing a standardized mini-access fluoroscopically-guided surgical protocol, fixation was established with two titanium pedicle screws placed into both pedicles, at the same level as the pars defect, without violating the facet joint. The cleaned pars defect was grafted; a curved titanium rod was then passed under the base of the spinous process of the affected vertebra, bridging the loose fragment, and attached to the pedicle screw heads, to uplift the spinal process, followed by compression of the defect. The patients were discharged three days after the procedure, with successful fusion at one-year follow-up. No rod breakage or implant-related complications were reported.

**Conclusions:** Where there is no evidence of frank spondylolisthesis or displacement and pain does not radiate below the knee, we recommend direct repair of the pars interarticularis fracture, especially in young active adults. We describe a modified form of the Buck screw procedure with a minimally invasive, image-guided method of pars interarticularis fixation. The use of image guidance simplifies the otherwise difficult visualization required for pars interarticularis screw placement and allows minimal skin and muscle dissection, which may translate into a more rapid postoperative recovery.

**Keywords:** Minimal Access; Spondylolysis Repair; Pedicle Screw.

### 173. Catheter Virtual Lumbar Discectomy (the Epidural Cocktail for Lumbar Disc Prolapse) A New Minimally Invasive Alternative, on an Outpatient Bases Bases

Mohamed M. Mohi Eldin

*The Internet Journal of Minimally Invasive Spinal Technology*, 5 (1) (2012)

**Objective:** After six weeks of conservative management of lumbar disc disease patients, some will require additional treatment. Surgeries available do not offer clear, safe options free of complications in all cases. Moreover, some reported postoperative complications are more difficult to treat than the original illness. I am offering a new modified intervention for such cases. The purpose of this study was to assess the safety and effectiveness of epidural cocktail instillation for lumbar degenerative diseases, confirm its indications, and evaluate the clinical outcomes of patients.

**Material and Methods:** A total of 60 patients underwent epidural cocktail injection for lumbar degenerative indications by one neurological spine surgeon. The mean follow-up was 12 months. Follow-up images were taken to assess results and determine any injection-related issues.

**Results:** The most prevalent diagnoses were disc bulges, especially in young patients. The mean severity of LBP decreased by 80% at 3-month follow-up, and 60% at 1-year follow-up. The results of pain relief were best at early follow-up visits. Forty-two patients (70%) stated that they would undergo this procedure again.

**Conclusion:** Despite the supposed argument, the current study provides evidence that immediate pain relief and increase in function can be provided by the epidural cocktail injections with a very low rate of morbidity. The follow-up images showed, in

addition to the clinical improvement, definite structural decrease of the disc bulges in a way as if discectomy was done without any surgical or interventional intervention. That is why the name catheter virtual discectomy (C VD) was introduced.

**Keywords:** Lumbar Disc; Epidural Drugs; Degenerative Spine; Catheter; Cocktail; Minimally Invasive.

#### 174. Catheter Virtual Lumbar Discectomy (Early and 5 Year Follow-Up Results) A New Minimally Invasive Alternative, on an Outpatient Bases

Mohamed Mohi Eldin

*The Open Spine Journal*, 4 (17): 16-27 (2012)

After at least six weeks of conservative management of lumbar disc disease patients, some will require additional treatment. Surgeries available do not offer clear, safe options free of complications in all cases. Moreover, some reported postoperative complications are more difficult to treat than the original illness. I am offering a new modified intervention for such cases.

**Objectives:** the purpose of this study was to assess the safety and effectiveness of epidural cocktail instillation for lumbar degenerative diseases, confirm its indications, and evaluate the clinical outcomes of patients.

**Study Design:** Patients were prospectively selected to receive catheter virtual discectomy (CVD) in a prospective, randomized, blinded, crossover cohort study.

**Setting:** the enrollment took place from January 2007 through February 2012 in major tertiary Hospitals in Cairo, including Cairo University Hospitals, Naser Institute Hospital, and Al-Helal Hospital.

**Material & Methods:** A total of 100 patients underwent epidural cocktail injections for lumbar degenerative indications by one neurological spine surgeon. the mean follow-up was 48 months.

**Outcomes Assessment:** After one week, one month and every 3 month thereafter, for the first year, then yearly, the pain was assessed using visual analogue score (VAS). Any decrease in VAS of more than two scales was defined as a significant VAS improvement. Patients were screened for any major or minor complications. the patients were then followed for three up to five years to determine the outcome of treatment. Follow-up images were taken to assess results and determine any injection-related issues.

Results the most prevalent diagnoses were disc bulges, especially in young ages. the mean severity of LBP decreased by 80% at 3-month follow-up, and 60% at 1-year follow-up. the results of pain relief were best at early follow-up visits.

Forty two patients (70%) stated that they would undergo this procedure again. the late 5 year follow up, if not superimposed by an additional new insult, and after exclusion of the 14 patients who did not complete the study, had a stationary clinical course.

**Limitations:** Fourteen patients did not complete the study, with reasons ranging from loss to follow-up (not returning) to pursuing exclusion criteria items. Eighty six patients were included in the final analysis.

**Conclusion** Despite the supposed argue, the current study provides evidence that immediate pain relief and increase in function can be provided by the epidural cocktail injections with a very low rate of morbidity. the follow-up images showed, in addition to the clinical improvement, definite structural decrease of the disc bulges in a way as if discectomy was done without any surgical or interventional intervention. That is why the name catheter virtual discectomy (CVD) was introduced.

**Keywords:** Lumbar disc; Epidural drugs; Degenerative spine; Catheter; Cocktail; Minimally invasive.

#### 175. Coflex-Augmented Lumbar Microdecompression/ Microlaminectomy (Comparative Pilot Study)

Mohamed M. Mohi Eldin

*The Internet Journal of Minimally Invasive Spinal Technology*, 5 (1): (2012)

**Objective:** in this study, we selected patients older than 40 years of age with degenerative segmental stenosis & neurogenic claudication and analyzed whether the augmented lumbar microdecompression /microlaminectomy with the implantation of the coflex device is beneficial when compared with microdecompression / microlaminectomy surgery alone.

**Methods:** Twenty five patients were treated with decompression augmented with the C oflex device, and 25 patients were treated with decompression alone during the same period. Clinical results were assessed using the pre- and postoperative visual analogue scale (VAS) and activities of daily living (ADL). Patients satisfaction was assessed using the validated outcome measurement, the Oswestry Disability Index Questionnaire (ODI). Radiologic results were assessed according to pre-and postoperative heights and segmental angles at the treated level.

**Results:** the mean age of the patients in the C oflex device group was 46.9 years, and the in the decompression group was 50 years. the mean pre- and postoperative VAS scores were 8.8 and 3.4, respectively, in interspinous devices group and 7.2 and 2.2 in the decompression group. Both groups of patients showed significant improvement in their VAS and ADL scores in comparison with their preoperative scores.

Radiologically, there were significant differences in disc heights and foraminal height between the two groups.

**Conclusions:** the C oflex device was helpful in alleviating pain and improving ADL performance. It corrected segmental scoliosis and restricted extension. the addition of coflex device to the microdecompression procedure, improves the clinical and radiological outcomes much, in properly-selected cases.

**Keywords:** Interspinous Spacer; C Oflex Device; Lumbar Microlaminectomy; Spinal Stenosis; Neurogenic Intermittent Claudication.

#### 176. Role of Endoscopy in Management of Hydrocephalus

Nasser M. F. El-Ghandour

*Hydrocephalus*, (2012)

A significant advance in the treatment of hydrocephalus has been the evolution of endoscopy. Hydrocephalus represents the classic indication for a neuroendoscopic approach. Currently, hydrocephalus remains the most frequent intracranial disease treated endoscopically. the success of neuroendoscopy in recent years has relied heavily on the success of endoscopic third ventriculostomy in the treatment of obstructive hydrocephalus. Endoscopic third ventriculostomy has become a well established procedure for the treatment of noncommunicating hydrocephalus. in our experience, third ventriculostomy has been successful in controlling obstructive hydrocephalus caused by posterior fossa tumors, and it was much more superior than

shunting in terms of morbidity and incidence of procedure failure. the role of endoscopy in the treatment of complex hydrocephalus is indispensable. Our results of using endoscopy in the treatment of these cases are encouraging. Endoscopic cyst fenestration has led to avoiding or eliminating the need for shunts in some cases, simplification of complex shunts and reduction of shunt revision rate. It can be also used as an adjunct to shunting. It improves the results of shunting, and it plays a crucial role in shunt revision and retrieval of malfunctioning ventricular catheters. in addition to tumor biopsy sampling, the endoscope has been used for the resection of colloid cysts and other intraventricular lesions. Our results of using endoscopy in the treatment of these cases are excellent. the use of the neuroendoscope provides the unique ability to perform tumor resection, tumor biopsy sampling, restoration of obstructed cerebrospinal fluid pathways (e.g. foramen of Monro and aqueduct of Sylvius), performing endoscopic third ventriculostomy, and cerebrospinal fluid sampling, all can be done in a single procedure. Over the last few years, the field of neuroendoscopy has been expanded to treat a wide array of neurosurgically managed conditions. A seemingly limitless number of neurosurgical applications await the endoscope. in the future, one can expect routine use of the endoscope in the management of hydrocephalus, either as the primary surgery or as an adjunct. the continued evolution of this modality will rely on new technological advances, improved understanding of endoscopically demonstrated neurosurgical anatomy, discovery of new applications, and the training of neurosurgeons. Endoscopy is expected to become a routine procedure in modern neurosurgical practice and training. Pediatric neurosurgeons should acquire the needed skill in using endoscopy in order to manage one of the most common neurosurgical problems in children, which is hydrocephalus.

#### Dept. of Nuclear Medicine

### 177. <sup>18</sup>F-Fluorodeoxyglucose Positron Emission Tomography/ Computed Tomography Finds Answers in Cancer Patients with Increasing Tumor Markers and Negative or Equivocal Conventional Imaging Modalities

Shahenda S. Salema and Mohamed A. Shahin

*Nucl Med Commun*, 33 (3): 314-321 (2012) IF: 1.404

The increase in tumor markers with negative or equivocal conventional imaging modalities represents a serious dilemma in the follow-up of previously treated cancer patients. Positron emission tomography/computed tomography (PET/CT) has emerged as a useful tool in oncological imaging in staging and restaging of most cancers.

**Objective:** This study explored the potential role of <sup>18</sup>F-fluorodeoxyglucose (FDG) PET/CT in the detection and localization of tumor recurrence in cancer patients with increasing serum tumor markers and negative or equivocal conventional imaging modalities.

**Materials and methods:** This prospective study was conducted on 105 previously diagnosed and treated cancer patients with different pathologies. All patients were referred for <sup>18</sup>F-FDG PET/CT scans because of increasing tumor markers with negative or equivocal conventional imaging modalities. All patients underwent whole-body <sup>18</sup>F-FDG PET/CT scans. the findings were confirmed by clinical and/or radiological follow-up of at least 12 months and histopathologically whenever possible.

**Results:** PET/CT detected recurrence and/or metastases in 90 patients (85.7%), including 17 recurrences, 50 metastases, and 23 recurrences and metastases. the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of PET/CT scans were 95.7, 100, 100, 73.3, and 96.2%, respectively. These parameters were 95, 100, 100, 69, and 95% for PET scans alone and were 91.5, 100, 100, 57.9, and 92.3% for CT scans alone.

**Conclusion:** <sup>18</sup>F-FDG PET/CT is a powerful diagnostic tool in restaging of cancer patients. in most cases, PET/CT provides accurate results and helps resolve the clinical dilemma encountered in oncological patients with increasing serum tumor markers and negative or equivocal findings in conventional imaging modalities.

**Keywords:** Conventional imaging modalities; Positron emission tomography; Computed tomography; Tumor markers.

#### Dept. of Obstetrics and Gynecology

### 178. Is There A Place for Corifollitropin Alfa in IVF/ICSI Cycles? A Systematic Review and Meta-Analysis

Mahmoud Youssef, M Aboulfoutouh, El-Khyat W and F. Al-Inany

*Fertility and Sterility*, 97(4): 876-885 (2012) IF: 3.775

To evaluate the role of corifollitropin alfa, a newly developed weekly administrated long-acting recombinant FSH (rFSH), as an alternative for daily rFSH administration in women undergoing controlled ovarian stimulation in GnRH antagonist down-regulated in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI) treatment cycles.

**Design:** Systematic review and meta-analysis of randomized controlled trials.

**Setting:** University and private centers.

**Patient(S):** Infertile women undergoing IVF/ICSI treatment.

**Intervention (S):** Comparing long-acting rFSH corifollitropin alfa versus standard daily administrated rFSH in GnRH antagonist IVF/ICSI cycles.

**Main Outcome Measure(S):** Ongoing pregnancy rate, live birth rate, clinical pregnancy rate, miscarriage rate, duration of stimulation, amount of FSH, number of retrieved oocytes, number of mature oocytes, number of embryos obtained, fertilization rate, ovarian hyperstimulation syndrome (OHSS) incidence, and adverse events. Searches (of literature through November 2011) were conducted in Medline, Embase, Science Direct, the Cochrane Library, and databases of abstracts.

**Result(S):** Four randomized trials involving 2,326 women were included. There was no evidence of a statistically significant difference in ongoing pregnancy rate for corifollitropin alfa versus rFSH. There was evidence of increased ovarian response and risk of OHSS in corifollitropin alfa.

**Conclusion(S):** in view of its equivalence and safety profile, corifollitropin alfa in combination with daily GnRH antagonist seems to be an alternative for daily rFSH injections in normal responder patients undergoing ovarian stimulation in IVF/ICSI treatment cycles

**Keywords:** Corifollitropin alfa; GnRH antagonist.

### 179. Would Gestational Age and Presence of Brain Anomalies Affect Interobserver Reliability of Fetal Head Biometry? Using Off-Line Analysis of 3-D Dataset

Mona S. M. Salman, Hatem A. Mousa, Peter Twining, Nia W. Jones, David James, Mohamed Momtaz, Mona Aboulghar, Ahmad El-Sheikhah and George Bugg

*Ultrasound Med Biol*, 38 (1): 69-74 (2012) IF: 2.293

The objective was to assess interobserver reliability of fetal head biometry using archived three-dimensional (3-D) volumes and the impact of gestational age and presence of brain anomalies on examiners' performance. Seventy nine 3-D volume datasets of fetal head were examined: 27 were normal and 52 had brain abnormalities. Off-line analysis was done by three fetal medicine experts (E1, E2 and E2), all were blinded to history and patient details. Measurements of the biparietal diameter (BPD), head circumference (HC), lateral ventricle (Vp) and transcerebellar diameter (TCD) were compared between examiners and to two-dimensional (2-D) measurements. Comparisons were made at two gestational age groups ( $\leq 22$  and  $>22$  weeks) and in presence and absence of brain anomalies. The intraclass coefficient showed a significantly high level of measurement agreement between 3-D examiners and 2-D, with values  $>0.9$  throughout ( $p < 0.001$ ). Bias was evident between 3-D examiners. E2 produced smaller measurements. The mean percentage difference between this examiner and the other two in BPD, HC, Vp and TCD measurements was significant, of 1.6%, 1%, 4.9% and 1.8%, respectively. E1 measured statistically larger for HC and TCD. E3 measured significantly larger for only BPD. The presence of anomalies was of no influence on the 3-D examiners' performance except for E3 who showed bias in BPD measurements only in cases with brain anomalies. Unlike other examiners, bias of E2 was only seen at gestational age group  $\leq 22$  weeks. Limits of agreement in measurements between observers were narrow for all parameters but were widest for the Vp measurements, being  $\pm 23\%$  of the mean difference. Despite the above bias, the actual mean difference between examiners was small and unlikely to be of any clinical significance. Off-line measurement of fetal head biometry using 3-D volumes is reliable. In our study, presence of brain anomalies was unlikely to influence the reproducibility of measurements. Gestational age seemed to be of an impact on examiners' bias. Among experts this bias may be of no clinical significance.

**Keywords:** 3-D Ultrasound; Off-Line analysis; Fetal head Biometry; Interobserver variation.

### 180. The Value of Fallopian Tube Sperm Perfusion in the Management of Mild-Moderate Male Factor Infertility

Waleed El-Khayat, Akmal El-Mazny, Nermeen Abou-Salem and Aly Moafy

*Int. J. Gynecol Obstet*, 117 (2012): 178-181 (2012) IF: 2.045

To investigate whether fallopian tube sperm perfusion (FSP) would improve pregnancy rates compared with standard intrauterine insemination (IUI) in cases of male factor infertility. Methods: in a randomized controlled trial at a university teaching hospital in Egypt, 120 couples with mild or moderate male factor infertility underwent a mild controlled ovarian stimulation

protocol (clomiphene citrate plus human menopausal gonadotropin). Women were randomly allocated to group 1 (FSP via Foley catheter with 4 mL of inseminate) or group 2 (standard IUI with 0.5 mL of inseminate) ( $n=60$  for both). The main outcome measure was clinical pregnancy rate. Results: There were no significant differences between the groups in terms of baseline clinical characteristics, semen parameters, or characteristics of stimulation cycles. The pregnancy rate was significantly higher in group 1 than in group 2 (16 [26.7%] vs 7 [11.7%];  $P=0.04$ ). There was no significant difference in the incidence of multiple pregnancy, abortion, or ectopic pregnancy between the groups. Conclusion: Fallopian tube sperm perfusion is an effective technique in the management of mild-moderate male factor infertility and should, therefore, be considered before resorting to more sophisticated techniques of assisted reproduction.

**Keywords:** Fallopian tube sperm perfusion; Infertility; Intrauterine insemination.

### 181. The Use of Vaginal Natural Progesterone for Prevention of Preterm Birth in Ivf/Icsi Pregnancies

Mona M Aboulghar, Mohamed A Aboulghar, Yahia M Amin, Hisham G Al-Inany, Ragaa T Mansour and Gamal I Serour

*Reprod Biomed Online*, 25: 133-138 (2012) IF: 2.042

The aim of this study was to evaluate the effect of vaginal natural progesterone on the prevention of preterm birth in IVF/intracytoplasmic sperm injection (ICSI) pregnancies. A single-centre prospective placebo-controlled randomized study was performed. A total of 313 IVF/ICSI pregnant patients were randomized into two groups for either treatment with daily 400 mg vaginal natural progesterone or placebo, starting from mid-trimester up to 37 weeks or delivery. Amongst the patients, there were 215 singleton and 91 twin pregnancies. There was no significant difference in risk of preterm birth among all patients (OR 0.672, 95% CI 0.42–1.0). There was a significantly lower preterm birth rate in singleton pregnancies in the natural progesterone arm (OR 0.53, 95% CI 0.28–0.97) and no significant difference between both arms in twin pregnancies (OR 0.735, 95% CI 0.36–2). In conclusion, the administration of 400 mg vaginal natural progesterone from mid trimester reduced the incidence of preterm birth in singleton.

**Keywords:** Ivf/Icsi; Preterm birth; Singleton pregnancy; Twin pregnancy; Vaginal natural progesterone.

### 182. Does A Single Endometrial Biopsy Regimen (S-Ebr) Improve Icsi Outcome in Patients with Repeated Implantation Failure? A Randomised Controlled Trial

Amal Shohayeb and Waleed El-Khayat

*Eur J. Obstet Gyn R B*, 164: 176-179 (2012) IF: 1.974

**Objective:** to evaluate the effect of a single endometrial biopsy regimen (S-EBR) in the cycle preceding the ICSI cycle in patients with repeated implantation failure. Study design: This was a prospective randomized controlled trial which included two-hundred infertile women with a history of repeated implantation failure. The subjects were randomly divided into two groups. Group A subjects underwent hysteroscopy and endometrial scraping by Novak curette in the cycle preceding the ICSI cycle,

while group B subjects underwent hysteroscopy without endometrial scraping. Implantation rate, clinical pregnancy rate, abortion rate and live birth rate were compared between both groups.

**Results:** the number of retrieved oocytes in group A was 11.6 3 and in group B was 11.6 2.8 with no statistically significant difference ( $p = 0.787$ ). There were statistically significant differences regarding the implantation rate, the clinical pregnancy rate and live birth rate. the implantation rate in group A was 12% while in group B it was 7% ( $p = 0.015$ ), the clinical pregnancy rate was 32% in group A while it was only 18% in group B ( $p = 0.034$ ) and the live birth rate was 28% in group A while it was 14% in group B ( $p = 0.024$ ).

**Conclusions:** the single endometrial biopsy regimen (S-EBR) performed during hysteroscopy has statistically significant higher implantation rate, clinical pregnancy rate and live birth rate than hysteroscopy without endometrial scraping.

**Keywords:** Implantation failure; Endometrial scraping; Repeated implantation failure.

### 183. Can Dopamine Agonist at A Low Dose Reduce Ovarian Hyperstimulation Syndrome in Women at Risk Undergoing Icsi Treatment Cycles? A Randomized Controlled Study

Amany Shaltout, Amal Shohyab and Mohamed A.F.M. Youssef

*European Journal of Obstetrics & Gynecology and Reproductive Biology*, 165: 254-258 (2012) IF: 1.974

Dopamine agonists were proposed as a preventive strategy for severe ovarian. the aim of this randomized controlled study is to evaluate the role of dopamine agonist at lower doses (0.25 mg) as a preventive strategy of severe hyperstimulation syndrome (OHSS) in women at high risk in IVF/ICSI treatment cycles.

**Study design:** Two hundred women at risk to develop OHSS undergoing IVF/ICSI treatment cycle were included; the study group received 0.25 mg of cabergoline for 8 days from the day of HCG administration versus no treatment for the prevention of OHSS. Reduction of the incidence OHSS was the primary outcome.

**Results:** the overall incidence of OHSS was significantly reduced, almost 50%, in cabergoline group in comparison with control group (RR: 0.5, 95% CI: 0.29–0.83), with absolute risk reduction following cabergoline administration 11% (ARR: 0.11, 95% CI: 1.09–20.91). the corresponding number needed to treat (NNT) was 9.

**Conclusion:** Prophylactic treatment with the dopamine agonist, cabergoline, at lower doses (0.25 mg) reduces the incidence of OHSS in women at high risk undergoing IVF/ICSI treatment.

**Keywords:** Dopamine agonist; Ohss; RCT; Cabergoline.

### 184. Placental Protein 13 as an Early Predictor in Egyptian Patients with Preeclampsia, Correlation to Risk and Association with Outcome

Walid S. El Sherbiny, Ahmed Soliman and Aml S. Nasr

*J Invest Med*, 60 (5): 818-822 (2012) IF: 1.964

**Introduction:** Placental protein 13 (PP13) is a protein expressed only in the placenta. It is involved in gluing the placenta to the uterus and remodeling the maternal arteries to expand them.

Women who subsequently develop preterm preeclampsia have low first trimester maternal serum.

**Aim of Work:** the aim of this work was to assess the value of PP13 as an early marker for screening of preeclampsia and to correlate it with the PP13 messenger RNA (mRNA).

**Patients and Methods:** as a part of the Antenatal Screening Project, 100 women in the first trimester of pregnancy were selected and subdivided into 2 groups: 50 women who developed preeclampsia in their third trimester (patient group) and 50 women who completed normal uncomplicated pregnancy until full term (control group). Placental protein 13 level was measured using the commercially available enzymelinked immunosorbent assay kit and PP13 mRNA was tested using reverse transcription polymerase chain reaction.

**Results:** the maternal serum PP13 level in the preeclamptic group was (157.9 T 45.5 pg/mL), which is significantly lower than that of the control group (225.3 T 67.3 pg/mL), with highly statistically significant difference (P G 0.0001). the frequency of maternal PP13 mRNA expression was lower in the preeclamptic group (28%) compared to that in the control group (76%), with highly statistically significant difference (P G 0.0001).

**Conclusion:** Combined serum PP13 level assay and PP13 mRNA expression are reliable markers for early detection of preeclampsia, and we recommend doing it as a routine investigation during the first trimester.

**Keywords:** Preeclampsia; Pp13; Enzyme-Linked Immunosorbent Assay; Mrna; Rt-Pcr.

### 185. Metalloprotease (ADAM12-S) as a Predictor of Preeclampsia: Correlation with Severity, Maternal Complications, Fetal Outcome, and Doppler Parameters

Walid El-Sherbiny, Ahmed Nasr and Aml Soliman

*Hypertension in Pregnancy*, : 1-9 (2012) IF: 1.694

**Objectives:** to compare the first trimesteric serum level of ADAM12-S in women who developed mild and severe preeclampsia and in healthy gravidas and to correlate these changes with the severity of the disease, maternal complications, fetal outcome, and Doppler cerebroplacental ratio (CPR). Design. Comparative prospective observational study. Setting: University hospital.

**Methods:** Serum samples were obtained from 414 women in their first trimester, of which 259 women completed their pregnancy without complications and 155 women developed preeclampsia later in their pregnancies. All were subjected to history taking, examination, laboratory investigations, obstetric ultrasound, and Doppler CPR.

**Results:** ADAM12-S was significantly decreased in patients with severe and in mild preeclampsia compared with the controls. Moreover, there was strong negative correlation with disseminated intravascular coagulopathy (DIC) and HELLP syndrome, cesarean delivery, postpartum hemorrhage, and neonatal intensive care unit admission. ADAM12-S had medium negative correlation with systolic blood pressure and diastolic blood pressure, accidental hemorrhage, cesarean hysterectomy, prematurity, and low birth weight. in addition, it had a weak negative correlation with intracranial hemorrhage, residual hypertension, and intrauterine fetal death. ADAM12-S had strong positive correlation with CPR. There were no correlation with



eclampsia, intrauterine growth retardation, acute pulmonary edema, and acute renal failure.

**Conclusion:** ADAM12-S is significantly decreased in severe and mild preeclampsia and is correlated with CPR, severity of preeclampsia, maternal complications, and fetal outcome. It is recommended to measure ADAM12-S in the first trimester to predict maternal complications and fetal outcome in pregnancies complicated by preeclampsia.

**Keywords:** Preeclampsia; Adam12-S; Elisa; Doppler cerebroplacental ratio; Perinatal morbidity and mortality; Hellp; Intrauterine growth restriction.

### 186. Laparoscopic and Laparotomic Approaches for Endometrial Cancer Treatment: A Comprehensive Review

Ingolf Juhasz-Böss, Hisham Haggag, Sascha Baum, Stephanie Kerl, Achim Rody and Erich Solomayer

*Arch Gynecol Obstet*, (2012) IF: 1.277

**Objective:** Endometrial cancer (EC) is the most common gynecological malignancy in the developed world, particularly among postmenopausal women. Endoscopic surgery is gaining more popularity among surgeons as a safe and feasible option for treatment of endometrial carcinoma, providing the possibility of adequate lymph node excision.

**Methods:** A comprehensive review. Results the advantages of laparoscopy prevail over laparotomy and authors report lower peri-operative complication rates, less blood loss, lower transfusion rates, and shorter hospital stay, as well as a better quality of life (QoL) after laparoscopic surgery, in contrast to conventional abdominal surgery. This was confirmed by a metaanalysis of four randomized controlled studies. This is also true for obese risky patients to whom laparotomies carry indolent side effects. In addition, with more training and experience this procedure would be even more feasible and safer.

**Conclusions:** Because of the increasing importance of economic efficiency in health care, the endoscopic approach will continue to play a more important role in the future treatment of EC providing a better treatment option for the coming patients. As a promising therapeutical option, it should be offered to all patients with an early stage EC.

**Keywords:** Endometrial cancer therapy; Laparoscopy; Peri-Operative complication; Oncological safety.

### 187. The Significance of Progesterone/Estradiol Ratio on the Day of HCG on the ICSI Outcome in Both Obese and Non-Obese Patients

Amal A. Shohaye, Mostafa M. Ragaee and Waleed El-Khayat

*Middle East Fertility Society Journal*, 17: 236-242 (2012)

**Aim:** to study the significance of progesterone/estradiol (P/E2) ratio on the outcome of ICSI cycles and if this relation would differ in obese vs. non-obese patients.

**Method:** Retrospective analysis of the results of 143 patients undergoing their first ICSI cycles at Kaser-elaini ART unit. All the included patients had long protocol for ovarian stimulation. P/E2 ratio was correlated to the pregnancy rate in all the included patients then they were classified into two groups according to their BMI into two groups. Group 1: with BMI > 30 and group 2: with BMI < 30. Different outcome parameters were compared

between the two groups including peak estradiol and progesterone levels on day of HCG, P/E2 ratio in addition to the number of retrieved oocytes, their maturity, fertilization rate and the pregnancy rate.

**Results:** Although elevated levels of peak estradiol in non-obese patients  $4.43 \pm 5.02$  compared to obese patients  $3.27 \pm 2.24$  and the difference is statistically significant (p value = 0.017) in addition to significant difference in levels of peak progesterone which is elevated in non-obese patients  $1.64 \pm 1.38$  compared to obese patients  $1.41 \pm 1.1$  (p value = 0.038). However, no significant difference was detected between the two groups regarding the progesterone/estradiol ratio (p value = 0.989), also no statistical difference was found regarding the number of retrieved oocytes, number of mature oocytes and the rate of fertilization in each group. The pregnancy rate showed near values in each group 36.9% in non-obese patients' vs. 29.4% in obese patients which was not found to be statistically significant between the two groups.

**Conclusion:** P/E2 ratio cannot be used as a reliable predictor for pregnancy rate, and this is not different between obese and non-obese patients. No significant difference was found between obese and non-obese patients regarding peak progesterone, estradiol level on day of neither HCG nor other ICSI outcomes including number of retrieved oocytes, fertilization rate or the pregnancy rate.

**Keywords:** P/E2 Ratio; Icsi; Bmi.

### 188. Conversion of Icsi Cycles to Iui in Poor Responders to Controlled Ovarian Hyperstimulation

Amal Shohieb, Mona Mostafa and Waleed El-Khayat

*Middle East Fertility Society Journal*, 17: 42-46 (2012)

**Aim:** Comparison between the results of the oocyte retrieval technique and the conversion to the intra-uterine insemination (IUI) technique in cases with poor ovarian response to the controlled ovarian hyperstimulation (COH) procedure.

**Patients and methods:** It is a retrospective observational study in women with poor ovarian response to COH which is defined as estradiol (E2) peak level <1000 pg/mL or with 64 follicles which are P14 mm in diameter. Four hundred and sixteen cases were reported as poor responders in 2 IVF centers since December 2007 to July 2010. One hundred and fifty two cases of them proceeded to the oocyte retrieval procedure. These cases were assigned as group (A). Sixty eight cases converted to IUI and were assigned as group (B). One hundred and ninety six cases canceled their cycles. These cases were not included in the current study. Our data were collected from the databases of two in Vitro Fertilization (IVF) centers and analyzed retrospectively to compare the results of the different applied techniques in the studied groups. The main measured outcome parameters were the clinical pregnancy rate and the live birth rate.

**Results:** the group of cases proceeded to the oocyte retrieval procedure had a higher basal Follicle Stimulating Hormone (FSH) level, needed a longer duration of stimulation with higher Human Menopausal Gonadotropin (HMG) doses and had higher E2 peak levels. The clinical pregnancy rates and the live birth rates were higher in the group proceeded to the oocyte retrieval than the group converted to IUI but the difference was not statistically significant.

**Conclusion:** as the pregnancy rates difference between both groups was not statistically significant the conversion to IUI could be considered a useful substitute to the oocyte retrieval

procedure in the poor responder cases. However, to adopt this conclusion, further confirmation in other prospective studies with larger sample size is a must.

**Keywords:** Controlled ovarian hyperstimulation; ICSI; Ntrauterine insemination; Oocyte retrieval; Poor response.

### 189. Does the Addition of LH Activity to FSH Make Gonadotrophins More Superior? A Systematic Review and Meta-Analysis

Hesham Al-Inany, Amr Wahba, Hatem Abu Hashim, Human Fatemi and Ahmed Abousetta

*Evidence Based Women's Health Journal*, : 113-120 (2012)

The contribution of luteinizing hormone (LH) activity to follicle-stimulating hormone (FSH) in ovarian stimulation in improving the outcome of IVF/intracytoplasmic sperm injection (ICSI) has been an area of major debate.

**Objective** to systematically locate, review, and analyze the best available evidence on the value of additional LH activity in ovarian stimulation in IVF and/or ICSI irrespective of the source of LH.

**Design** Systematic review of properly randomized trials comparing FSH only [as recombinant FSH (recFSH)] vs. LH-containing protocols (derived either from a urinary source or developed by recombinant technology) in women undergoing IVF and/or ICSI with desensitization achieved either by long GnRH agonist or GnRH antagonist protocols.

A meticulous search was carried out using electronic databases and hand searches of the literature.

**Results** Thirty-one trials were identified. Only nine trials reported on live birth rate and ovarian hyperstimulation (OHSS) rates. Pooling of the trials showed that the live birth rate did not show a statistically significant difference [recFSH (304/1120; 27.14%) vs. FSH/LH (324/1110; 29.19%) ( $P = 0.29$ ; odds ratio (OR)=0.90, 95% confidence interval (CI) = 0.75–1.09)]. OHSS rates also did not show a significant difference [recFSH (34/1888; 1.80%) vs. FSH/LH (29/1843; 1.57%) ( $P = 0.79$ ; OR= 1.08, 95% CI = 0.63–1.83)]. the clinical pregnancy rate significantly favored additional LH activity [(recFSH (748/2758; 27.1%) vs. FSH/LH (838/2772; 30.2%),  $P = 0.008$ ; OR = 0.85 95% CI =0.76–0.96)], whereas FSH-only protocols (recFSH) yielded a higher number of retrieved oocytes compared with LH-containing protocols (FSH/LH) ( $P = 0.002$ ; mean difference = 1.25, 95% CI= 0.48–2.02).

**Conclusion** LH activity is not paramount in ovarian stimulation.

**Keywords:** Lh; Gonadotrophins; Ivf; ICSI; Infertility.

### 190. Atosiban Versus Nifedipine for Prevention of Preterm Labor: Systematic Review and Meta-Analysis using Direct and Indirect Evidence

Ahmed Abou-Setta, Hesham G. Al-Inany and Jaro Wex

*Evidence Based Women's Health Journal*, 2: 27-46 (2012)

The objective of our study was to review the efficacy and safety of atosiban and nifedipine using both direct and indirect evidence. Data sources We performed electronic (e.g. MEDLINE, EMBASE, CENTRAL) and hand searches (last search August 2011) to identify randomized controlled trials (RCTs) comparing atosiban with nifedipine directly, or either drug with betamimetics, in order to allow for indirect analyses.

**Methods of study selection:** A review was conducted of published, unpublished, and ongoing RCTs comparing atosiban with nifedipine directly, or either drug with betamimetics, in pregnant women under threat of preterm labor. Tabulation, integration, and results Data were extracted for an intention-to-treat analysis, and meta-analysis was performed using a random-effects model. Data from direct and indirect evidence were combined using inverse variance. Four RCTs were identified that compared atosiban with nifedipine, with another 31 RCTs comparing either drug with betamimetics. Data for the majority of outcomes were unavailable. When evidence was available, the meta-analysis showed that there were no clear differences in the significant effects exerted by the two drugs. All safety outcomes were in favor of atosiban: there were lower incidences of adverse drug reactions, flushing, gastrointestinal tract upset, hypotension, palpitation, and tachycardia in women prescribed atosiban, with the exception of nausea, which was more frequent in such women. on combining direct and indirect evidence, we also identified a higher probability of treatment failure within 7 days of initiation of treatment (birth or alternative tocolytic therapy) and higher incidence of headache in women receiving nifedipine.

**Conclusion:** Both drugs seem to have a similar positive effect on prolongation of pregnancy; however, the safety profile of atosiban is considerably better.

**Keywords:** Atosiban; Betamimetics; Meta-analysis; Nifedipine; Preterm labor; Tocolysis.

### 191. Peer Review of Manuscripts Submitted to Medical Journals

Mohamed Abdelfattah Mahmoud Youssef

*Middle East Fertility Society Journal*, 17: 139-143 (2012)

Journal editors usually rely on the views of independent experts (peers) in making decisions on an author's scholarly work, research, or ideas and material submitted for publication. the peer reviewer serves the editor by substantiating the quality of the manuscript, and serves the author by giving constructive criticism (1). the use of peers to assess the work of fellow scientists goes back at least 200–300 years (2–6). 2. Is peer review an important process? This peer review process first and foremost serves as a powerful quality control mechanism to make sure only sound, good and interesting research to the international community is published, helps to determine novelty or originality, credibility, and clarity of data and to measure the quality of the manuscript and also provides feedback to authors, so they can improve papers that will go on to be published. in other words, the prevention of work that does not meet the standards of the field from being published, is the reviewers' responsibility. Consequently, it encourages authors to meet the accepted standards of their discipline and prevents the publication of irrelevant or faked data.

**Keywords:** Peer Review.

### 192. Can the International Index of Erectile Function Be Used as a Diagnostic Tool to the Severity of Vasculogenic Erectile Dysfunction

Abdelrahman Elnashar, Amr M. Gadallah, Alaa A. Abdelaal, Islam F. Soliman and Mohamed A.F.M. Youssef

*Middle East Fertility Society Journal*, 17: 101-104 (2012)

The objective of this observational study was to compare the International Index of Erectile Function (IIEF-5) with penile

duplex in the diagnosis of vasculogenic erectile dysfunction severity. 150 subjects complaining of erectile dysfunction for >6months have been divided into two groups according to their response to intracavernous injection (ICI) test; 50 patients who showed good response(E4) and one hundred patients who showed poor response(E4) up to maximum dose of 1cc Quadmix with abnormal penile duplex. the results of the duplex are correlated to the IIEF-5 score of the patients.

Findings ,There is statistically significant difference between mean value of IIEF-5 in both good and poor responders (P-value=0.0000), significant difference between mean value of (age, duration, PSV, EDV, diameter of artery after injection, percent of increase in arterial diameters and RI) between the good and poor responders. There was no evidence of statistically significant difference between mean value of IIEF-5 in both arteriogenic and venogenic subgroups of poor responders group. There was neither evidence of statistically significant correlations between IIEF-5 and penile duplex results in both good and poor responders groups, nor between IIEF-5 and penile duplex results in arteriogenic and venogenic and combined subgroups.

Conclusion IIEF-5 might not be a suitable diagnostic tool of the severity of vascular affection in ED.

**Keywords:** Penile Duplex; Ici; Quadmix.

### 193. Hanging Attitudes in Obstetrics and Gynecology - How Evidence Based Medicine is Changing Our Practice?

Amr Hassan Hussein EL Said Wahba

*Evidence Based Medicine -Closer to Patients or Scientists,* (2012)

The aim of this chapter is to explore different aspects of evidence based medicine including background on its development, motives towards changing our attitudes in practice and how can evidence be extracted. the chapter will also highlight the major role of evidence based medicine in changing attitudes towards evidence based practice which ensures safety and efficiency of the health service provided, in the field of obstetrics and gynecology; a domain that has greatly participated in the establishment of evidence based medicine and evidence based practice. Many examples on how evidence based medicine has changed attitudes in practice will be displayed to demonstrate and emphasize this role.

### 194. Evidence-Based Medicine: Essentials of Research Design and Methodology

Akmal El-Mazny

*Book Published by Lap Lambert Academic Publishing,* (2012)

Evidence-based medicine (EBM) aims to apply the best available research evidence to clinical decision making, and to assess the strength of evidence of the risks and benefits of treatments and diagnostic tests. in this era of evidence-based health care, both clinicians and researchers need to master EBM in order to critically appraise the medical research articles, and to judge the implications and reliability of reported results. the purposes of this book are to discuss how to practice EBM, the various types of research designs, the basic process by which research studies are conducted, and the research-related considerations such as scientific writing and research publishing. This book also offers a

fundamental knowledge of conducting and interpreting biomedical statistics, and guides researchers through the processes of data management. Finally, I hope that this book will provide the "know how" for all researchers and health-care professionals.

### 195. Hypertension in Pregnancy: Classification and Management

Akmal El-Mazny

*Book Published by Lap Lambert Academic Publishing,* (2012)

Hypertensive states during pregnancy include preeclampsia/eclampsia, gestational hypertension, chronic hypertension, and preeclampsia superimposed on chronic hypertension. Preeclampsia is a medical condition where hypertension appears in pregnancy, usually in the second or third trimester, in association with significant proteinuria. Eclampsia is a new onset of seizures in a woman with preeclampsia. Accurate preeclampsia statistics are difficult. The single most significant risk factor is having had preeclampsia in a previous pregnancy. There are many different mechanisms for preeclampsia that may cause endothelial dysfunction; with subsequent damage to the maternal endothelium, kidneys and liver. Preeclampsia is a major cause of maternal and perinatal mortality and morbidity worldwide. Intensive monitoring in women who are at increased risk may lower the incidence of adverse outcome. A pregnancy complicated by severe preeclampsia, especially at term, should be terminated; otherwise, expectant management may be indicated.

### 196. Gynecologic Endoscopy: Indications and Techniques

Akmal El-Mazny

*Book Published by Lap Lambert Academic Publishing,* (2012)

The human dream was to see the interior of the body. Endoscopy is a procedure that uses a narrow telescope to view the interior of a viscus or a preformed space. in gynecology, endoscopes are used most often to diagnose conditions by direct visualization of the peritoneal cavity (laparoscopy) or the inside of the uterus through a transcervical approach (hysteroscopy). Endoscopy has affected every area of gynecology, from diagnosis to therapy, from reproductive medicine to urogynecology and oncology. Laparoscopy is indicated mainly for the investigation of pelvic pain and subfertility, as well as the diagnosis of endometriosis and adhesions. Hysteroscopy is considered the gold standard technique for the assessment of the uterine cavity. It is essential that the surgeon fully understands all aspects of the use of endoscopic equipment; and should be aware of the potential risks of the procedure and their management.

### Dept. of Ophthalmology

### 197. Electrophysiological Assessment of Optic Nerve and Retinal Functions Following Intravitreal Injection of Bevacizumab (Avastin)

Tamer A. Macky and Mohamed M. Mahgoub

*J. Ocul Pharmacol Th.,* (2012) IF: 1.509

**Purpose:** to evaluate the retinal and optic nerve functions of bevacizumab when injected intravitreal in human eyes using

electrophysiological tests; Electroretinogram (ERG) and Visual Evoked Potentials (VEP).

**Methods:** Fifty five eyes of 55 patients with choroidal neovascular membrane (CNV) who were prepared for intravitreal injections of 1.25mg bevacizumab underwent baseline ERG and VEP in both eyes before, and at 1 and 6 weeks after the intravitreal injections.

**Results:** Mean age was 50 years ranging from 24-62 years, with 32 AMD and 23 myopic patients. Mean baseline best corrected visual acuity (BCVA) was 4/60, and mean final BCVA at 6 weeks was 6/60. There was no statistically significant reduction of the post-injection (1 and 6 weeks) ERG A and B waves or the VEP waves' amplitudes and latency, or in the contralateral non-injected eyes. on the contrary, there were statistically significant improvement at 1 and 6 weeks in the photopic B-wave of the injected and fellow eyes (p values=0.046, and <0.001).

**Conclusions:** Intravitreal bevacizumab did not appear to be toxic to the retina or the optic nerve at a concentration of 1.25 mg.

### 198. Clinical Findings, Orbital Imaging, and Intraoperative Findings in Patients with Isolated Inferior Rectus Muscle Paresis or Underaction

Ahmed Awadein

*J. Aapos*, 16:345-349: 345-349 (2012) IF: 1.028

**Purpose:** to present the clinical findings, orbital imaging, and intraoperative findings of patients with inferior rectus muscle underaction and to determine whether specific findings can help discern the underlying cause.

**Methods:** A retrospective observational study was performed on patients presenting with isolated inferior rectus muscle underaction between January 2007 and October 2011. Patient history, ocular motility, fundus torsion, Lancaster red-green plots, and radiographic findings were analyzed. for patients who had surgery, intraoperative findings also were considered.

**Results:** A total of 28 patients with inferior rectus muscle underaction were identified. of these, 13 (46%) presented with inferior rectus muscle underaction after orbital trauma; 25 (89%) showed no increase in hypertropia .4D on head tilt to either side. Fundus intorsion was present in all patients. of 15 patients evaluated by Lancaster red-green testing, 12 (80%) showed subjective intorsion. Twenty patients underwent orbital imaging via computed tomography or magnetic resonance imaging, and the results in 8 (40%) revealed obvious changes in the inferior rectus muscle. Nineteen patients underwent surgery; intraoperatively, the muscle appeared grossly normal in 8 patients (42%) and showed posterior muscle slippage in 4 (26%). Less common findings included stretched scar formation, flap tear, missing tissue, extensive muscle adhesions, or inability to identify the muscle.

**Conclusions:** Clinical findings in patients with inferior rectus muscle underaction are not sufficiently different to identify the cause, and orbital imaging identified a specific abnormality in only 40% of cases.

**Keywords:** Inferior Rectus; Trauma; Intorsion; Flap Tear; Orbital Imaging.

### 199. Comparison of Superior Oblique Suture Spacers and Superior Oblique Silicone Band Expanders

Ahmed Awadein and Ghada Gawdat

*J. Aapos*, 16:131-135: 131-135 (2012) IF: 1.028

**Purpose:** to compare suture spacers with silicone band expanders in superior oblique-weakening surgery.

**Methods:** We retrospectively reviewed the charts of consecutive patients who had superior oblique weakening with either suture spacers or silicone expanders and had been followed for a minimum follow-up of 6 months. the ductions, versions, and the degree of fundus torsion were analyzed in all patients before and after surgery. in addition, surgery time and postoperative complications were analyzed.

**Results:** the record review identified 25 patients, of whom 13 had been treated with superior oblique muscle suture spacers and 12 with superior oblique muscle silicone expanders. Both groups showed improved ductions and versions. in patients with Brown syndrome, complete normalization of superior oblique muscle overaction occurred in 67% of patients who had suture spacers and 67% of patients who had silicone expanders. in patients with A-pattern strabismus, normal function of the superior oblique muscle occurred in 75% of patients with suture spacers and 67% of patients with silicone expanders. Surgery time was significantly less in patients who had suture spacers. Severe orbital inflammation occurred in 1 patient around the silicone band and was managed by removal of the implant.

**Conclusions:** Both suture spacers and silicone expanders improved the comitance of versions and normalized superior oblique muscle function. Longer surgery time and more severe inflammatory reaction are possible drawbacks of silicone expanders.

**Keywords:** Superior oblique; Brown syndrome; Super oblique overaction; A-Pattern; Suture spacers; Silicone band expanders.

### 200. Selective Laser Trabeculoplasty in Egyptian Patients with Primary Open Angle Glaucoma

Ahmed M. Abdelrahman and Rasha M. Eltanamly

*Middle East African Journal of Ophthalmology*, 19 (3): 299-303 (2012)

**Purpose:** to assess the change in intraocular pressure(IOP) in Egyptian patients after selective laser trabeculoplasty(SLT) as a primary or adjunctive treatment for primary open angle glaucoma (POAG).

**Materials and Methods:** one hundred and six eyes with POAG were enrolled in this prospective study. Patients were divided into two groups: recently diagnosed cases with no preoperative medications (group 1) and patients with confirmed glaucoma on medical therapy (group 2).all patients underwent360 SLT.patients were evaluated to 18 months postoperatively. DAta were analysed on postoperative changes in IOP,number of medications and complications.A p value less than 0.05 was statistically significant.

**Results:** A statistically significant drop in IOP occurred, from 19.55 +/-4.8 mmHg preoperatively, to 16.03 +/-2.8 mmHg postoperatively (p< 0.001). Each group had a statistically significant drop in IOP (p<0.001). There was a statistically significant decrease in the number of medications in the number of medications in group 2 from 2.25 +/-0.97 medications

preoperatively to 1.0 +/- 1.3 medications postoperatively (p=0.004). No serious complications occurred for the duration of the study.

**Conclusion:** SLT can be safely and effectively used as primary or adjunctive therapy for the treatment of POAG.

**Keywords:** Laser; Primary open angle glaucoma; Selective laser trabeculoplasty; Treatment.

### 201. First Experience with Bak-Free Travoprost 0.004% in Topical Glaucoma Medication

Ahmed Salah Gado and Tamer Ahmed Macky

*Clinical Ophthalmology*, 6: 1-4 (2012)

Benzalkonium chloride (BAK)-free travoprost 0.004% (Travatan Z®), Alcon Laboratories, Inc, Fort Worth, TX) is a new formulation that was developed with the aim of creating a formulation of travoprost that would maintain the intraocular pressure (IOP)-lowering efficacy and have an improved overall safety profile, particularly improved ocular surface tolerability.

**Methods:** Thirty newly diagnosed primary open-angle glaucoma (POAG) patients were treated with BAK-free travoprost 0.004%. IOP readings were recorded at baseline before initiating treatment, at 4-6 weeks, and after 12 weeks of starting treatment. In addition, patient demographics, subjective symptoms (ie, burning, foreign-body sensation, itching, and stinging), and objective clinical signs such as conjunctival hyperemia were collected. Subjective symptoms were evaluated using a four-point scale ranging from "no symptoms," "mild symptoms," "moderate symptoms" to "severe symptoms." as for clinical signs, severity of conjunctival hyperemia was evaluated. All other adverse events were collected.

**Results:** BAK-free travoprost 0.004% provided an IOP decrease in all patients, with an overall mean of  $28.3 \pm 2.1$  mmHg at baseline to a mean of  $18.7 \pm 1.6$  mmHg at 4-6 weeks, and a mean of  $18.4 \pm 1.4$  mmHg after 12 weeks. Both subjective symptoms and objective clinical signs were very few after treatment.

**Conclusion:** the results demonstrate that BAK-free travoprost 0.004% is an effective, well tolerated, and safe medication in POAG patients

**Keywords:** Primary open-angle glaucoma; Poag; Benzalkonium chloride; Travatan.

### 202. Dysfunctional Tear Film, Etiology, Diagnosis, and Treatment in Oculoplastic Surgery

Mark R. Levine and Essam El Toukhy

*Smith AndNesi'S Ophthalmic Plastic and Reconstructive Surgery (Third Edition)* (2012)

Dry eye syndrome (DES) is a complex and very prevalent disease which affects more than ten million people, primarily women, in the United States alone. When you consider the number of contact lens wearers, computer users, patients who live and/or work in dirty environments, and patients with autoimmune disease, the number is certainly higher.

### Dept. of Orthopaedic

### 203. Arthroscopic Inferior Capsular Shift Long-Term Follow-Up

Basim A. Fleega and Mohamed T. El Shewy.

*the American Journal of Sports Medicine*, 40 (5): 1126-1132 (2012) IF: 3.792

Neer and Foster's open inferior capsular shift to treat acquired cases of anteroinferior shoulder instability due to an overstretched and redundant capsule is described with good results. Recently, new arthroscopic techniques were described to manage this problem.

**Purpose:** to assess the results of a new arthroscopic reinforced inferior capsular shift technique based on Neer and Foster's open inferior capsular shift.

**Study Design:** Case series; Level of evidence, 4.

**Methods:** This new technique of arthroscopic inferior capsular shift was used to treat 108 patients with anteroinferior shoulder instability due to capsular redundancy as confirmed clinically and during arthroscopy. It reduces the size of the redundant capsular pouch and reinforces the thinned-out capsule. Intraoperatively, patients with associated labral tears (n = 25) and patients with open rotator intervals (n = 8) were excluded, and only 75 patients with pure capsular redundancy were included in this study.

**Results:** Patients were followed for a minimum of 7 years. All 75 patients had patulous and redundant capsules. Three patients (4.0%) had a redislocation after a significant trauma. the range of motion preoperatively was 168.16 7.5in forward elevation, 64.76 7.9in external rotation, and T5.0 6 T0.8 in internal rotation. Postoperatively, it was 167.26 5.8in forward elevation, 59.956 4.9in external rotation, and T7.1 6 T1.0 in internal rotation. the American Shoulder and Elbow Surgeons (ASES) (70.76 to 97.53; P\0.001), Constant (90.02 to 99.24; P\0.001), and University of California, Los Angeles (UCLA) (21.97 to 33.84; P.001) scores demonstrated significant improvement postoperatively.

**Conclusion:** This novel technique of arthroscopic capsular shift addresses the problem of capsular redundancy present in many cases of anteroinferior shoulder instability. It tries to achieve a capsular shift based on the principles of Neer. the long-term results are very good.

**Keywords:** Arthroscopy; Shoulder; Dislocation; Capsular shift.

### 204. Tendon Transfer for Treatment of Internal Rotation Contracture of the Shoulder in Brachialplexus Birth Palsy

H. Abdel-Ghani, K. A. Hamdy, N. Basha and Y. N. Tarraf

*Journal of Hand Surgery (European Volume)*, 37 (8): 781-786 (2012) IF: 1.171

We retrospectively analyzed 63 patients with internal rotation contracture of the shoulder secondary to brachial plexus birth palsy treated with subscapularis sliding combined with either latissimus dorsi transfer (group A: n = 18) or latissimus dorsi and teres major transfer (group B: n = 45) to the rotator cuff. the mean age at time of surgery was 43 months (SD 21 months; range 8 months to 9 years). We used a modification of the Gilbert shoulder grading system for assessment. All patients showed statistically significant improvement of active shoulder abduction and external rotation without significant differences between the two groups. Significant external rotation contracture of the

shoulder (inability to touch the abdomen with the wrist extended) occurred in 42 of 63 patients, and there was a greater incidence of external rotation contracture in group B. We conclude that surgery should be restricted to latissimus dorsi transfer without teres major transfer to avoid external rotation contractures. Our modification of the Gilbert grading system appears to be valid and applicable.

**Keywords:** Shoulder internal rotation contracture; Brachial plexus birth palsy; Latissimus; Teres major transfer.

#### Dept. of Pathology

### 205. Virtual Microscopy Beyond the Pyramids, Applications of Wsi in Cairo University for E-Education & Telepathology

Essam Ayada and Yukako Yagib

*Anal Cell Pathol*, 34: 1-3 (2012) IF: 0.917

Telepathology, the practice of pathology at a long distance, has advanced continuously since 1986. The progress of telepathology passed through four stages: Static, Dynamic, Hybrid & Whole Slide Imaging. Materials and methods: A pilot project between the Italian Hospital in Cairo & the Civico Hospital in Palermo was completed successfully, applying the static & dynamic techniques of telepathology. This project began in 2003 and continued till now. In 2004, centers in Venice, London and Pittsburgh participated actively in our project. Results: Over eight years we consulted on many problematic pathological cases with specialized pathological centers in Italy, UK & USA. In addition to the highly specialized scientific value, we saved a lot of time and money. Conclusion: We concluded from our experience that telepathology is a very useful and applicable tool for additional consulting on difficult pathological cases especially for emerging countries. In view of this success we have already established our Digital Telepathology Unit in Cairo University, using the WSI technique in teaching which was greatly successful and encouraged us to build a huge digital pathology library which will expand our telepathology & E-learning programs to cover staff and students in Egypt and Eastern Mediterranean.

**Keywords:** Telepathology; Egypt; Cairo university; Italy; Ucdmc; Wsi; E-Learning.

#### Dept. of Pediatrics

### 206. Exome Sequencing Can Improve Diagnosis and Alter Patient Management

Tracy J. Dixon-Salazar, Jennifer L. Silhavy, Nitin Udpa, Jana Schroth, Stephanie Bielas, Ashleigh E. Schaffer, Jesus Olvera, Vineet Bafna, Maha S. Zaki, Ghada H. Abdel-Salam, Lobna A. Mansour, Laila Selim, Sawsan Abdel-Hadi, Naima Marzouk Tawfeg Ben-Omran, Nouriya A. Al-Saana, F. Mijgan Sonmez, Figen Celep, Matloob Azam, Kiley J. Hill, Adrienne Collazo, Ali G. Fenstermaker, Gaia Novarino, Naiara Akizu, Kiran V. Garimella, Carrie Sougnez, Carsten Russ, Stacey B. Gabriel and Joseph G. Gleeson

*Science Translational Medicine*, 4 (138): 1-12 (2012) IF: 7.804

The translation of "next-generation" sequencing directly to the clinic is still being assessed but has the potential for genetic diseases to reduce costs, advance accuracy, and point to

unsuspected yet treatable conditions. To study its capability in the clinic, we performed whole-exome sequencing in 118 probands with a diagnosis of a pediatric-onset neurodevelopmental disease in which most known causes had been excluded. Twenty-two genes not previously identified as disease-causing were identified in this study (19% of cohort), further establishing exome sequencing as a useful tool for gene discovery. New genes identified included EXOC8 in Joubert syndrome and GFM2 in a patient with microcephaly, simplified gyral pattern, and insulin-dependent diabetes. Exome sequencing uncovered 10 probands (8% of cohort) with mutations in genes known to cause a disease different from the initial diagnosis. Upon further medical evaluation, these mutations were found to account for each proband's disease, leading to a change in diagnosis, some of which led to changes in patient management. Our data provide proof of principle that genomic strategies are useful in clarifying diagnosis in a proportion of patients with neurodevelopmental disorders.

**Keywords:** Exome sequencing; Patient management.

### 207. Deferasirox for Up to 3 Years Leads to Continued Improvement of Myocardial T2\* in Patients with $\beta$ -Thalassemia Major

Dudley J. Pennell, John B. Porter, Maria Domenica Cappellini, Lee Lee Chan, Amal El-Beshlawy, Yesim Aydinok, Hishamshah Ibrahim, Chi-Kong Li, Vip Viprakasit, Mohsen S. Elalfy, Antonis Kattamis, Gillian Smith, Dany Habr, Gabor Domokos, Bernard Roubert and Ali Taher

*Hematologica*, 97 (6): 842-848 (2012) IF: 6.424

Prospective data on cardiac iron removal are limited beyond one year and longer-term studies are, therefore, important. Design and **Methods:** Seventy-one patients in the EPIC cardiac substudy elected to continue into the 3<sup>rd</sup> year, allowing cardiac iron removal to be analyzed over three years.

**Results:** Mean deferasirox dose during year 3 was 33.6±9.8 mg/kg per day. Myocardial T2\*, assessed by cardiovascular magnetic resonance, significantly increased from 12.0 ms ±39.1% at baseline to 17.1 ms ±62.0% at end of study (P<0.001), corresponding to a decrease in cardiac iron concentration (based on ad hoc analysis of T2\*) from 2.43±1.2 mg Fe/g dry weight (dw) at baseline to 1.80 ±1.4 mg Fe/g dw at end of study (P<0.001). After three years, 68.1% of patients with baseline T2\* 10 to <20 ms normalized (≥20 ms) and 50.0% of patients with baseline T2\* >5 to <10 ms improved to 10 to <20 ms. There was no significant variation in left ventricular ejection fraction over the three years. No deaths occurred and the most common investigator-assessed drug-related adverse event in year 3 was increased serum creatinine (n=9, 12.7%).

**Conclusions:** Three years of deferasirox treatment along with a clinically manageable safety profile significantly reduced cardiac iron overload versus baseline and normalized T2\* in 68.1% (32 of 47) of patients with T2\* 10 to <20 ms.

**Keywords:** Deferasirox; Myocardial T2; Thalassemia major; Iron chelation.

### 208. High-Throughput Mutation Analysis in Patients with A Nephronophthisis-Associated Ciliopathy Applying Multiplexed Barcoded Array-Based Pcr Amplification and Next-Generation Sequencing and Next-Generation Sequencing

Jan Halbritter, Katrina Diaz, Moumita Chaki, Jonathan D Porath, Brendan Tarrier, Clementine Fu, Jamie L Innis, Susan J Allen, Robert H Lyons, Constantinos J Stefanidis, Heymut Omran, Neveen A Soliman and Edgar A Otto

*Journal of Medical Genetics*, 49: 756-767 (2012) IF: 6.365

**Objective** to identify disease-causing mutations within coding regions of 11 known NPHP genes (NPHP1- NPHP11) in a cohort of 192 patients diagnosed with a nephronophthisis-associated ciliopathy, at low cost.

**Methods** Mutation analysis was carried out using PCR-based 48.48 Access Array microfluidic technology (Fluidigm) with consecutive next-generation sequencing. We applied a 10-fold primer multiplexing approach allowing PCR-based amplification of 475 amplicons (251 exons) for 48 DNA samples simultaneously. After four rounds of amplification followed by indexing all of 192 patient-derived products with different barcodes in a subsequent PCR, 2×100 paired-end sequencing was performed on one lane of a HiSeq2000 instrument (Illumina). Bioinformatics analysis was performed using ‘CLC Genomics Workbench’ software. Potential mutations were confirmed by Sanger sequencing and shown to segregate.

**Results** Bioinformatics analysis revealed sufficient coverage of 30× for 168/192 (87.5%) DNA samples (median 449×) and of 234 out of 251 targeted coding exons (sensitivity: 93.2%). for proof-of-principle, we analysed 20 known mutations and identified 18 of them in the correct zygosity state (90%). Likewise, we identified pathogenic mutations in 34/192 patients (18%) and discovered 23 novel mutations in the genes NPHP3 (7), NPHP4 (3), IQCB1 (4), CEP290 (7), RPGRIP1L (1), and TMEM67 (1). Additionally, we found 40 different single heterozygous missense variants of unknown significance.

**Conclusions** We conclude that the combined approach of array-based multiplexed PCR-amplification on a Fluidigm Access Array platform followed by next-generation sequencing is highly cost-efficient and strongly facilitates diagnostic mutation analysis in broadly heterogeneous Mendelian disorders.

**Keywords:** Nephronophthisis; Ciliopathy; High-throughput mutation analysis; Next-generation sequencing.

### 209. $\beta$ -Ureidopropionase Deficiency: Genotype, Phenotype and Protein Structural Consequences IN 16 Patients

André B.P. van Kuilenburg, Doreen Dobritzsch, Judith Meijer, Michael Krumpel, Laila A. Selim, Mohamed S. Rashed, Birgit Assmann, Rutger Meinsma, Bernhard Lohkamp, Tetsuya Ito, Nico G.G.M. Abeling, Kayoko Saito, Kaoru Eto, Martin Smitka, Martin Engvall, Chunhua Zhang, Wang Xu, Lida Zoetekouw and Raoul C.M. Hennekam

*Biochimica Et Biophysica Acta-Molecular Basis of Disease*, 1822: 1096-1108 (2012) IF: 5.387

$\beta$ -ureidopropionase is the third enzyme of the pyrimidine degradation pathway and Catalyse the conversion of N-carbamyl- $\beta$ - Aminobutyric acid to  $\beta$ -alanine and  $\beta$ -aminoisobutyric acid,

Ammonia and  $\text{CO}_2$ . to date, only five genetically confirmed patients with a complete  $\beta$ -ureidopropionase deficiency have been reported. Here, we report on the clinical, biochemical, and molecular findings of 11 newly identified  $\beta$ -ureidopropionase deficient patients as well as the analysis of the mutations in three dimensional framework. Patients presented mainly with neurological abnormalities (intellectual disabilities, seizures, abnormal tonus regulations, microcephaly and malformations on neuroimaging) and markedly elevated levels of N- carbamyl-  $\beta$ - Alanine and Ncarbamyl-  $\beta$  - amino isobutyric acid in urine and plasma. Analysis of UPB1 encoding  $\beta$  -ureidopropionase, showed 6 Novel Missense mutations and one novel splice- site mutation. Heterozygote expression of of the 6 mutant enzymes in *Eshreshia coli* showed that all mutations yielded mutant Bureidopropionase proteins with significant decrease activity. Analysis of homology model of human  $\beta$ - ureidopropionase generated using the crystal structure of the enzyme from *Drosophila melanogaster* indicated that the point mutations p.G235R, p.R236WAND p.S264R lead to aminoacid exchanges in the active site and therefore affect substrate binding and catalysis.. the mutation L13S, R326Q, and T359M resulted most likely in folding defects and oligomer assembly impairment. Two mutations were identified in several unrelated  $\beta$ -ureidopropionase patients, indicating that  $\beta$ -ureidopropionase deficiency may be more common than anticipated.

**Keywords:**  $\beta$ -Ureidopropionase; Up  $\beta$ 1; Neurological abnormalities; Homology modeling; Functional and structural protein analysis.

### 210. Molecular Mechanisms of Ursodeoxycholic Acid Toxicity & Side Effects: Ursodeoxycholic Acid Freezes Regeneration & Induces Hibernation Mode

Magd A. Kotb

*Int. J. Mol. Sci.*, 13: 8882-8882 (2012) IF: 2.598

Ursodeoxycholic acid (UDCA) is a steroid bile acid approved for primary biliary cirrhosis (PBC). UDCA is reported to have “hepato-protective properties”. Yet, UDCA has “unanticipated” toxicity, pronounced by more than double number of deaths, and eligibility for liver transplantation compared to the control group in 28 mg/kg/day in primary sclerosing cholangitis, necessitating trial halt in North America. UDCA is associated with increase in hepatocellular carcinoma in PBC especially when it fails to achieve biochemical response (10 and 15 years incidence of 9% and 20% respectively). “Unanticipated” UDCA toxicity includes hepatitis, pruritus, cholangitis, ascites, vanishing bile duct syndrome, liver cell failure, death, severe watery diarrhea, pneumonia, dysuria, immune-suppression, mutagenic effects and withdrawal syndrome upon sudden halt. UDCA inhibits DNA repair, co-enzyme A, cyclic AMP, p53, phagocytosis, and inhibits induction of nitric oxide synthetase. It is genotoxic, exerts aneugenic activity, and arrests apoptosis even after cellular phosphatidylserine externalization. UDCA toxicity is related to its interference with drug detoxification, being hydrophilic and anti-apoptotic, has a long half-life, has transcriptional mutational abilities, down-regulates cellular functions, has a very narrow difference between the recommended (13 mg/kg/day) and toxic dose (28 mg/kg/day), and it typically transforms into lithocholic acid that induces DNA strand breakage, it is uniquely co-mutagenic, and promotes cell transformation. UDCA beyond PBC is unjustified.

**Keywords:** Ursodeoxycholic acid; Primary biliary cirrhosis; Neonatal cholestasis; Vanishing bile duct syndrome; Toxicity; Side effects; Primary sclerosing cholangitis; Psc; Extrahepatic biliary atresia; Neonatal hepatitis.

### 211. Rare Coagulation Disorders: A Study of 70 Cases in the Egyptian Population

M. Abdelwahab and N. Khaddah

*Haemophilia*, : 1-3 (2012) IF: 2.597

Few Rare Bleeding Disorders registries (RBD) exist, none in Africa. Rare coagulation defects, such as factor (F)I, FII, FV, FV +FVIII, FVII, FX, FXI and FXIII deficiencies are transmitted as autosomal recessive traits with more prevalence in Muslim countries where consanguineous marriages are frequent. However, epidemiological information on the real distribution of these deficiencies is still limited and consequently when compared with the common bleeding disorders, most of these rare disorders are not well characterized clinically and do not have well-established treatment strategies. The clinical data of some big rare coagulation disorders registries such as the Italian, Iranian and North American have been reported.

Only several small scale studies have been reported in Africa with none to date in the Egyptian population. Aim to compare the clinical spectrum of some RBD in Egypt with other published data and to see if they behave differently in a population with many historical ethnic variations. Methods A local hospital registry was started and patients were studied over 3 years.

Assessment included detailed bleeding history, diagnostic events, clinical manifestations and treatment received. FX and FV deficiencies were classified according to the North American Rare Bleeding Disorders Registry and FVII deficiency according to the severity scoring system.

Treatment was provided according to UKHCDO guidelines in view of resource constraint and patient's previous bleeding history. Results We report the full clinical data of 70 patients, 61.4 % males and 38.6% females with the vast majority the offspring of consanguineous marriages.

Afibrinogenemia is the most prevalent constituting 28.6% of the rare coagulation disorders, FV deficiency (10 homozygous and one heterozygous) constituting 15.7% and 20% of patients had FVII deficiency (6 severe, 7 mild and 1 moderate). FX deficiency (11 homozygous and 2 heterozygous) was reported in 18.6% and FXIII deficiency in 11.4%. One patient had combined FV and FVIII deficiency and 3 had FII deficiency.

Intracranial hemorrhage occurred in 10% of our study group, joint bleeds in 12.9%, muscle bleeds in 7.1%, oral bleeding in 48.6%, epistaxis in 50%, bleeding per rectum in 17.1%, hematuria in 7.1%, post-circumcision bleeding in 14.3% and umbilical bleeding in 30% mainly in afibrinogenemia patients. Most patients received on demand therapy usually on initial presentation and 5 are on prophylactic therapy. Conclusion the prevalence of these rare coagulation deficiencies and bleeding symptoms is different in the Egyptian population than elsewhere and so further studies including bigger numbers of patients could serve as an important source for clinicians in different parts of the world in view of rarity of these conditions.

**Keywords:** Rare; Coagulation; Egypt.

### 212. Growth Charts of Down Syndrome in Egypt: A Study of 434 Children 0-36 Months of Age

Hanan H. Afifi, Mona S. Aglan, Moushira E. Zaki, Manal M. Thomas and Angie M.S. Tosson

*Am J Med Genet A*, : 2647-2655 (2012) IF: 2.391

The aim of the study was to construct new reference growth charts for weight, length and head circumference of Egyptian children with Down syndrome (DS) from birth to 36 months of age. These specific charts may be used by health professionals involved in medical, physical and developmental care of Egyptian children with Down syndrome. The study included 434 children with non-disjunction trisomy 21, 0-36 months of age.

They were 54.4% males and 45.6% females and had no concomitant chronic disease (congenital heart disease, gastrointestinal malformations, hypothyroidism, and blood disorders). Overall, 1,955 observations were performed of weight, length and head circumference. The data for each sex were divided into 37 different age groups with 1-month intervals. All measurements were taken using standardized equipments and following the international recommendations. Values were statistically analyzed and growth curves were plotted as means and standard deviations (SD). Growth measurements evaluated in all age groups of both sexes were significantly lower than those of the controls. There was a gender difference in weight, length and head circumference, males with Down syndrome had higher values. In conclusion, we suggest that these new growth charts specific for Down syndrome children may be used in optimizing direct Egyptian DS children care and in providing anticipatory guidance in term of optimal physical growth and early detection of hidden factors affecting growth.

**Keywords:** Down syndrome; Growth charts; Egyptians; Anthropometry.

### 213. Sustained Viral Response and Hematological Adverse Events During Chronic Hepatitis C Infection Treatment

Mortada El-Shabrawi and Mona Isa

*Hepatitis Monthly*, 12 (2): 122-123 (2012) IF: 2.19

Hepatitis C virus (HCV), as a causative agent of chronic liver disease, has infected approximately 175 million people (almost 3%) of the world's population; and 3 to 4 million new cases are added to this figure annually (1).

Chronic HCV infection may progress to severe outcomes in the form of cirrhosis and hepatocellular carcinoma (HCC) (2). Currently, there is no effective HCV vaccine on the horizon due to a lack of a susceptible small animal model, an absence of neutralizing antibodies, and a high degree of viral genomic diversity and mutagenicity; therefore, successful treatment of HCV infection is very much needed. A few years ago, the standard of care (SOC) for chronic HCV infection consisted of subcutaneous injection of conventional Interferon (IFN)- $\alpha$ -2, 3 times per week, plus an oral, daily dose of Ribavirin (RBV) for 24 to 48 weeks (2, 3). This therapy is not ideal because of a very low sustained virologic response [(SVR) i.e., HCV RNA undetectable 6 months after the end of treatment].

**Keywords:** Infection; Hepatitis C; Treatment.



### 214. Saliva and Sera Iga and Igg in Egyptian Giardia-Infected Children

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*Parasitol Res*, 111: 571-575 (2012) IF: 2.149

Giardiasis is a gastrointestinal infection of wide distribution that is more prevalent in childhood. Easy and rapid diagnosis of giardiasis is essential for reduction of this infection. This cross-sectional study included 62 children in which collection of saliva, stool and serum samples was performed. An enzyme-linked immunosorbent assay (ELISA) technique was evaluated to detect IgA and IgG responses in both saliva and serum samples. Twenty-two children were positive for *Giardia duodenalis* infection by direct examination of faecal specimens, 20 non-infected and 20 infected with other parasites. Salivary and serum IgA and IgG responses against *G. duodenalis* infection were significantly higher in *Giardia* parasitized than non-*Giardia* parasitized children ( $p < 0.001$ ). This concludes that specific salivary IgA may serve as a diagnostic tool and specific salivary IgG as a screening tool in monitoring the exposure of various populations to *Giardia duodenalis*. The advantage of salivary assays over serum immunoglobulin assay is being easy and noninvasive in sampling technique which is important especially for young children.

**Keywords:** Saliva; Immunoglobulin; Giardia.

### 215. Prenatal Diagnosis for Thalassaemia in Egypt: what Changed Parents' Attitude?

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*Prenatal Diag*, 32 (8): 777-782 (2012) IF: 2.106

To present the current status of the prenatal diagnosis services and results from the largest thalassaemia center in Egypt treating 3000 patients. Traditionally, prenatal diagnosis has not been successful in reducing the births of affected children in Egypt, because the majority of women undergoing prenatal diagnosis continued to have affected pregnancies.

**Methods:** Seventy-one pregnant mothers at risk for  $\beta$ -thalassaemia underwent prenatal diagnosis by chorionic villus sampling ( $n=57$ ) or amniocentesis ( $n=14$ ) between 11 to 14 weeks of gestation. Molecular characterization of fetal DNA by reverse dot blot hybridization and polymerase chain reaction-amplification refractory mutation system techniques was conducted in all cases.

**Results:** Twenty-four women (33.8%) were found to have affected fetuses; 100% of these women opted to terminate the pregnancy. The change in attitude towards termination of pregnancy was related to in-depth counseling of the religious aspects towards prenatal diagnosis and termination of pregnancy. Forty-eight women (66.2%) with normal or carrier fetuses for  $\beta$ -thal requested human leukocyte antigen typing of the fetal material to determine if the fetus was a human leukocyte antigen match for their existing thalassaemic siblings.

**Conclusion:** This study demonstrates that prenatal diagnosis is feasible and acceptable in Egypt, a Muslim country, provided an in-depth discussion, which also addresses the religious considerations of prevention, is held with the couples.

**Keywords:** Thassaemia; Prenatal diagnosis; Parents attitude; Egypt.

### 216. Mutation Analysis of *NPHS1* in a Worldwide Cohort of Congenital Nephrotic Syndrome Patients

Bugsu Ovunc, Shazia Ashraf, Virginia Vega-Warner, Detlef Bockenhauer, Neveen A. Soliman Elshakhs and g Mark Joseph

*Nephron Clinical Practice*, 120: 139-146 (2012) IF: 2.038

Congenital nephrotic syndrome (CNS) is defined as nephrotic syndrome that manifests within the first 3 months of life. Mutations in the *NPHS1* gene encoding nephrin, are a major cause for CNS. Currently, more than 173 different mutations of *NPHS1* have been published as causing CNS, affecting most exons. **Methods:** We performed mutation analysis of *NPHS1* in a worldwide cohort of 20 families (23 children) with CNS. All 29 exons of the *NPHS1* gene were examined using direct sequencing. New mutations were confirmed by demonstrating their absence in 96 healthy control individuals. **Results:** We detected disease-causing mutations in 9 of 20 families (45%). Seven of the families showed a homozygous mutation, while two were compound heterozygous. In another 2 families, single heterozygous *NPHS1* mutations were detected. Out of 10 different mutations discovered, 3 were novel, consisting of 1 splice site mutation and 2 missense mutations. **Conclusion:** Our data demonstrate that the spectrum of *NPHS1* mutations is still expanding, involving new exons, in patients from a diverse ethnic background.

**Keywords:** Mutation analysis; Congenital nephrotic syndrome; *Nphs1*.

### 217. Orphan Kidney Diseases

Neeven A. Soliman

*Nephron Clinical Practice*, 120: 194-199 (2012) IF: 2.038

Rare kidney diseases are a unique subset of renal disorders that are often termed 'orphan' as a result of a multitude of reasons: the small number of patients with the consequent lack of well-defined natural history and course of many of these diseases, limited awareness among the medical community, and finally the significant cost of developing novel therapeutics which makes many of these diseases unattractive targets for the pharmaceutical industry.

Nevertheless, in the last decade the study and clinical management of rare kidney disease patients has been the focus of many investigative efforts. In recent years we have witnessed an enormous expansion in our knowledge of the genetic nature of a number of rare kidney diseases. Moreover, the investigation of the role of genetic disruption aiming at elucidating the pathogenesis of different and complex renal diseases has helped not only in understanding the disease states, but has also given us fundamental insights into a number of kidney developmental and physiological functions.

This article will give an overview of orphan renal diseases with particular emphasis on monogenic kidney diseases. It will also focus on the classification of these diseases while highlighting a prominent example in each category.

**Keywords:** Rare diseases; Monogenic kidney diseases; Molecular genetics; Nephronophthisis; Ciliopathies; Genetic nephrotic syndrome; Podocytopathies.

### 218. Glutathione S-Transferase Gene Polymorphisms in Neonatal Hyperbilirubinemia

Eman Abdel Ghany Abdel Ghany, Nouran Fahmy Hussain and Shahira Kamal Anis Botros

*Journal of Investigative Medicine*, 60: 18-22 (2012) IF: 1.964

**Background:** Glutathione S-transferases (GSTs) are a polymorphic superfamily of multifunctional enzymes known to play an important role in the detoxification of several substances. GSTM1 and GSTT1 are present in the liver in relatively high levels. Polymorphisms of the GSTM1 and GSTT1 genes may affect ligandin functions that are important in bilirubin transportation.

**Objective:** the aim of this study was to investigate the role of GSTM1 and GSTT1 gene polymorphisms as risk factors for neonatal jaundice.

**Methods:** This study was conducted on 72 neonates with pathologic hyperbilirubinemia (bilirubin 915 mg/dL) and 112 neonates with bilirubin level less than 15 mg/dL as a control group. GSTM1 and GSTT1 genotypes were assessed by multiplex polymerase chain reaction.

**Results:** GSTM1 null genotype was significantly higher in the patient compared with control groups (P = 0.005; odds ratio = 2.43; 95% confidence interval, 1.29-4.55) and was significantly associated with higher bilirubin levels compared with the wild genotype (P < 0.001). There was no statistically significant difference in the GSTT1 genotypes between the patient and the control groups. In the patient group, total bilirubin levels did not vary significantly among the null and wild GSTT1 genotypes (P = 0.108).

**Conclusions:** Neonates with the GSTM1 null genotype are at high risk to develop pathologic hyperbilirubinemia and may have higher bilirubin levels

**Keywords:** Bilirubin; Glutathione S-Transferases (Gsts); Neonates; Jaundice.

### 219. Echocardiogram Done Early in Neonatal Sepsis: what Does it Add?

Rania H. Tomerak, Ayman A. El-Badawy, Gehan Hussein, Nermin R.M. Kamel and Abdel Rahman A. Razak

*J. Invest Med*, 680-684 (2012) IF: 1.964

**Background:** One of the major organs affected in neonatal sepsis is the heart. Echocardiogram provides real-time information on the cardiovascular performance rather than dependence on the clinical signs alone, which might lead to misjudgment. Aim of the Work: to assess left ventricular (LV) functions in septic neonates early after admission using transthoracic color Doppler Echocardiography.

**Patients and Methods:** Echocardiography was done to 30 septic and 30 nonseptic newborns who were divided among 4 groups (septic full-term, 14; septic preterm, 16; nonseptic full-term, 21; and nonseptic preterm, 9). Comparisons were made among the 4 groups using analysis of variance and post hoc test regarding the systolic function (using ejection fraction and fractional shortening), the diastolic function (using the early atrial peak/atrial peak flow velocity ratio), and the global LV function (using myocardial performance index).

**Results:** the E-wave and the early peak flow velocity/atrial peak flow velocity ratio were significantly lower in the septic neonates, whether full-term or premature, compared to their corresponding

age groups in the nonseptic newborns, suggesting LV diastolic dysfunction (P < 0.001 and P < 0.014, respectively). No difference was found in the diastolic function between the full-term and the preterm neonates whether lying within the septic group or in the nonseptic group. Myocardial performance index was significantly higher in the septic neonates who died than in the survivors (P < 0.001).

**Conclusion:** Neonatal sepsis is associated with LV diastolic dysfunction.

**Keywords:** Echocardiogram, Neonatal sepsis, E/A Ratio, Myocardial performance index, Diastolic dysfunction.

### 220. Double-Blind, Placebo-Controlled Trial on the Effect of Piracetam on Breath-Holding Spells

Happy Sawires and Osama Botrous

*Eur J Pediatr*, 171 (7): 1063-1067 (2012) IF: 1.879

Breath-holding spells (BHS) are apparently frightening events occurring in otherwise healthy children. The aim of this study was to evaluate the efficacy of piracetam in the treatment of breath-holding spells. Forty patients with BHS (who were classified into two groups) were involved in a double-blinded placebo-controlled prospective study. Piracetam was given to group A while group B received placebo. Patients were followed monthly for a total period of 4 months. The numbers of attacks/month before and monthly after treatment were documented, and the overall number of attacks/month after treatment was calculated in both groups. The median number of attacks/month before treatment in the two groups was 5.5 and 5, respectively, while after the first month of treatment, it was 2 and 5, respectively. The median overall number of attacks/month after treatment in both groups was 1 and 5, respectively.

There was a significant decline of number of attacks after piracetam treatment compared to placebo (p value < 0.001). There were no reported side effects of the piracetam throughout the study period. In conclusion, piracetam is a safe and effective drug for the treatment of breath-holding spells in children.

**Keywords:** Piracetam; Breath-holding Spells; Pallid spells.

### 221. Sleep of Children Living in Institutional Care Facilities

Maha K. Abou-Khadra

*Sleep and Breathing*, 16 (3): 887-894 (2012) IF: 1.839

Purpose to describe sleep patterns and problems among institutionalized children. Methods in this cross-sectional study, the caregivers of 118 children, aged 4-12 years from six institutional care facilities completed the Children's Sleep Habits Questionnaire (CSHQ). Results the mean ( $\pm$ SD) of night bedtime was 21:05 $\pm$ 2:52, mean morning wake-up time was 06:58 $\pm$ 0:31, mean total sleep duration was 10 $\pm$ 1.1 h, and mean night-sleep duration was 9.5 $\pm$ 0.9 h. The percentage of children who took a daytime nap was 34.7% (n=41) and the mean duration of nap was 0.5 $\pm$ 0.7 h. The most frequently reported sleep problems were bedtime resistance, daytime sleepiness and night awakening. Children with bedtime at or after 9 PM, night-sleep duration less than 10 h and daytime napping had more disturbed sleep. Conclusions Sleep problems are common among this sample of institutionalized children.

**Keywords:** Institutionalized children; Sleep patterns; Sleep.

### 222. Renal Involvement in Childhood-Onset Systemic Lupus Erythematosus in Egypt

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*Rheumatol Int.*, (2012) IF: 1.431

Lupus nephritis has been described as the most serious complication of systemic lupus erythematosus (SLE) and the strongest predictor of poor outcome. While the incidence of childhood SLE is relatively low, renal involvement appears to be more common and more severe in childhood SLE. This study aims to characterize the features and outcome of renal involvement in childhood-onset SLE based on a study of 100 Egyptian patients (mean age at diagnosis 10.1 years, range 2-17 years). Initial data regarding disease manifestations and biopsy findings were reviewed. Disease activity was assessed using SLEDAI scores. Follow-up data (mean duration 6 years) were noted regarding specific treatment, response, complications and renal survival. Initial renal involvement was present in 78 patients, including 66 with hypertension and 23 with renal impairment. Pathologically, class IV nephropathy was found in 18 patients, class V in 9 and low-grade lesions (class II-III) in 49. Twenty patients required follow-up biopsy, and all transformations were observed. SLEDAI scores significantly decreased from initial (mean  $\pm$  SD) of  $21.4 \pm 7.3$  to  $13.4 \pm 7.8$ , in association with response to therapy ( $P < 0.0001$ ). Poor response was associated with initial hypertension and renal impairment but not with initial SLEDAI score or pathological class. The projected renal survival was 82.4 and 64.7% 5 and 10 years from diagnosis. Early renal involvement in childhood SLE is common, serious and requires proper evaluation and management.

**Keywords:** Childhood; Lupus nephritis; Renal survival; Sledai score.

### 223. Study of Serum Heparin in Hereditary Hemolytic Anemias

Amal El Beshlawy, Ibrahim Alaraby, Mohamed S.E.M. Abdel Kader, Dina H. Ahmed and Hossam E.M. Abdelrahman

*Hemoglobin*, 36 (6): 555-570 (2012) IF: 1.304

The aim of this study was to assess the level of hepcidin in hereditary chronic hemolytic anemias and to correlate the serum hepcidin levels to the need for blood transfusions (frequency of blood transfusions and the serum ferritin level). Seventy pediatric patients with hereditary chronic hemolytic anemias, attending to hematology clinics of Cairo University and Misr University for Science and Technology (MUST) hospitals were the subjects of this study [53 patients with  $\beta$ -thalassemia major ( $\beta$ -TM), 10 patients with  $\beta$ -thalassemia intermedia ( $\beta$ -TI), four patients with congenital spherocytosis and three patients with sickle cell disease] (38 males and 32 females); their ages ranged from 1-14 years. Seventy normal children, age- and sex-matched, served as the control group. The results of this study revealed decreased hepcidin levels in patients (all types of congenital chronic hemolytic anemias) [mean  $\pm$  SD (standard deviation) =  $22.9 \pm 6.0$ ] compared to controls (mean  $\pm$  SD =  $132.4 \pm 16.7$ ) with highly significant statistical difference in between. Hepcidin levels were higher in  $\beta$ -TM patients (mean  $\pm$  SD =  $23.7 \pm 6.2$ ) than in  $\beta$ -TI patients (mean  $\pm$  SD =  $21.8 \pm 4.0$ ), the hepcidin to ferritin ratio was significantly less than one. In  $\beta$ -TM patients, the mean  $\pm$  SD was  $0.03 \pm 0.004$ , and in  $\beta$ -TI patients the mean  $\pm$  SD

=  $0.025 \pm 0.002$ , with highly significant statistical difference with hepcidin-to-ferritin ratios in controls being mean  $\pm$  SD =  $2.3 \pm 0.7$ . Hepcidin and hepcidin/ferritin ratios can be used as good markers of hemolytic anemia and iron overload as they have very high sensitivity (99.0 and 99.0%, respectively) and very high specificity (98.0 and 97.0%, respectively). Our findings highlight the potential usefulness of hepcidin measurement as a diagnostic tool. The use of hepcidin as an adjuvant therapy with iron chelators is important as it has a vital role in combating hemosiderosis.

**Keywords:** Hereditary hemolytic anemias; Hepcidin; thalassemia; Iron overload disorders.

### 224. Isolation of Poliovirus Shedding Following Vaccination in Children with Antibody Deficiency Disorders

Nermeen M. Galal, Laila Bassiouny, Eman Nasr and Naglaa Abdelmeguid

*Journal of Infection in Developing Countries*, 6 (12): 881-885 (2012) IF: 1.191

Prolonged excretion of oral poliovirus may occur in primary antibody deficiency states. Those patients who persistently excrete the virus may pose the risk of aiding viral propagation in the environment. This study therefore aimed to identify the potential for prolonged poliovirus shedding by patients diagnosed with congenital antibody deficiency disorders.

**Methodology:** A cohort of children later diagnosed with antibody deficiency disorders was included in the study. Patient history was taken for each participant, with emphasis on vaccination data. Laboratory investigations included immunoglobulin profiles and stool sample collection at one month intervals from each patient, with follow-up for six months. The virus isolates were detected using enzyme-linked immunosorbent assay (ELISA) and molecular reverse transcription polymerase chain reaction (RT-PCR) techniques.

**Results:** on the initial sample screens, one patient revealed excretion one for Sabin-like strain 1 (SL1) and one patient revealed excretion for Sabin like strain 2 (SL2). Only one patient continued to shed the virus (SL1) on three successive samples and on follow-up. There was no correlation between the level of immunoglobulins and duration of virus shedding.

**Conclusion:** the study demonstrates the low occurrence of prolonged vaccine polioviruses shedding in a group of children exposed to a live vaccine.

**Keywords:** Polio-Ivdpv- Immunodeficiency.

### 225. Empirical Antibiotic Treatment and the Risk of Necrotizing Enterocolitis and Death in Very Low Birth Weight Neonates

Eman A. Abdel Ghany and Aliaa A. Al

*Ann Saudi Med*, 32 (5): 521-526 (2012) IF: 1.071

Antibiotics are one of the most overused drugs in the neonatal unit. Our objective was to assess associations between the duration of the initial antibiotic course and subsequent necrotizing enterocolitis (NEC) and/or death in very low birth weight (VLBW) neonates with sterile initial postnatal culture results.

**Design and Setting:** A retrospective cohort analysis of VLBW neonates admitted to a tertiary center during the period from 1 January 2008 to 31 December 2009.

**Patients and Methods:** the study included VLBW neonates who had been inborn and admitted to the neonatal intensive care unit within the first 24 hours after birth. We used descriptive statistics to characterize the study population, and multivariate analyses to evaluate associations between therapy duration, prolonged empirical therapy, and subsequent NEC and/or death.

**Results:** of 328 VLBW neonates admitted to our center, 207 (63%) survived >5 days and received initial empirical antibiotic treatment for  $\geq 5$  days. the median duration of initial empirical antibiotic therapy was 7 days (range 5-10 days). Those neonates were more likely to be of younger gestational age, lower birth weight, and to have lower Apgar scores ( $P < .001$ ,  $.001$  and  $.017$ , respectively). Each empirical treatment day was associated with increased odds of death (OR 1.45, CI 1.24-1.69), NEC (OR 1.32, CI 1.05-1.65), and the composite measure of NEC or death (OR 2.13, CI 1.55-2.93).

**Conclusion:** the use of prolonged initial empirical antibiotic therapy in VLBW neonates with initial sterile culture results may be associated with an increased risk of NEC or death and should be used with caution.

**Keywords:** Nec; Death; Neonates; Antibiotic.

## 226. Prevalence of Hepatitis C Virus Infection and Human Immunodeficiency Virus in A Cohort of Egyptian Hemophiliac Children

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*Ann Saudi Med*, 32 (2): 200-202 (2012) IF: 1.071

The risk of blood-borne infections, especially hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infection still remains in developing countries among children receiving blood products as hemophiliacs, but the risk is not known in Egypt. the objective of this study was to detect the prevalence of HCV and HIV infection among hemophiliac children to know the magnitude of the problem and determine potential risk factors.

**Patients and Methods:** This was a cross-sectional study conducted on 100 hemophiliac children that assessed the liver clinically and by laboratory tests. All children were screened for HCV and HIV antibodies by enzyme-linked immunosorbent assay. Those with positive HCV antibody titre were tested by polymerase chain reaction (HCV-PCR).

**Results:** Forty were positive for HCV antibodies with 19 children (47.5%) HCV-PCR positive as well. the mean age, average frequency of bleeds/year, dose of replacement therapy/year and alanine aminotransferase (ALT) levels were significantly high in HCV-antibody and PCR positive patients as compared to HCV antibody and PCR negative ones. None of our patients had clinical evidence of hepatic involvement or was co-infected with HIV.

**Conclusion:** HIV infection does not appear to be a current health problem in Egyptian hemophiliac children though the prevalence of HCV infection is still high.

**Keywords:** Hiv; Hcv; Hemophilia; Egypt.

## 227. High-Flux and Low-Flux Dialysis Membranes and Levels of Intercellular Adhesion Molecule-1 and Vascular Cell Adhesion Molecule-1 in Children with Chronic Kidney Failure

Happy K Sawires, Waleed A Mohamed and Mona F Schaalan

*Iranian J. of Kidney Diseases*, 6 (5): 366-372 (2012) IF: 0.87

**Introduction:** During hemodialysis, the expression of different adhesion molecules changes, thus serving as markers of biocompatibility of dialysis membranes. Our aim was to investigate whether low-flux and high-flux dialysis membranes have different effects on the concentration of adhesion molecules and their association with leukocytes and pro-inflammatory cytokines.

**Materials and Methods:** We enrolled 80 pediatric patients on hemodialysis. Baseline levels of intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) were measured. the patients were classified into 2 groups to use either low-flux filters or high-flux filters for 3 months. at the end of the 3 months, predialysis samples were obtained for measurement of ICAM-1, VCAM-1, TNF- $\alpha$  and interleukin-1. Post-dialysis samples were collected for measurement of CBC, ICAM-1, VCAM-1, TNF- $\alpha$ , and interleukin-1. Forty volunteers were involved as a control group.

**Results:** Both TNF- $\alpha$  and IL-1 were higher in the patients compared to the control group ( $P < .001$ ). Compared to the control group, there was a significant increase in ICAM-1 and VCAM-1 ( $P < .001$ ) in both groups predialysis and postdialysis. the postdialysis increments

of ICAM-1 with the high-flux membranes were significantly less compared to the low-flux membranes ( $P < .001$ ). Serum ICAM-1 and VCAM-1 significantly correlated with TNF- $\alpha$  and interleukin-1 in all groups.

**Conclusions:** the postdialysis increments of the adhesion molecules are due to the effect of dialysis membranes, which is less with the use of high-flux filters.

**Keywords:** Dialysis membranes; Intracellular adhesion molecule-1; Vascular cell adhesion molecule -1.

## 228. The Expanded Clinical Profile and the Efficacy of Colchicine Therapy in Egyptian Children Suffering from Familial Mediterranean Fever: A Descriptive Study

Hala Salah El-Din Talaat, Mohamed Farouk Mohamed, Nihal Mohamed El Rifai and Mohamed Ali Gomaa

*Italian Journal of Pediatrics*, 38-66 (2012) IF: 0.791

Familial Mediterranean fever (FMF) is an autosomal recessive disease characterized by self-limiting recurrent attacks of fever and serosal inflammation, leading to abdominal, thoracic or articular pain.

**Objective:** to detect variable clinical presentations of different groups of FMF patients and the efficacy of colchicine therapy in treatment of these groups of FMF after one year.

**Methods:** 70 patients with already diagnosed FMF and following-up at the Rheumatology Clinic, Children's Hospital - Cairo University were enrolled. the diagnosis of FMF was determined according to Tel Hashomer criteria for FMF. All patients were subjected to a questionnaire containing detailed history, demographic status, colchicine dosage to control attacks,

clinical manifestations, history of other diseases and development of amyloidosis and a treatment regimen was developed. Then, Response to colchicine treatment was evaluated as complete, incomplete and unresponsive.

**Results:** Out of seventy patients, 40 were males (57.1%) and 30 were females (42.9%) with a male to female ratio (M:F) of 1.3:1. Fever was the most common presenting feature, followed by abdominal pain, and arthritis; these were documented in 95.7%, 94.3%, and 77.1% of cases, respectively. Mild to moderate disease severity score was detected in a significant proportion of heterozygotes and gene-negative group than the homozygotes. All patients received colchicine therapy; 22.9% of them showed complete response, 74.3% showed incomplete response and 2.9% showed no response to therapy. the mean of colchicine dose needed to control attacks was significantly lower in heterozygotes than the homozygotes. Also patients' response to colchicine therapy was significantly better in the heterozygous group.

**Conclusion:** Heterozygous patients presenting with severe phenotype should be further analyzed for less common second MEFV mutation using gene sequencing.

**Keywords:** Familial mediterranean fever; Clinical presentations; Efficacy; Colchicine.

### 229. Tracheal Colonization in Preterm Infants Supported with Nasal Continuous Positive Airway Pressure

Hany Aly, Magda Badawy, Rania H. Tomerak, Amani A. El-Kholy and Abeer S. Hamed

*Pediatr Int.*, 54: 356-360 (2012) IF: 0.626

The aim of this study was to examine endotracheal bacteriological status in premature infants who are supported by nasal continuous positive airway pressure (CPAP) without any history of tracheal intubation.

**Methods:** in this prospective study, we enrolled 60 premature infants with respiratory distress; of these, 30 were supported by CPAP without tracheal intubation, and 30 were intubated and mechanically ventilated. Infants were enrolled at a postnatal age of <24 h. Endotracheal (ET) cultures were taken at 24 h and at the 5th day of life. in the CPAP group, a suction catheter was sterilely inserted into the trachea while directly visualizing the vocal cords using a laryngoscope.

**Results:** ET cultures taken on the 1st day of life showed colonization in 7/30 (23%) in the CPAP group versus 19/30 (63%) in the mechanically ventilated group ( $P = 0.002$ ). Tracheal cultures on day 5 were positive in 5/30 (17%) and 11/30 (37%), respectively ( $P = 0.093$ ). *Klebsiella* ssp. represented the most frequently isolated organism in both groups. A positive tracheal culture at 5 days was associated with a longer duration of respiratory support in the CPAP group ( $P = 0.05$ ) but not in the ventilation group. Endotracheal culture at 5 days was associated with mortality in the ventilation group (8/11 vs 5/19,  $P = 0.02$ ), but not in the CPAP group (1/5 vs 2/25,  $P = 0.45$ ). Early endotracheal cultures did not relate with mortality in either of the groups.

**Conclusion:** the trachea of premature infants supported with CPAP is at risk for bacterial colonization. Predisposing factors, mechanisms and clinical implications of these novel findings need to be studied.

**Keywords:** Continuous positive airway pressure; Gram-negative bacilli; Pneumonia; Premature neonates; Ventilator-associated pneumonia.

### 230. Magnesium Concentrations in Acute Asthmatic Children

Maha Amin, Mohammed Abdel-Fattah and Safa S. Zaghloul

*Iranian Journal of Pediatrics*, 22 (4): 463-467 (2012) IF: 0.292

**Objective:** Magnesium (Mg) is thought to be an important element in the pathogenesis of acute asthma attacks. We hypothesized that erythrocytic Mg would be decreased during an acute asthma exacerbation. We aimed at investigating plasma and erythrocytic Mg in acute asthmatic children.

**Methods:** This case-control study included 30 Egyptian outpatients with acute asthma. Thirty healthy matched children were included as controls. All candidates had measurements of plasma and erythrocytic Mg levels before and after treatment.

**Findings:** No significant differences were detected in plasma Mg levels between cases and controls ( $1.53 \pm 0.33$  mmol/L versus  $1.67 \pm 0.50$  mmol/L respectively,  $P = 0.2$ ). However, erythrocytic Mg levels were significantly reduced in cases when compared to controls ( $1.06 \pm 0.43$  mmol/L versus  $2.57 \pm 0.59$  mmol/L respectively,  $P < 0.001$ ). Plasma Mg levels did not significantly change in acute asthmatics before and after their rescue treatment ( $1.53 \pm 0.33$  mmol/L versus  $1.68 \pm 0.31$  mmol/L respectively,  $P = 0.07$ ). in contrast, the study detected a significant increase in erythrocytic Mg levels in cases after their treatment from acute attacks ( $1.06 \pm 0.43$  mmol/L versus  $1.56 \pm 0.23$  mmol/L respectively,  $P < 0.001$ ), with significant negative correlation with severity of attack (Spearman's  $\rho = -0.647$ ,  $P < 0.001$ ).

**Conclusion:** Erythrocytic Mg levels were significantly lower during the acute asthma, and were negatively correlated with severity of exacerbation, while plasma Mg did not significantly change. Only erythrocytic Mg levels were significantly elevated after receiving rescue treatment.

**Keywords:** Asthma; Children; Erythrocytes; Magnesium.

### 231. Urinary Levels of Leukotriene E4 in Acute Asthmatic Children

Mohammed Abdel Fattah, Nehal El Rifai and Nadia Swelam

*Journal of Pediatric Sciences*, 4 (2): 1067 (2012)

Increased production of cysteinyl leukotrienes (CysLTs) within the airways causes acute asthma. Leukotriene E4 (LTE4) is a potent constricting mediator and is excreted in urine. This study hypothesized that uLTE4 levels would be increased in acute asthma in Egyptian children.

**Aim Of The Work:** the study measured urinary LTE4 (uLTE4) in children with acute asthma and compared them to a matched healthy control group.

**Patients and Methods:** the study included 40 acute Egyptian asthmatic children and 40 age- and sex-matched controls. All candidates were subjected to a complete clinical study (thorough history and physical examination), with emphasis on severity of asthma attack according to Global Initiative for Asthma Guidelines. Measurement of urinary creatinine was performed for all study candidates. Measurement of uLTE4 (pg/mg creatinine) was performed using commercial ELISA kit.

**Results:** Levels of uLTE4 were significantly higher in cases compared to controls ( $305.48 \pm 34$  pg/mg creatinine versus

175.55 ± 79 pg/mg creatinine respectively, 95% CI (17.7; 242.1), p=0.024). Levels of uLTE4 were significantly higher in cases with moderate and severe attacks in comparison to those with mild attacks. There was a significant positive correlation between severity of the attack and uLTE4 levels (Spearman's rho = 0.446, p=0.004).

**Conclusions:** Levels of uLTE4 are significantly elevated during acute asthma episodes in children. the significant direct correlation between severity of these attacks and uLTE4 levels make uLTE4 a possible marker for monitoring acute asthma exacerbations in children.

**Keywords:** Asthma; Acute; Ulte4; Children.

### 232. Pediatric Preparedness for Bioterrorism: A New Horizon in Developing Countries

Mortada El-Shabrawi, Mona Schaalán and Fetouh Hassanin

*Journal of Bioterrorism & Biodefense*, 3-11 (2012)

Bioterrorism is the threat of deliberate release of viruses, bacteria, or other germs (agents) used to cause illness or death in people, animals, or plants. These agents are typically found in nature, but it is possible that they could be intentionally changed to increase their virulence, ability to cause disease, resistance to current medicines and dissemination into the environment. These noxious biological agents can be spread through the air, through water, or in food.

**Keywords:** Pediatric preparedness; Bioterrorism.

### 233. Predictive Accuracy of Serum Hyaluronic Acid as A Non-Invasive Marker of Fibrosis in A Cohort of Multi Transfused Egyptian Children with $\beta$ -Thalassaemia Major

Mortada H.F. El-Shabrawi, Maha Y. Zein El Abedin, Naglaa Omar, Naglaa M. Kamal Sayed Abou Elmakarem, Sahar Khattab, Hussein M. El-Sayed, Ahmed El-Hennawy and Ali S.M. Ali

*Arab Journal of Gastroenterology*, 13: 45-48 (2012)

Liver disease remains a major cause of morbidity and mortality in patients with  $\beta$ -thalassaemia major ( $\beta$ -TM); therefore, its identification at an early stage is of great significance. Serum hyaluronic acid (HA) is considered as a non-invasive marker that appears early before pathological changes occur. We aim to determine the predictive accuracy of HA in detecting and staging hepatic fibrosis in  $\beta$ -TM patients.

**Patients and methods:** 30 Egyptian children with  $\beta$ -TM, and 15 age and sex-matched controls were studied. All had abdominal ultrasonography (US), measurement of serum amino-transferases (ALT, AST); hepatitis C, B and human immunodeficiency viruses (HCV, HBV, HIV) sero-markers, serum ferritin and HA. Liver biopsy was done for patients and fibrosis was scaled using Metavir scoring system and liver iron concentration (LIC) was measured.

**Results:** Twenty patients (67.7%) had sero-markers of HCV, none had HBV or HIV. Serum HA was significantly higher in patients (90.78 ± 28.79 ng/ml) compared to controls (21.1 ± 13.24 ng/ml) with p < 0.05. No difference between HCV infected and non-infected patients was detected. Positive significant correlation was detected between serum HA and stages of fibrosis by histopathology and US. No correlation was found between serum HA and age, sex, weight, height, haemoglobin level,

platelet count, AST, serum ferritin, necro-inflammatory grade, and LIC.

**Conclusions:** Serum HA is a valuable non-invasive marker that may contribute to the assessment of liver fibrosis in multi-transfused children and adolescents with  $\beta$ -TM, irrespective of concomitant HCV infection.

**Keywords:** Hyaluronic Acid; Liver Fibrosis;  $\beta$ -Thalassaemia; Liver Fibrosis.

### 234. Clinical Outcome of Children with Post Bacillus Calmette and Guerin Vaccination Complications: A Single Center Experience

Nermeen M. Galal

*World Journal of Vaccines*, 2: 50-54 (2012)

Bacillus Calmette ET Guerin (BCG) vaccine, compulsory in endemic areas, remains the only available vaccine for prevention of Tuberculosis (TB) despite its modest protective value. Complications may arise in healthy/ immunocompromized hosts.

**Methods:** Children presenting with BCG vaccine related complications in the form of lo- cal/distant complications were enrolled from 2007-2010 at Cairo University Pediatric hospital.

**Objectives:** Assess out- come of BCG related complications in a group of children with post vaccination incidents, identify risk factors for complications among vaccinated children and identify cases of underlying Primary Immunodeficiency (PID) among presenting cases.

**Results:** Fifty one eligible patients were included, forty three were proved immunocompetent, and eight had underlying primary immunodeficiency disorders. Presentations included localized axillary lymphadenopathy, cervical sinuses, granulomatous lesions and disseminated forms Faulty injection sites were strongly associated with complications (p value < 0.001). Patients without underlying PID had larger scar size and younger age at presentations (p values: 0.02, 0.0001 respectively). Resolution of lesions was observed in 97% (95% CI 97% ± 3%) of cases without underlying PID versus fatal outcome in all cases with underlying immune defects.

**Conclusion:** Local BCG related complications do not necessarily indicate underlying PID, disseminated complications are more serious and warrant further investigations. If PID is suspected, vaccination should be deferred to avoid its potentially fatal outcome.

**Keywords:** Bcg related complications; Primary immunodeficiency.

### 235. Immunophenotyping of Lymphocyte Subpopulations and Pre-Inflammatory Mediators in Neonatal Sepsis

Mostafa Zakaria and Mona Rafaat,

*Advances in Environmental Biology*, 6 (11): 2948-2952 (2012)

Sepsis is one of the major causes of neonatal morbidity and mortality. the present study was designed to elucidate the changes in the lymphocyte subsets and in the pre-inflammatory mediators; IL-6 and IL-1b in full-term neonates with sepsis Patients and methods: A prospective study was carried out at the neonatology intensive care unit of Cairo University in the period from June 2007 to June 2009 and included 96 full term neonates, classified

into 2 groups. A Septic group (n = 50) and a control group (n=46). the parameters.

**studied serially were:** complete blood count, differential WBCs, blood culture, C- reactive protein. The lymphocyte subsets including; CD3+, CD4+, CD8+, NK cells, and B cells. Also the interleukins including; IL-1b and IL-6, and the immunoglobulins (Igs) including IgA, IgG, and IgM.

**Results:** CRP, IL1-b, and IL6 were significantly higher in the sepsis group than in the control group. IL-6 > 90 pg ? ml was an excellent marker with high sensitivity and specificity. A significantly elevated absolute and percentage counts of CD19+, CD 4+ and NK cells in the septic group, while total lymphocytic count, CD3+ and CD8 + were not significantly different.

**Conclusion:** this study has shown that the combination of IL-6 with CRP can offer a good diagnostic accuracy in the detection of sepsis in neonates. NK cells are elevated in documented sepsis and it may be considered as an early diagnostic marker.

**Keywords:** Neonates; Sepsis; lymphocytes; Pre-Inflammatory Mediators; Immunop henotyping.

### 236. Correlation between Serum Insulin Growth Factor I Deficiency and Occurrence of Retinopathy of Prematurity

Mostafa Zakaria, Mansour Hassan and Mona Rafaat

*Australian Journal of Basic and Applied Science*, 6 (9): 577-582 (2012)

Retinopathy of prematurity (ROP) is a blinding disease, initiated by the lack of retinal vascular growth after preterm birth. in Vitro, lack of insulin-like growth factor I (IGF-I) prevents normal retinal vascular growth. the present study was conducted to determine if low serum IGF-I levels in premature infants is associated with a higher incidence of retinopathy and therefore may be used as a prognostic factor for the occurrence of such events. Patients and

**Methods:** A prospective study was carried out at the neonatology intensive care unit of Cairo University in the period from June 2007 to June 2009 and included forty infants the inclusion criteria were: gestational age under 32 weeks or weight at birth < 1,500 g. Twenty healthy full term infants selected randomly during the same time period constituted the control group.

**Results:** of the 40 premature babies recruited, 17 (42.5%) developed some degree of retinopathy during the course of the study, among the 17 cases of ROP diagnosed, 35% (n =6) developed stage 1 retinopathy, 47% (n =8) stage 2 and 18% (n =3) stage 3. Mean serum IGF-I values were measured at birth and at 3 weeks and were found significantly lower at birth and after 3 weeks in ROP group in comparison to normal. Moreover, infants with stage 2 ROP and sage 3 ROP showed significantly lower mean values of IGF-I than cases with stage 1 ROP.

**Conclusion:** Our study suggests that Low levels of serum IGF-I in preterm infants appears to predict an increased risk of ROP, as well as other severe perinatal morbidities associated with preterm birth. the observed relationship between ROP and lower levels of IGF1 opens up the possibility of treatment with an IGF1 substitute, especially since birth.

**Keywords:** Retinopathy; Prematurity; Insulin growth factor.

### 237. MEFV Gene Mutations in Egyptian Children with Familial Mediterranean Fever: Clinical Versus Genetic Diagnosis

Samia Salah, Mostafa Zakaria, Mona Azez and Hoda Marzouk

*Advances in Environmental Biology*, 6 (11): 2894-2900 (2012)

To determine the frequencies of MEFV gene mutations in a cohort of Egyptian patients in whom FMF was diagnosed and to explore the presence of a possible correlation between the diverse genotypes and the phenotypic expressions of the disease.

**Patients and methods:** This cross sectional study was conducted in the Rheumatology clinic, New Children Hospital, Cairo University in the period from February 2010 to February 2012. It included 61 patients with the clinical diagnosis of FMF. All patients were screened for the presence of the 3 commonest mutations: M680I, V726A and M694V. Mutations were analyzed by amplification refractory mutation system (ARMS).

**Results:** Positive mutations were found in 17 patients (27.87%). V726A gene mutation was the most frequent mutation (19.7%), followed by M680I mutation (11.5%), whereas M694V mutation was reported in one patient (1.6%). the attacks were significantly more frequent in patients with positive mutations compared to patients with negative mutations while no significant differences were observed between the 2 groups regarding the presenting symptoms. There were no significant differences between patients with positive M680I and positive V726A regarding their clinical presentations and laboratory findings. Only one of our patient with V726A gene mutation developed amyloidosis.

**Conclusion:** There is no consistency in the association between specific MEFV mutations and phenotypic features. in other words, specific FMF mutations are not the sole determinants of the disease severity nor for the development of amyloidosis. Further studies are needed to identify new MEFV mutation or MEFV- related genes and to explore the other factors behind the wide phenotypic variations of the disease.

**Keywords:** Mefv gene mutations; Familial; Mediterranean fever; Amyloidosis.

### 238. Assessment of Risk Factors of Pediatric Urolithiasis in Egypt

Mostafa Zakaria, Sherif Azab and Mona Rafaat

*Translation Andrology and Urology*, 1 (4): 209-215 (2012)

Pediatric urolithiasis is a significant medical problem, which has seen an increasing incidence in developing countries. the main objective of the present study was to investigate the clinical characteristics and the most important risk factors that contribute to stone formation in Egyptian children.

**Patients and methods:** This prospective study was carried out at the outpatient clinics of Cairo university children's hospital as well as October 6 University hospitals, between November 2008 and March 2012. One hundred and fifty children (100 males, 50 females; mean age 3.5 years; range, 1-14 years) suffering from urinary stones were included. the mean follow-up duration; 33.1 months. All patients underwent detailed medical and family histories, dietary habits and physical examination, including Growth percentiles. Laboratory investigations were performed including: complete urine analysis and culture and sensitivity tests, urine collection in 24-h to quantity urinary volume, pH, calcium, uric acid, magnesium, creatinine, oxalate and citrate. Blood samples were obtained to measure (serum creatinine,

calcium, phosphorus, uric acid level, and alkaline phosphatase and electrolyte levels, in addition to pH and pCO<sub>2</sub> values). Radio-sonographic investigation of the abdomen and pelvis was also performed.

**Results:** the commonest presentations were abdominal pain in 42 children (28%) and gross hematuria in 35 patients (23%). Urinary tract infection was the most common risk factor, 60 patients (40%) had UTI, 70% of them had recurrent infections. Genito-urinary abnormalities, as a risk factor, were detected in 38 children (25%), with vesico-urethral reflux being the commonest abnormality (18/38). Metabolic risk factors were detected in 34 children (23%) with hypercalciuria and hyperoxaluria being the commonest metabolic abnormalities. Treatments used were, ESWL in 69 patients (46%), endoscopic interventions in 40 children (27%) and open surgery in 15 children (10%). the remaining 26 children (17%) were managed conservatively

**Keywords:** Pediatric; Urolithiasis; Uti; Metabolic; Hypercalciuria.

### 239. Outpatient Blind Percutaneous Liver Biopsy in Infants and Children: Is It Safe

Mortada H. El-Shabrawi, Hanaa M. El-Karaksy, Sawsan H. Okahsa, Naglaa M. Kamal, Gamal El-Batran and Khaled A. Badr

*Saudi Journal of Gastroenterology*, 18 (1): 26-33 (2012)

We aim to investigate the safety of outpatient blind percutaneous liver biopsy (BPLB) in infants and children with chronic liver disease (CLD).

**Patients And Methods:** BPLB was performed as an outpatient procedure using the aspiration Menghini technique in 80 infants and children, aged 2 months to 14 yrs, for diagnosis of their CLD. Patients were divided into three groups: Group 1 (<1 year), group 2 (1-6 yrs), and group 3 (6-14 yrs). the vital signs were closely monitored 1 hr before biopsy, and then 1, 2, 6, and 24 hrs after biopsy. Twenty-four hours pre- and post-biopsy complete blood counts, liver enzymes, prothrombin time (PT), and abdominal ultrasonography, searching for a biopsy-induced hematoma, were done for all patients.

**Results:** No mortality or major morbidities were encountered after BPLB. the rate of minor complications was 17.5% including irritability or "pain" requiring analgesia in 10%, mild fever in 5%, and drowsiness for >6 hrs due to oversedation in 2.5%. There was a statistically significant rise in the 1-hr post-biopsy mean heart and respiratory rates, but the rise was non-significant at 6 and 24 hrs except for group 2 where heart rate and respiratory rates significantly dropped at 24 hrs. No statistically significant difference was noted between the mean pre-biopsy and the 1, 6, and 24-hrs post-biopsy values of blood pressure in all groups. the 24-hrs post-biopsy mean hemoglobin and hematocrit showed a significant decrease, while the 24-hrs post-biopsy mean total leucocyte and platelet counts showed non-significant changes. the 24-hrs post-biopsy mean liver enzymes were non-significantly changed except the 24-hrs post-biopsy mean PT which was found to be significantly prolonged, for a yet unknown reason(s).

**Conclusions:** Outpatient BPLB performed by the Menghini technique is safe and well tolerated even in infants and young children. Frequent, close monitoring of patients is strongly recommended to achieve optimal patient safety and avoid potential complications.

**Keywords:** Blind percutaneous liver biopsy; Complications; Infants; Children.

### 240. Management of Portal Hypertension in Children: A Focus on Variceal Bleeding

Mortada H.F. El-Shabrawi, Mona Isa and Naglaa M. Kamal

*Journal of Gastroenterology and Hepatology Research*, 21 1(2): 20-26 (2012)

Treatment of the primary cause of many chronic liver diseases (CLDs) may not be possible and serious complications like portal hypertension (PH) must be prevented or controlled enabling the child with CLD to live with a good quality of life. Early detection of PH is achieved by history taking, examination, imaging techniques as well as esophagogastroduodenoscopy (EGD). Primary prevention of first episode of variceal hemorrhage involves use of non-selective  $\beta$ -blocker (NSBB) and rubber band endoscopic variceal ligation (EVL).

Management of acute variceal bleeding includes effective resuscitation, prompt diagnosis, control of bleeding and prevention of complications. Prevention of secondary variceal hemorrhage is through a combination of EVL plus pharmacological therapy, other therapies include surgical porto systemic shunt (PSS) and Meso-Rex bypass.

The goal of this review is to highlight the pediatrician role in management of variceal bleeding in children with PH in order to improve their survival and avoid its life threatening complications exceeds 12 mm Hg[1]. PH associated with chronic liver disease (CLD) poses distinctive risks, including luminal gut bleeding, ascites and hepatic encephalopathy. PH can also be present in the absence of CLD in the setting of portal vein obstruction (PVO). A major cause of cirrhosis-related morbidity and mortality is the development of variceal hemorrhage, a direct consequence of portal hypertension.

Variceal hemorrhage may be lethal, although effective interventions have resulted in a threefold decrease in mortality over the past three decades. in one study mortality between 1980 and 2000 decreased from 9% to 0% in Child-Turcotte-Pugh (CTP) class A patients, from 46% to 0% in CTP B patients and from 70% to 30% in CTP C patients.

Much of this improvement has resulted from more effective interventions before, during and after a bleeding episode.

**Keywords:** Chronic Liver Disease; Portal Hypertension.

### 241. Diversity in Auxology: Between Theory and Practice

M. Hermanussen, L.S. Lieberman, V. Schöfnfeld Janewa, C. Scheffler, A. Ghosh, B. Bogin, E. Godina, M. Kaczmarek, M. El-Shabrawi, E.E. Salama, F.J. Rühli, K. Staub, U. Woitek, P. Blaha, C. Aßmann, S. van Buuren, A. Lehmann, T. Satake, H.H. Thodberg, E. Jopp, S. Kirchengast, J. Tutkuvieni, M.H. McIntyre, U. Wittwer-Backofen, J.L. Boldsen, D.D. Martin and J. Meier

*J. Biol. Clin. Anthropol.*, 160-174 (2012)

Auxology has developed from mere describing child and adolescent growth into a vivid and interdisciplinary research area encompassing human biologists, physicians, social scientists, economists and biostatisticians. the meeting illustrated the diversity in auxology, with the various social, medical, biological and biostatistical aspects in studies on child growth and development.

**Keywords:** Child growth; Adolescent growth; Child development; Height; Weight; Body mass.



### 242. Adiponectin: an Adipocyte-Derived Hormone, and its Gene Encoding in Children with Chronic Kidney Disease

Manal F Elshamaa, Samar M Sabry, Marwa M El-Sonbaty, Eman A Elghoury, Nahed Emara, Mona Raafat, Dina Kandil and Gamila Elsaaid

*Bmc Research Notes*, 5 (174): 2-8 (2012)

**Background:** the prevalence of cardiovascular disease (CVD) and inflammation is high in patients with chronic kidney disease (CKD). Adiponectin (ADPN) is an adipocytokine that may have significant anti inflammatory and antiatherosclerotic effects. Low adiponectin levels have previously been found in patients with high risk for CVD.

**Methods:** on seventy eight advanced CKD (stages 4 and 5) pediatric patients undergoing maintenance hemodialysis (MHD) or conservative treatment (CT) the following parameters were studied: body mass index, left ventricular mass index (LVMI), serum adiponectin, cholesterol, HDL cholesterol, high sensitivity C-reactive protein (hs CRP), interleukin 6 (IL6) and single-nucleotide polymorphisms (SNPs) in the ADIPOQ gene at positions 45, and 276. Seventy age- and gender-matched healthy subjects served as control subjects.

**Results:** Markedly ( $P=0.01$ ) elevated plasma adiponectin levels were observed in CKD patients, especially CT patients, compared to control subjects. The wild type of ADIPOQ 45T > G (T) allele is the main gene for patients and controls. MHD and CT patients had significantly higher frequency of the TT genotypes of +276G > T gene ( $P=0.04$ ) compared with control subjects. A significant positive correlation was observed between plasma adiponectin and IL6 level, whereas negative correlations were found between adiponectin level, cholesterol, HDL cholesterol and hs CRP. In a stepwise backward multiple regression model only IL6 ( $P=0.001$ ) was independently associated with plasma adiponectin levels. The adiponectin gene the 276 GT+TT genotypes were associated with a higher level of adiponectin.

**Conclusions:** the present study demonstrated that ADPN is related to several metabolic and inflammatory CV risk factors in a manner consistent with the hypothesis that this protein might have a protective role against these factors. We observed an association between the +276G>T SNP in the adiponectin gene and CKD in children. Genetic variation of +276 gene seemed to have a positive impact on circulating adiponectin levels in CKD patients.

**Keywords:** Adiponectin; Single Nucleotide Polymorphisms; CKD; Children; Inflammation.

### 243. Clinical Scenario of Primary Dyslipidaemia in the Paediatric Age Group; an Egyptian Experience

Rania Hosny Tomerak, Nermeen Mofteh Gala, Sawsan Hassan Abdelhady and Khaled A. Naem

*Journal of Pakistan Medical Association*, 62 (4): 321-328 (2012)

To study the frequency of occurrence of the different forms of primary dyslipidaemia, to display their various clinical presentations and their lipid profile before and six months after therapy.

**Methods:** Prospective study was conducted in the Cairo University Childrens' Hospital- Twenty primary dyslipidaemic cases were included with history taking, clinical examination, electrocardiography and echocardiography. Investigations included: Total cholesterol, total triglycerides, LDL-C and HDL-

C using enzymatic colorimetric methods, ApoA1, Apo B100 were evaluated using a Behring nephelometer. Different therapeutic modalities were offered and reassessment of laboratory tests was done every three months.

**Results:** Parents were consanguineous in 75%. Eleven cases had hypercholesterolaemia; eight had xanthoma, one had xanthelasma, two had hypo pigmentation, three had corneal arcus, one had lipaemia retinalis and six had cardiac manifestations among which one case had myocardial infarction and one case died. Three cases had hypertriglyceridaemia; three had milky plasma, two had xanthoma, two had lipaemia retinalis, one case had pancreatitis and none had cardiac manifestations. Six cases had mixed hyperlipidaemia; five had xanthoma, three had lipaemia retinalis and two had cardiac manifestations. After six months of multi-drug use, the laboratory lipid profile was unsatisfactory in majority of the cases.

**Conclusion:** Primary dyslipidaemia may present early and paediatricians should have high index of suspicion. These children should be put on early strict lipid reduction protocols to prevent complications.

**Keywords:** Paediatric cardiovascular disease; Xanthoma; Pancreatitis; Myocardial infarction.

### 244. Does Bloody Aspirate Reflect the State of Upper Gastrointestinal Mucosa in A Critically Ill Newborn?

Rania H. Tomerak, Ayman A. El Badawy, Ayman E. Eskander, and Amira H. Mahmoud

*Arab J. Gastroenterol*, 13: 130-135 (2012)

Critically ill newborns have many risk factors to develop stress related mucosal lesions (SRML). We used upper endoscopy to evaluate the presence of SRML in these neonates, to know the specificity and sensitivity of the bloody gastric aspirate to detect SRML and to identify the risk factors associated with the presence of SRML and bloody gastric aspirate.

**Patients and Methods:** This is a cross-sectional study done on 100 critically ill newborn after becoming clinically stable. SRML were diagnosed if there is hyperaemia, erosions or ulcers in the oesophagus, stomach, and/or the duodenum.

**Results:** SRML were found in 77% of neonates in the NICU though frank bloody aspirate was detected in only 22% of neonates. The presence of bloody aspirate showed low sensitivity (24.68%) and high specificity (86.96%) for the presence of SRML. The presence of bloody gastric aspirate showed a double fold risk for the presence SRML (OR=2.184, CI=0.584-8.171). Factors associated with SRML included respiratory distress ( $p=0.000$ , risk=4.006), the use of nasogastric tube ( $p=0.017$ , OR=3.281) and the use of triple antibiotics ( $p=0.001$ , risk=1.432). Factors associated with the presence of bloody gastric aspirate included the use of nasogastric tube (OR=1.629,  $p=0.000$ ) and the presence of haemostatic disorders (OR=3.143,  $p=0.039$ ). It was also associated with lower haemoglobin levels ( $p=0.000$ ).

**Conclusion:** SRML represents an under-diagnosed problem in NICUs. Absence of bloody gastric aspirate does not exclude the presence of SRML

**Keywords:** Stress related mucosal lesions; Endoscopy and newborns.

#### 245. Red Blood Cell Transfusion in Preterm Infants: Changes in Glucose, Electrolytes and Acid Base Balance

Shereen Abdelghaffar, Yasmeen Mansi, Reem Ibrahim and Dina Mohamed

*Asian Journal of Transfusion Science*, 6 (1): 36-41 (2012)

Preterm neonates comprise the most heavily transfused group of patients, and about 85% of extremely low birth weight newborns receive a transfusion by the end of their hospital stay. The aim of this study was to assess the possible metabolic effects of RBC transfusion on preterm infants, especially during the first 2 weeks of life, and its relation to blood volume.

**Materials and Methods:** This study was conducted on 40 preterm neonates with gestational age of less than or equal to 34 weeks. They received RBCs transfusion during first 2 weeks of life. Venous blood samples of infants were collected 2 to 4 hours before and 1 hour after the end of transfusion to evaluate hemoglobin (Hb) level, hematocrit, acid-base, electrolytes, and glucose status. Then, infants were classified into two main groups: those who received RBCs volume less than or 20 ml/kg and those who received RBCs volume more than 20 ml/kg.

**Results:** Infants received a mean volume of  $20.38 \pm 3.2$  ml/kg RBCs (range, 10.9 - 26.6 ml/kg) at a median age of  $9.8 \pm 3.6$  days. After transfusion, a significant increase of mean Hb ( $P < 0.001$ ), mean Hct ( $P < 0.001$ ), pH ( $P < 0.001$ ),  $pO_2$  ( $P < 0.05$ ), and a significant decrease of the  $pCO_2$  ( $41.46 \pm 8.8$  torr vs  $35.4 \pm 9.34$  torr;  $P < 0.001$ ) were observed. In addition, there was a significant increase of serum  $K^+$  ( $P < 0.001$ ), and a significant decrease of  $Ca^{+2}$  ( $P < 0.001$ ). A positive correlation was found between the  $K^+$  intake and the changes of kalemia ( $r = 0.99$ ;  $P = 0.00$ ). Furthermore, we observed an inverse correlation between the patients' calcium intake and the changes of calcemia ( $r = -0.35$ ;  $P = 0.02$ ). On comparing the changes in clinical and biochemical variables between two groups after transfusion, we observed a significant increase in mean Hb and Hct associated with a significant decrease in mean serum  $Ca^{+2}$  ( $P < 0.001$ ) in the group receiving the larger blood volume.

**Conclusion:** RBC transfusion was effective in improving anemia, oxygenation, increasing pH, and decreasing  $CO_2$  and  $Ca^{+2}$ . However, from a more clinically relevant point of view, we demonstrated the development of hyperkalemia, especially in infants with a previously borderline hyperkalemia.

**Keywords:** Transfusion; Acid; Balance; Electrolytes.

#### 246. Clinical Characterization and Nphp1 Mutations in Nephronophthisis and Associated Ciliopathies: A Single Center Experience

Neveen A Soliman, Friedhelm Hildebrandt, Edgar A Otto, Marwa M Nabhan, Susan J Allen, Ahmed M Badr, Maha Sheba, Sawsan Fadda, Ghada Gawdat and Hassan El-Kiky

*Saudi Journal of Kidney Diseases and Transplantation*, 223 (5): 1090-1098 (2012)

Nephronophthisis (NPHP) is a recessive disorder of the kidney that is the leading genetic cause of end-stage renal failure in children. Egypt is a country with a high rate of consanguineous marriages; yet, only a few studies have investigated the clinical and molecular characteristics of NPHP and related ciliopathies in the Egyptian population. We studied 20 children, from 17

independent families, fulfilling the clinical and the ultrasonographic criteria of NPHP.

Analysis for a homozygous deletion of the NPHP1 gene was performed by polymerase chain reaction on the genomic DNA of all patients. Patients were best categorized as 75% juvenile NPHP, 5% infantile NPHP, and 20% Joubert syndrome-related disorders (JSRD). The mean age at diagnosis was  $87.5 \pm 45.4$  months, which was significantly late as compared with the age at onset of symptoms,  $43.8 \pm 29.7$  months ( $P < 0.01$ ). Homozygous NPHP1 deletions were detected in six patients from five of 17 (29.4%) studied families. Our study demonstrates the clinical phenotype of NPHP and related disorders in Egyptian children. Also, we report that homozygous NPHP1 deletions account for 29.4% of NPHP in the studied families in this cohort, thereby confirming the diagnosis of type-1 NPHP. Moreover, our findings confirm that NPHP1 deletions can indeed be responsible for JSRD.

**Keywords:** Chronic Kidney Disease; Joubert Syndrome Related Disorders; Nephronophthisis; Molecular Genetic Analysis.

#### 247. Echocardiographic Study of Infants of Diabetic Mothers Versus Macrosomic Infants of Non-Diabetic Mothers - an Egyptian Experience

Nayera Attia, Mohamed Fathallah, Hebatalla Attia, Mervat El Feky, Hala El Rabei, Reham Shaker, Mohamed Farouk and Mortada El-Shabrawi

*Journal of Medicine and Biomedical Sciences*, : 0-0 (2012)

**Aim:** The infant of diabetic mother (IDM) is exposed to in-utero to a deranged metabolic milieu that might affect its heart as detected by echocardiography. This study aimed at comparing the echocardiographic findings of infants of controlled or uncontrolled gestational or pre-gestational diabetic mothers, macrosomic infants of nondiabetic mothers, and healthy full term neonates.

**Methods:** A prospective case-control study was conducted on 20 IDMs (group 1), 20 macrosomic infants of non-diabetic mothers (group 2) and 20 controls. All infants were evaluated regarding serum insulin level, and chest x-ray and echocardiographic findings in the first three days of life. Maternal glycated hemoglobin (HbA1c) was measured at or shortly after delivery.

**Results:** There was a significantly higher percentage of congenital heart diseases among IDMs as well as a significantly higher percentage among pregestational compared to gestational subgroups ( $p < 0.05$ ). Patent ductus arteriosus (PDA) was much frequently encountered in IDMs. Echocardiography revealed a significantly higher interventricular septum dimension in diastole (IVSD) in IDMs as compared to the controls ( $p < 0.05$ ). A significant negative correlation between HbA1c, end diastolic dimensions (EDD) and left atrium thickness (LA) was noted. Ejection fraction (EF%) was significantly negatively correlated with random blood sugar and significantly positively correlated with HbA1c. End systolic dimensions (ESD) were significantly negatively correlated with HbA1c in IDMs.

**Conclusion:** Maternal diabetes is associated with myocardial dysfunction in IDMs. The most common echocardiographic findings are PDA, thickened myocardium and significant septal hypertrophy. Women with good glycemic control can expect favorable pregnancy outcomes compared to the general population.

**Keywords:** Echocardiography; Infant of diabetic mothers; Macrosomia.

#### 248. Disorders of the Gallbladder and the Biliary System

Mortada El-Shabrawi

*Textbook of Clinical Pediatrics- Second Edition, 3: (2012)*

Although gallbladder and biliary tract diseases are relatively uncommon in infants and children, pediatric patients comprise a relatively big number of cholecystectomies, with a rising rate in recent years. Pediatric gallbladder stones (cholelithiasis) and bile duct stones (choledocolithiasis) are most commonly associated with hemolytic diseases or hemoglobinopathies; however, other risk factors are recognized.

Extended administration of total parenteral nutrition (TPN) support and prolonged survival after extensive bowel resection increase the risk of gallbladder disease, a cause that will likely continue to increase as survival rates improve in extremely low birth weight infants. In addition, as childhood obesity reaches near-epidemic proportions in many Western countries, gallbladder disease related to dietary factors is increasing. Gallbladder and biliary tract diseases should be in the differential diagnosis of any pediatric patient who presents with right upper quadrant pain, jaundice, or unremitting dyspepsia with normal endoscopic gastric findings.

Asymptomatic gallstones and symptomatic pigment gallstones in children are common indications for surgery. Noncalcified gallstones due to long-term cholestasis or TPN may respond to medical therapy with cholagogues such as ursodeoxycholic acid (UDCA). Aside from gallstones, the pediatric population can experience anatomical abnormalities including hydrops of the gallbladder, extrahepatic biliary atresia (EHBA), and choledochal cysts discussed below. Other anomalies as intrahepatic biliary hypoplasia, Caroli disease, perforations, and biliary dyskinesia are beyond the scope of this chapter.

#### Dept. of Pharmacology

#### 249. Effects of Topiramate on Diabetes Induced by Streptozotocin in Rats

Amani Nabil Shafik

*European Journal of Pharmacology, 684: 161-167 (2012)*

IF: 2.516

Topiramate currently approved for marketing as antiepileptic drug also possesses anti-diabetic activity. The aim of this study was to determine the antidiabetic effect of topiramate in a rat model of diabetes mellitus.

Diabetes was induced by a single injection of streptozotocin to fasted rats. Diabetic animals were divided into untreated; insulin treated; topiramate treated with 25, 50 and 100 mg/kg; and combined insulin plus topiramate treatment in the previous doses. All medications were given once daily started after the rise of blood glucose for three weeks. Control rats were divided into untreated; vehicle treated and rats given topiramate in the previous doses. Body weight, blood-glucose and insulin levels were measured.

Histopathological examination, immunohistochemical and morphometric studies of islets of the pancreas were done.

Topiramate 50 and 100 mg/kg resulted in a significant decrease in the blood glucose and increase in the insulin levels as well as the number of islets and the count and mass of beta cells. Combined treatment to diabetic rats with insulin and topiramate induced a better response than either alone. Further experimental and clinical studies are needed to explore the different mechanisms of action of topiramate as antidiabetic both in insulin dependent and non-insulin-dependent diabetes mellitus.

**Keywords:** Diabetes mellitus; Pancreatic hormone receptor; Streptozotocin; Topiramate.

#### Dept. of Physiology

#### 250. Effect of Recombinant Erythropoietin on Ischemia-Reperfusion Induced Apoptosis in Rat Liver

Heba M. Shawky, Sandra M. Younan, Leila A. Rashed and Heba Shoukry

*J. Physiol Biochem, 68: 19-28 (2012) IF: 1.711*

Ischemia reperfusion (I/R) can not be avoided in liver transplantation procedures and apoptosis is a central mechanism of cell death after liver reperfusion. Protective effect of recombinant erythropoietin (rh EPO) on liver apoptosis has not been clearly investigated.

This work investigated intraportal (i.p) rhEPO protective effect in a rat model of hepatic I/R induced apoptosis and its appropriated time and dose of administration. Eight groups were included (n=10/group): sham-operated, I/R (45 min ischemia and 2h reperfusion), preconditioned rhEPO I/R (24h or 30 min before ischemia) and post-conditioned rhEPO I/R (before reperfusion) using two different rhEPO doses (1000 and 5000 IU/Kg). When compared with the sham-operated group, the I/R group showed significant increase of serum levels of aspartate and alanine aminotransferases (AST, ALT), hepatic caspase-9 activity ( $894.99 \pm 176.90$  RFU/mg/min versus  $458.48 \pm 82.96$  RFU/mg/min) and Fas ligand (FasL) expression, histopathological damages and significant decrease in the antiapoptotic Bcl-xL/apoptotic Bax ratio ( $3.38 \pm 2.1$  versus  $3.35 \pm .77$ ). rh EPO improved ALT and AST but failed to reduce FasL expression in all groups compared to the I/R group. 30 min and 24h Preconditioning with rhEPO (1000 IU/Kg) increased Bcl-xL / Bax ratio and reduced caspase-9 activity and the same effect was observed when higher dose was given 24h before ischemia.

Preconditioning was more effective than post-conditioning in improving caspase-9 activity and no dose dependent effect was observed. In conclusion, single i.p rhEPO injection 30 min before ischemia has an advantage over rhEPO post-conditioning in improving post-hepatic I/R induced apoptosis with no additional time and dose dependent effect which may provide a potentially useful guide in liver transplantation procedures.

**Keywords:** Ischemia; Reperfusion-apoptosis; Erythropoietin.

### 251. An Evaluation of Anti-Diabetic and Anti-Lipidemic Properties of Momordica Charantia (Bitter Melon) Fruit Extract in Experimentally Induced Diabetes

Ibraheem Mohammady, Samah Elattar, Sanaa Mohammed and Madeha Ewais

*Life Science Journal*, 9 (2): 363-374 (2012) IF: 0.073

**Aim:** Momordica charantia is reported to possess hypoglycemic activity. This study aims at investigating the effect of Momordica charantia extract on glucose tolerance and some biochemical parameters in alloxan induced diabetes, comparing it to the effect of rosiglitazone maleate, an oral hypoglycemic drug, and to suggest the possible mechanisms of its action.

**Main methods:** Rats were divided into 5 groups: normal control, rats received bitter melon, diabetic control, diabetic treated with rosiglitazone (4mg/kg BW), and diabetic received Momordica charantia (300 mg/kg BW). After 4 weeks, OGTT, serum insulin, lipid profiles, glycohemoglobin% (HbA1c%), liver enzymes activity and glycogen content, intestinal absorption and diaphragm uptake of glucose and histopathological studies on the pancreas were evaluated.

**Key findings:** Bitter melon (BM) induced a significant improvement of OGTT and induced a significant decrease in HbA1c% ( $p < 0.05$ ), significantly increased insulin release from the pancreas and serum insulin level, increased glucose uptake by rat diaphragm and decreased intestinal glucose absorption ( $p < 0.05$ ). BM improved lipid profile. In addition, BM significantly increased liver glycogen content and reduced liver enzyme activity compared to the diabetic control. BM treatment of diabetic rats resulted in significant hypoglycemic and hypolipidemic effects as compared to rosiglitazone ( $p < 0.05$ ).

**Significance:** Results demonstrated anti-diabetic effects of bitter melon may be through increasing insulin release and serum insulin, increasing glucose uptake by muscles and decreasing intestinal glucose absorption and a hypolipidemic effect and this recommend its therapeutic use in diabetes.

**Keywords:** Momordica charantia; Diabetes; Glucose absorption; Rat diaphragm glucose uptake; Rosiglitazone maleate.

### 252. Nerve Conduction Velocity of Sciatic Nerve in High Fat Diet Induced Obesity in Rats: Effect of Corn Oil and Omega 3 Fatty Acids Supplement

Laila Ahmed El sayed, Samah Elattar and Nashwa Eltablawy

*Life Science Journal*, 9 (3): 2301-2314 (2012) IF: 0.073

Obesity is a major susceptibility factor leading to the development of various conditions of the metabolic syndrome. In obese rats, slowing of motor nerve conduction velocity was observed. Fatty acids metabolism disturbance is very important in the occurrence of peripheral neuropathy. The aim of this work is to consider the role that balanced diets high in omega 6&9 PUFA (corn oil) or supplying rats with omega 3, play in modulating the impaired nerve function in obese rats.

**Methods:** Thirty two adult male albino rats were randomly assigned to receive normal chow (NC) (n=8) or high fat diet HFD (n=24), for 12 weeks. After 12 weeks, body weight and body mass index (BMI) were measured and the NC group (n=8) continue their normal chow diet, Group 1 (NC) and served as a control group and the obese rats were randomly divided into 3

groups, 8 rats each: Group 2: Ob + HFD group, they continue their high animal fat diet, Group 3: Ob+HFD + corn oil group, they are obese rats received high fat diet containing corn oil and Group 4: Ob + HFD + Omega 3 group, they are obese rats, fed high animal fat diet supplemented with omega 3 (0.4 g/kg) daily. After five weeks, the final body weight was measured and BMI was calculated and blood samples were collected for measuring fasting plasma glucose level and insulin level and homeostasis model assessment of insulin resistance (HOMA-IR) test were evaluated. Plasma cholesterol, triglycerides and free fatty acids (FFAs) were measured.

The rats were then killed and sciatic nerves were carefully dissected for measuring the nerve conduction velocity (NCV). Superoxide dismutase activity (SOD), malondialdehyde (MDA) and tumor necrosis factor alpha (TNF $\alpha$ ) were estimated in the nerve tissue of the 4 groups.

**Results:** The results of this study showed a significant increase of body weight (gm) and BMI (kg/m<sup>2</sup>) in high fat diet group ( $p < 0.05$ ) after 12 weeks of the start of the diet when compared to the control group (NC).

There were significant elevations in the final weight (gm) and BMI (kg/m<sup>2</sup>), a significant elevation in insulin level ( $\mu$ IU/l) and HOMA-IR test, a significant increase in nerve malondialdehyde (MDA), and tumor necrosis factor alpha (TNF $\alpha$ ) and a significant decrease in superoxide dismutase activity (SOD) and nerve conduction velocity (NCV) (m/s) after 5 weeks of high fat diet in (Ob+HFD) group, when compared to NC group. Changing diet composition for 5 weeks in Ob+ HFD+corn oil and Ob+HFD+omega 3 groups, did not induce any significant variation in body weight, BMI, or fasting blood glucose level as compared to Ob+HFD group.

Insulin level ( $\mu$ IU/l) and HOMA-IR test were significantly decreased in Ob+ HFD+corn oil and Ob+HFD+omega 3 groups compared to Ob+HFD group. Plasma cholesterol levels (mg/dl), triglycerides (mg/dl), and free fatty acids (FFA) (mmol/l) were significantly decreased after 5 weeks diet in Ob+ HFD+corn oil or Ob+HFD+ Omega 3 groups when compared to mean values of Ob+HFD group. Tissue malondialdehyde (MDA) and tumor necrosis factor alpha (TNF $\alpha$ ) were significantly decreased but superoxide dismutase (SOD) activity was significantly increased in Ob+HFD+corn oil and Ob+HFD+omega3 groups compared to Ob+HFD. NCV (m/s) in Ob+HFD+ corn oil group was significantly increased compared to Ob+ HFD and their values in Ob+HFD+ corn oil group showed no significant variation as compared to NC group. While there was a significant increase in NCV in Ob+ HFD+Omega 3 group as compared to Ob+ HFD group, there was still a significant decrease compared to NC group.

**Conclusion:** the results of this study may have important clinical and speculative implications. Corn oil or omega 3 supplementation may be effective in obesity induced neuropathy. The mechanism of their effects is multifactorial including improving insulin sensitivity, correction of dyslipidemia, reducing oxidative stress and an anti-inflammatory effect.

This possibility should be carefully considered and examined in future trials of essential fatty acid supplementation.

**Keywords:** Nerve conduction velocity; Obesity; Oxidative stress; Inflammation; Corn oil; Omega3; Insulin resistance.

### 253. Role of Heme Oxygenase -1 Induction and Type 5 Phosphodiesterase Inhibition in Hepatic Ischemia Reperfusion Injury in Male Albino Rats

Hassan M. Eissa; Mohammad E. Saleh; Laila A. Elsayed and Hend A. Hassan

*Life Science Journal*, 9(3): 1711-1724 (2012) IF: 0.073

**Objective:** Ischemia and reperfusion (I/R) injury is a pathophysiologic process whereby hypoxic organ damage is accentuated following return of blood flow and oxygen delivery to the compromised tissue. Both hemeoxygenase producing carbon monoxide and nitric oxide synthase producing nitric oxide are involved in cytoprotection against ischemia and reperfusion. the aim of the present study was to investigate the possible hepatic cytoprotective effects of pretreatment with cobalt (III) protoporphyrin IX chloride (Copp) and sildenafil citrate during ischemia, separately and in combination on hepatic I/R injury assessed by serum alanine transaminase (ALT), a marker of hepatic IR injury, and necrotic index.

**Materials and methods:** the study was carried out using fifty male albino rats belonging to the local strain age eight weeks with body weight 165 to 200 gm. Rat were divided randomly into five groups, each included 10 rats: group I( control sham-operated), group II(hepatic I/R, ischemia for 45 minutes followed by reperfusion for 2 hours), group III(Copp pretreatment and I/R), and group IV (I/R with sildenafil injection during ischemia), and group V(Copp pretreatment and sildenafil injection during ischemia). After two hours of reperfusion following ischemia, animals were killed and blood is collected for serum ALT determination and hepatic tissues were used for determining histological evidence of hepatocellular injury assessed by necrotic index. Liver samples are also used for determining HO-1 gene expression and total hepatic nitrite content.

**Results:** Hepatic ischemia and reperfusion (group II) resulted in hepatocellular injury as revealed by significant increases ( $p < 0.05$ ) in mean value of serum levels of ALT and necrotic index. This was accompanied by significant ( $p < 0.05$ ) increases in the mean values of hepatic HO-1 gene expression and total hepatic nitrite content compared to the control group. Induction of HO-1, by pretreatment of rats with Copp (group III) resulted in hepatocellular protection as evident by significant decreases ( $p < 0.05$ ) in mean values of serum level of ALT and necrotic index. This was accompanied by significant increases in the mean values of hepatic HO-1 gene expression and insignificant change ( $p > 0.05$ ) in total hepatic nitrite content compared to group II. Sildenafil citrate injection during ischemia (group IV) also resulted in hepatocellular protection as evident by significant decreases ( $p < 0.05$ ) in mean values of serum levels of ALT and necrotic index accompanied by significant increases ( $p < 0.05$ ) in the mean values of hepatic HO-1 gene expression and total hepatic nitrite content compared to group II. Compared to group III, sildenafil injection during ischemia produced insignificant changes ( $p > 0.05$ ) in the mean value of serum level of ALT and necrotic index. However, HO-1 gene expressions was significantly ( $p < 0.05$ ) decreased while total nitrite content was significantly ( $p < 0.05$ ) increased. Compared to group II pretreatment of rats with Copp and Sildenafil injection during ischemia (group V) produced significant decreases ( $p < 0.05$ ) in the mean value of serum levels of ALT, necrotic index while hepatic HO-1 gene expression and total nitrite content were significantly ( $p < 0.05$ ) increased. Compared to group III and IV by pretreatment of rats with Copp and Sildenafil injection during

ischemia produced significant decreases ( $p < 0.05$ ) in the mean value of serum levels of ALT and necrotic index while hepatic HO-1 gene expression and total nitrite content were significantly ( $p < 0.05$ ) increased.

**Conclusion:** Induction of HO-1 gene expression and inhibition of phosphodiesterase type 5 could have synergistic hepatoprotective effects against I/R injury. Further investigations are recommended for using agents that are not hepatotoxic and can protect the liver and other organs from I/R injury.

**Keywords:** Hepatic ischemic; Reperfusion injury; Heme oxygenase-1; Nitric oxide; Phosphodiesterase Type 5 Inhibition.

### Dept. of Physiology of the nervous system - nerve disease

### 254. Feasibility and Validation of Spinal Cord Vasculature Imaging Using High Resolution Ultrasound

Foad Abd Allah, Shahram Majidi, Masaki Watanabe, Saqib A. Chaudhry and Adnan I. Qureshi

*J. Vasc Surg*, 56: 637-643 (2012) IF: 3.153

A noninvasive method of visualization of the anterior spinal artery such as ultrasound that can be utilized in emergent or intraoperative settings can reduce the risk of spinal cord ischemia.

**Objective:** We assessed the feasibility of imaging and characterizing blood flow in the anterior spinal artery using ultrasound with concurrent validation using a cadaveric model.

**Methods:** We developed a protocol for ultrasonographic assessment of anterior spinal artery based on anatomic, morphologic, and physiologic characteristics of anterior spinal artery and determined the feasibility in 24 healthy research participants using high frequency probe (3-9 MHz) through the left lateral paramedian approach in the area between T8 and T12. We ascertained the detection rate, depth of insonation, and flow parameters, including peak systolic velocity, end diastolic velocity, and resistivity indexes for both segmental arteries and anterior spinal artery within the field of insonation. We validated the anatomical landmarks using simultaneous spinal angiography and simulated anterior spinal artery flow in a cadaveric set-up.

**Results:** We detected flow in all segmental arteries at different levels of our field of insonation with mean depth (standard deviation) of insonation at 3.9 0.7 cm identified by characteristic high resistance flow pattern. Anterior spinal artery was detected in 15 (62.5%) research participants at mean depth ( standard deviation) of 6.4 1.2 cm identified by characteristic low resistance bidirectional flow. Age, gender, and body mass index were not correlated with either the detection rate or depth of insonation for anterior spinal artery. Simultaneous spinal angiography and simulated anterior spinal artery flow in a cadaveric set-up confirmed the validity of the anatomic landmarks by demonstrating concordance with results obtained from volunteer research participants.

**Conclusions:** the current study describes a technique for noninvasive imaging of spinal vasculature using ultrasound which may enhance our diagnostic capabilities in emergent and intraoperative settings.

**Keywords:** Spinal Vasculature; Ultrasound.

### 255. Role of Interleukin 6 and Alpha-Globulins in Differentiating Alzheimer and Vascular Dementias

Azza A. Helmy, Maged M. Abdel Naseer, Shahira El Shafie and Mona A.F. Nada

*Neurodegener Dis*, 9: 81-86 (2012) IF: 3.056

Inflammatory mechanisms and immune activation have been hypothesized to play a role in the pathogenesis of age-associated diseases, including Alzheimer's disease.

**Purpose:** the evaluation of inflammatory markers in patients with dementia, and to determine whether these markers can be used to differentiate between vascular dementia (VD) and Alzheimer's dementia (AD). **Patients and Methods:** Twenty demented patients (10 AD and 10 VD) and 20 non-demented controls were subjected to clinical evaluation, MRI brain scans and laboratory tests, including interleukin (IL) 6, C-reactive protein and serum protein electrophoresis.

**Results:** the results of this study revealed that serum levels of IL-6 and C-reactive protein were significantly elevated among patients with both types of dementia compared to normal elderly subjects. Although the mean IL-6 level was higher in patients with AD compared to patients with VD, this difference was not significant. the cutoff value at which the serum level of IL-6 gave maximum sensitivity and specificity was 14.25 pg/ml. Moreover, 1 - and 2 -globulins were able to discriminate between AD and VD (being significantly higher in AD).

**Conclusion:** IL-6 levels could be used to differentiate dementia from normal aging. Moreover, 1 - and 2 -globulins could differentiate between AD and VD. It can be concluded that inflammation plays an important role in both types of dementia.

**Keywords:** Alpha-1 Globulins; Alpha-2 Globulins; Alzheimer's Dementia; Inflammatory Markers; Interleukin 6; Serum Protein Electrophoresis; Vascular Dementia.

### 256. Vitamin D Deficiency in Women with Fibromyalgia in Saudi Arabia

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*Pain Medicine*, 13 (3): 452-458 (2012) IF: 2.346

The relation between low levels of 25-hydroxyvitamin D and nonspecific musculoskeletal pain, including fibromyalgia syndrome, is debatable. Many studies have reported "a positive relation" and others "found no relation." **Objectives:** to determine the prevalence of vitamin D deficiency among patients with fibromyalgia in a neurology clinic in the Kingdom of Saudi Arabia (KSA).

**Methods:** This study was done at a neurology clinic of Bugshan Hospital, Jeddah, KSA, from January to April 2011. Thirty female patients were diagnosed with fibromyalgia according to new clinical fibromyalgia diagnostic criteria; their serum vitamin D levels were screened. Vitamin D deficiency is defined as <20 ng/mL, vitamin D insufficiency is defined as 21–29 ng/mL, and vitamin D sufficiency is equal to or >30 ng/mL.

**Result:** Thirty female patients were included in the study. the mean age was 34.56 ± 8.1 years. Mean vitamin D level was 4.76 ± 1.46 ng/mL. A significant negative correlation between vitamin D level and widespread pain index was found. Thirty percent of the patients were Saudi Arabian of whom 100% were veiled; 70% were non-Saudi Arabian of whom 47.6% were veiled and 52.4% wore long pants and/or full sleeved clothes. Vitamin D deficiency was equally prevalent among veiled (4.77 ± 1.37 ng/mL) and

nonveiled (4.75 ± 1.68 ng/mL). Treatment with high-dose vitamin D resulted in clinical improvement in all patients.

**Conclusion:** Vitamin D deficiency is often seen in patients diagnosed with fibromyalgia in our population. This was equally true in veiled and nonveiled, but conservatively dressed populations. Effective treatment with high-dose vitamin D could lead to resolution of almost all symptoms. Further study of these populations and fortification of foods with vitamin D may be essential.

**Keywords:** Vitamin D; Fibromyalgia.

### 257. High Dose Erythropoietin Increases Brain Tissue Oxygen Tension in Severe Vasospasm After Subarachnoid Hemorrhage

Raimund Helbok, Ehab Shaker, Ronny Beer, Andreas Chemelli, Martin Sojer, Florian Sohm, Gregor Broessner, Peter Lackner, Monika Beck, Alexandra Zangerle, Bettina Pfausle, Claudius Thome and Erich Schmutzhard

*Bmc Neurology*, 12 (32): 2-6 (2012) IF: 2.167

Vasospasm-related delayed cerebral ischemia (DCI) significantly impacts on outcome after aneurismal subarachnoid hemorrhage (SAH). Erythropoietin (EPO) may reduce the severity of cerebral vasospasm and improve outcome, however, underlying mechanisms are incompletely understood. In this study, the authors aimed to investigate the effect of EPO on cerebral metabolism and brain tissue oxygen tension (PbtO<sub>2</sub>).

**Methods:** Seven consecutive poor grade SAH patients with multimodal neuromonitoring (MM) received systemic EPO therapy (30,000 IU per day for 3 consecutive days) for severe cerebral vasospasm. Cerebral perfusion pressure (CPP), mean arterial blood pressure (MAP), intracranial pressure (ICP), PbtO<sub>2</sub> and brain metabolic changes were analyzed during the next 24 hours after each dose given. Statistical analysis was performed with a mixed effects model.

**Results:** A total of 22 interventions were analyzed. Median age was 47 years (32–68) and 86% were female. Three patients (38%) developed DCI. MAP decreased 2 hours after intervention (P<0.04) without significantly affecting CPP and ICP. PbtO<sub>2</sub> significantly increased over time (P<0.05) to a maximum of 7 ± 4 mmHg increase 16 hours after infusion. Brain metabolic parameters did not change over time.

**Conclusions:** EPO increases PbtO<sub>2</sub> in poor grade SAH patients with severe cerebral vasospasm. the effect on outcome needs further investigation.

**Keywords:** Cerebral microdialysis; Erythropoietin; Multimodality monitoring; Subarachnoid hemorrhage.

### 258. Carotid Atherosclerosis: Socio-Demographic Issues, the Hidden Dimensions

Foad Abd-Allaha, Noha Abo-Kryshaa and Essam Balighb

*New Trends in Neurosonology and Cerebral Hemodynamics – an Update*, (2012)

The effect of conventional vascular risk factors on carotid atherosclerosis had been reported in many studies. Little is known about social and demographic issues on the development of carotid artery disease among different populations. the aim of our study is to demonstrate the prevalence of carotid atherosclerosis

among Egyptians and its difference in relations to other studies from industrialized countries.

**Methods:** We analyzed the data of 4733 Egyptian subjects who underwent extracranial carotid duplex scanning at the vascular laboratories of the largest tertiary referral hospital in Cairo from January 2003 to January 2008. Demographic and clinical data were correlated with ultrasound findings.

**Results:** Atherosclerotic carotid artery disease was present in 41% of the study population, significant and high grade disease detected in 2.5% of the study populations. Multivariate stepwise logistic regression analysis selected age, hypertension and diabetes mellitus and dyslipidemia as independent predictors of the presence of carotid atherosclerotic disease.

**Conclusion:** Hemodynamically significant extracranial atherosclerotic carotid disease is rare in Egyptians. Risk factors for carotid atherosclerosis are the same as in societies where carotid disease is more prevalent.

#### Dept. of Psychology

##### 259. Beliefs About Medications Predict Adherence to Antidepressants in Older Adults

Waleed Fawzi, Mohamed Yousry Abdel Mohsen, Abdel Hamid Hashem, Suaad Moussa, Elizabeth Coker and Kenneth C.M. Wilson

*International Psychogeriatrics*, 24 (1): 159-169 (2012) IF: 2.24

Adherence to treatment is a complex and poorly understood phenomenon. This study investigates the relationship between older depressed patients' adherence to antidepressants and their beliefs about and knowledge of the medication.

**Methods:** Assessment was under taken of 108 outpatients over the age of 55 years diagnosed with depressive disorder and treated for at least four weeks with antidepressants. Adherence was assessed using two self-report measures: the Medication Adherence Rating Scale (MARS) and a Global Adherence Measure (GAM). Potential predictors of adherence investigated included sociodemographic, medication and illness variables. In addition, 33 carers were interviewed regarding general medication beliefs.

**Results:** 56% of patients reported 80% or higher adherence on the GAM. Sociodemographic variables were not associated with adherence on the MARS. Specific beliefs about medicines, such as "my health depends on antidepressants" (necessity) and being less worried about becoming dependant on antidepressants (concern) were highly correlated with adherence. General beliefs about medicines causing harm or being overprescribed, experiencing medication side-effects and severity of depression also correlated with poor adherence. Linear regression with the MARS as the dependent variable explained 44.3% of the variance and showed adherence to be higher in subjects with healthy specific beliefs who received more information about antidepressants and worse with depression severity and autonomic side-effects.

**Conclusions:** Our findings strongly support a role for specific beliefs about medicines in adherence. Challenging patients' beliefs, providing information about treatment and discussing side-effects could improve adherence. Poor response to treatment and medication side-effects can indicate poor adherence and should be considered before switching medications.

**Keywords:** Compliance; Depression; Elderly; Side-Effects; Carers; Education; Cognition; Concordance.

#### Dept. of Public Health

##### 260. Urinary Bladder Cancer Risk Factors in Egypt: A Multicenter Case–Control Study

Yun-Ling Zheng, Sania Amr, Doa'a A. Saleh, Chiranjeev Dash, Sameera Ezzat, Nabil N. Mikhail, Iman Gouda, Iman Loay, Tamer Hifnawy, Mohamed Abdel-Hamid, Hussein Khaled, Beverly Wolpert, Mohamed A. Abdel-Aziz and Christopher Loffredo

*Cancer Epidem Biomar*, 6: 537-546 (2012) IF: 4.123

We investigated associations between tobacco exposure, history of schistosomiasis, and bladder cancer risk in Egypt.

**Methods:** We analyzed data from a case-control study (1,886 newly diagnosed and histologically confirmed cases and 2,716 age-, gender-, and residence-matched, population-based controls). Using logistic regression, we estimated the covariate-adjusted ORs and 95% confidence interval (CI) of the associations.

**Results:** Among men, cigarette smoking was associated with an increased risk of urothelial carcinoma (OR ¼ 1.8; 95% CI, 1.4–2.2) but not squamous cell carcinoma (SCC); smoking both water pipes and cigarettes was associated with an even greater risk for urothelial carcinoma (OR ¼ 2.9; 95% CI, 2.1–3.9) and a statistically significant risk for SCC (OR ¼ 1.8; 95% CI, 1.2–2.6). Among nonsmoking men and women, environmental tobacco smoke exposure was associated with an increased risk of urothelial carcinoma. History of schistosomiasis was associated with increased risk of both urothelial carcinoma (OR ¼ 1.9; 95% CI, 1.2–2.9) and SCC (OR ¼ 1.9; 95% CI, 1.2–3.0) in women and to a lesser extent (OR ¼ 1.4; 95% CI, 1.2–1.7 and OR ¼ 1.4; 95% CI, 1.1–1.7, for urothelial carcinoma and SCC, respectively) in men.

**Conclusions:** the results suggest that schistosomiasis and tobacco smoking increase the risk of both SCC and urothelial carcinoma.

**Impact:** This study provides new evidence for associations between bladder cancer subtypes and schistosomiasis and suggests that smoking both cigarettes and water pipes increases the risk for SCC and urothelial carcinoma in Egyptian men.

**Keywords:** Bladder cancer; U; Sc; Risk factors; Cigarette smoking; Waterpipe smoking; Schistosomiasis; Gender differences; Environmental tobacco smoke.

##### 261. Microscopic Observation Drug Susceptibility Assay in the Diagnosis of Multidrug-Resistant Tuberculosis

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*Int J Tuberc Lung D*, 16 (7): 941-946 (2012) IF: 2.731

**Background:** Early detection of multidrug-resistant Mycobacterium tuberculosis (MDR-TB) is of primary importance for both patient management and infection control. Optimal methods for identifying MDR-TB in a timely and affordable manner in resource-limited settings are not yet available.

**Objectives:** to evaluate the performance of a low technology but rapid drug susceptibility testing method, the microscopic observation drug susceptibility assay (MODS), in the concurrent detection of M. tuberculosis and its susceptibility to isoniazid (INH) and rifampin (RMP) directly from sputum specimens.

**Methods:** A total of 115 smear-positive TB patients admitted to

Abbasia Chest Hospital, Cairo, Egypt, were simultaneously tested using MODS and the BACTECT<sup>TM</sup> MGIT<sup>TM</sup> 960 mycobacterial detection system for the detection of *M. tuberculosis* and the identification of MDR-TB samples. RESULTS: MODS detected 112 (97.4%) samples and BACTEC MGIT detected 115 (100%) of the 115 isolates tested for susceptibility to INH, RMP and MDRTB, complete agreement between MODS and MGIT results was found among respectively 92.9%, 95.5% and 97.3% of samples. the sensitivity, specificity, and positive and negative predictive values of MODS in the detection of MDR-TB were respectively 95.3%, 98.6%, 97.6% and 97.1%. MODS results were obtained in a median of 8 days (range 5–21).

**Conclusion:** MODS is an optimal alternative method for timely and affordable identification of MDR-TB in resource-limited settings.

**Keywords:** Mycobacterium tuberculosis; Mdr-Tb; Mods; Bactec mgit 960; Egypt.

## 262. Assessment of Tobacco Dependence in Waterpipe Smokers in Egypt

Auf, R. A.; Radwan, G. N.; Loffredo, C. A.; El Setouhy, M.; Israel, E. and Mohamed, M. K

*The International Journal of Tuberculosis and Lung Disease*, 16 (1): 132-137 (2012) IF: 2.731

Waterpipe smoking is increasingly worldwide. Nevertheless, little is known about nicotine dependence in tobacco smokers who use waterpipes.

**Objective:** in the current work, we aimed to assess evidence of dependency among waterpipe smokers in Egypt who did not use cigarettes.

**Methods:** One hundred and fifty four male exclusive current waterpipe smokers were enrolled for the present study. We adapted the Fagerstrom test for nicotine dependence (FTND) and the reasons for smoking (RFS) scales and related these to smoking behaviors.

**Results:** Mean age of the subjects was 47±14 years, mean age of smoking initiation was 22±9 years, and average daily consumption was 4±8 hagers (tobacco units). Time to first smoking of the day ( $p<0.001$ ), smoking even when ill ( $p=0.003$ ), time to craving tobacco ( $p<0.001$ ), and hating to give up the first smoking of the day ( $p=0.033$ ) were each significantly associated with number of hagers smoked per day. the RFS subscales of addictive smoking, smoking to relieve negative affect, and smoking for stimulation were also associated with these variables.

**Conclusion:** the overall findings suggest that waterpipe smokers exhibit many of the same features of nicotine dependency attributed to cigarette smokers.

**Keywords:** Waterpipe smoking; Nicotine dependence; Rfs; Ftnd.

## 263. Public Opinion on Smoke-Free Policies Among Egyptians

G. N. Radwan, A. H. Emam, K. M. Maher, M. Mehrez, N. El-Sayed and G. M. El-Nahas

*Int. J. Tuberc Lung D*, 16 (10): 1412-1417 (2012) IF: 2.731

A smoke-free law was passed in 2007 and in 2010 its bylaw was issued and has led a drive to launch a smoke-free initiative by Ministry of Health and Population (MOHP) in Egypt which started in Alexandria, the second large city in Egypt.

**Objective:** to assess public opinion in regards to 100% smoke-free legislation and its implementation in Alexandria Governorate in Egypt.

**Design:** the Union Middle East Office in collaboration with the Central Agency for Public Mobilization and Statistics (CAPMAS) and the MOHP have conducted a cross sectional survey among 427 (206 males & 221 females) randomly selected adults covering the major 7 districts of Alexandria governorate.

**Results:** Almost all interviewed subjects (98%) expressed their support to the Government in enacting 100% smoke-free indoor legislation in all public places and transportation. Respondents endorsed the Government plan to implement the legislation ensuring 100% smoke-free public places. More than one third (33.5%) of all subjects indicated that they would increase the frequency of visits if the restaurants were smoke-free and 63% indicated no impact at all.

**Conclusion:** the results of the poll clearly support results concluded by different countries worldwide that smoke-free policies are popular and supported by the public.

**Keywords:** Opinion poll; Smoke-free Policies; Egypt.

## 264. An E-Learning Reproductive Health Module to Support Improved Student Learning and Interaction: A Prospective Interventional Study at A Medical School in Egypt

Rehab Abdelhai, Sahar Yassin, Mohamad F Ahmad and Uno GH Fors

*Bmc Med Educ*, 12 (11): (2012) IF: 1.152

The Public Health (PH) course at the medical college of Cairo University is based on traditional lectures. Large enrollment limits students' discussions and interactions with instructors. Aim: Evaluate students' learning outcomes measured by improved knowledge acquisition and opinions of redesigning the Reproductive Health (RH) section of the PH course into e-learning and assessing e-course utilization.

**Methods:** This prospective interventional study started with development of e-learning course covering the RH section, with visual and interactive emphasis, to satisfy students' diverse learning styles. Two student groups participated. the first received traditional lecturing, while the second volunteered to enroll in the e-learning course, taking online course quizzes. Both groups answered knowledge and course evaluation questionnaires and were invited to group discussions. Additionally, the first group answered another questionnaire about reasons for non-participation.

**Results:** Students participating in the e-learning course showed significantly better results, than those receiving traditional tutoring. Students who originally shunned the e-course expressed eagerness to access the course before the end of the academic year. Overall, students using the redesigned e-course reported better learning experiences.

**Conclusions:** an online course with interactivities and interaction, can overcome many educational drawbacks of large enrolment classes, enhance student's learning and complement pit-falls of large enrollment traditional tutoring.

**Keywords:** on-Line learning; E-Learning; Reproductive health; Public health; Medical education; Egypt.



### 265. Implementation, Barriers and Challenges of Smoke-Free Policies in Hospitals in Egypt

Ghada Nasr Radwan, Christopher A Loffredo, Rasha Aziz, Nagah Abdel-Aziz and Nargis Labib

*Bmc Research Notes*, 5 (568): 1-9 (2012)

Tobacco use is a serious public health challenge in North Africa, and health professionals play a vital role in tobacco control. In Egypt, limited data are available on the knowledge and attitudes of health care providers regarding tobacco control policies. Such data are especially relevant due to Egypt's tobacco control laws, adopted in 2007, prohibiting smoking in hospitals and other public places. This study surveyed 49 senior administrative staff, 267 physicians, 254 nurses, and 109 administrative employees working in El-Kasr El-Aini Hospital in Cairo, assessing their knowledge and attitudes regarding Egypt's tobacco control laws and barriers to their effective implementation in health care facilities. We also investigated the hospital's compliance with smoke-free policies.

**Results:** the majority (>90%) of the hospital workers knew that exposure to second-hand smoke is harmful to health. Physicians and nurses had a more favorable attitude towards the smoking ban when compared to administrative employees. Hospital staff identified the following barriers to successfully implementing the smoking ban: lax enforcement of tobacco control laws, the lack of penalties for violators, the lack of cessation programs, and the prevalence of smoking among physicians.

**Conclusions:** Overall, smoke-free policies were poorly enforced in this large teaching hospital in Cairo, Egypt. Interventions to address the identified barriers to their implementation could include the provision of cessation training and services as well as effective communication programs to educate health care workers at all levels regarding the dangers of second-hand smoke exposure and effective measures for protection.

**Keywords:** Health care staff; Fctc; Smoke-free policies.

### 266. Differential Characteristics of the Diabetes Epidemic Across Global Regions

Wasantha Jayawardene, Ahmed Youssef Agha, Samer Mattar, Nargis Labib and Mohammad Torabi

*The International Journal of Health, Wellness and Society*, 1 (4): 62-80 (2012)

This study performs a systematic review on the global distribution of diabetes, impaired glucose tolerance (IGT), and significance of risk factors for diabetes in various regions. A Medline search of articles from 1990 was conducted to identify 91 studies representing 57 countries considering year, sample characteristics, and diagnostic criteria.

Review was performed with World Health Organization classification of regions. Prevalence of diabetes was highest in Americas (14.8%), followed by Eastern-Mediterranean. Prevalence of IGT is highest in South-East Asia (12.1%), followed by Americas. Women have a higher prevalence of diabetes/IGT in many regions.

Urban areas have a higher prevalence. Undiagnosed cases are higher in developing countries. Obesity is the most potent risk factor for diabetes, followed by older age, and central-obesity. Diabetes/IGT prevalence is higher in women than in men, and diabetes prevalence is remarkably higher in urban areas than in rural areas. Primary prevention is emphasized in developing

regions. Interventions, which lead to lifestyle modifications, will reduce or delay the occurrence of diabetes. Early detection of undiagnosed cases of diabetes in developing countries is stressed.

**Keywords:** Diabetes; Impaired glucose Tolerance; Prevalence; Risk factors.

### Dept. of Rheumatology

### 267. Lichen Planus In Association With Adult-Onset Still's Disease Successfully Treated With Mycophenolate Mofetil

Yasser Emad, Yasser Ragab and Nashwa El-Shaarawy

*The Journal of Rheumatology*, 39 (6): 1305-1306 (2012) IF: 3.85

A 55-year-old woman presented with acute onset of spiking fever, symmetric polyarthritis with intense myalgia, and sore throat. Onset was associated with diffusely itchy purple papules involving the trunk, anterior chest wall, and upper and lower limbs. Initial laboratory investigations showed elevated erythrocyte sedimentation rate (90 mm/h), elevated C-reactive protein (17.8 mg/dl), negative rheumatoid factor (RF), negative anti-citrullinated protein antibody, and negative antinuclear antibody (ANA). Complete blood count showed leukocytosis with white blood cell count  $14.7 \times 10^3/\mu\text{l}$ , anemia with hemoglobin 9.6 g/dl, thrombocytosis with platelet count  $802 \times 10^3/\mu\text{l}$ , and 2-fold increase in serum ferritin levels (350 ng/ml, normal values up to 150 ng/ml). Other laboratory investigations showed elevated liver enzymes [aspartate transaminase 69 IU/l, alanine transaminase 125 IU/l, and elevated creatine phosphokinase (CPK) levels 320 IU/l, normal 40–120 IU/l] with negative virology screening for viral hepatitis. Skin biopsy showed focal thinning of the epidermis with focal destruction of basal layers and focal dermal mononuclear infiltrate, features consistent with the diagnosis of lichen planus (LP; Figure 1). No history of medications known to induce LP was given by the patient. The case fulfilled the Yamaguchi criteria for classification of adult-onset Still's disease (AOSD) 1, with the presence of 3 major criteria (spiking fever, arthritis, and leukocytosis) and 3 minor criteria (sore throat, liver dysfunction, and negative ANA and RF).

### 268. Knee Enthesitis and Synovitis on Magnetic Resonance Imaging in Patients with Psoriasis Without Arthritic Symptoms

Yasser Emad, Yasser Ragab, Tamer Gheita, Ashraf Anbar, Hoda Kamal, Ahmed Saad, Hanan Darweesh, Nashwa El-Shaarawy, Amr Azab, Ahmed Ismail, Johannes J. Rasker and Knee Enthesitis

*The Journal of Rheumatology*, 39 (10): 1979-1986 (2012)

IF: 3.695

This case-control study was designed to evaluate magnetic resonance imaging (MRI) findings of knee joints in patients with psoriasis without clinical peripheral or axial joint involvement, and to correlate MRI findings with disease and demographic variables.

**Methods:** in total 48 patients with psoriasis and no clinical evidence of synovitis or enthesitis in any peripheral or axial joints were enrolled. A random sample of 20 healthy subjects without knee or other joint complaints and matched for age and sex served as controls. All patients and controls

underwent enhanced MRI studies of both knee joints, and MRI findings were compared.

**Results:** Among 48 patients (96 knees), a total of 90 enthesal lesions were detected, with no enthesitis in 2 cases (6.3%). Signs of continuing inflammation bilaterally were frequently found: soft tissue edema (STE; n = 52), bone marrow edema (BME; n = 20), perienthesal BME (n = 3), cartilaginous erosions (n = 42), and bone erosions (n = 27). In controls, 2 (10%) subjects had BME and another 5 (25%) showed cartilaginous erosions. None showed evidence of enthesitis. Significant correlations were observed between the number of enthesal lesions of both knees vs. STE (present vs. absent;  $r = 0.314$ ,  $p = 0.030$ ) and STE (number of lesions;  $r = 0.351$ ,  $p = 0.014$ ). Enthesitis (unilateral vs. bilateral) was significantly and positively correlated with STE ( $r = 0.304$ ,  $p = 0.036$ ), cartilaginous erosions ( $r = 0.304$ ,  $p = 0.036$ ), and villous projections ( $r = 0.347$ ,  $p = 0.016$ ).

**Conclusion:** Subclinical synovitis and enthesitis are frequently found in the knee joint of patients with psoriasis. These may be an early sign of psoriatic arthritis.

**Keywords:** Knee enthesitis; Enhanced magnetic resonance imaging; Psoriasis; Subclinical synovitis; Seronegative spondyloarthropathy.

### 269. Giant Intraosseous Synovial Cyst with Intraarticular Communication with the Ankle Joint in Longstanding Rheumatoid Arthritis

Yasser Emad Amin, Yasser Ragab, Nashwa El-Shaarawy and Ahmed Kamal

*The Journal of Rheumatology*, 39 (1): 180-181 (2012) IF: 3.695

The term "intraosseous synovial cyst" is used to designate the epiphyseal cyst-like lesions seen in a variety of clinical settings. Extraarticular synovial cysts in rheumatoid arthritis (RA) have rarely been documented in case reports. The same is true for giant intraosseous synovial cysts with intraarticular communication. We describe an adult case of RA with uncontrolled disease, involving a giant intraosseous synovial cyst in the lower end of the tibia and communicating with the ankle joint. A 56-year-old woman with longstanding aggressive RA presented with chronic pain around the ankle joint of 6 months' duration. After control of synovitis with a combination of disease-modifying antirheumatic drugs, the patient still complained of pain around the right ankle and the lower end of the tibia. Magnetic resonance imaging (MRI) was done to further evaluate the cause of the pain. A contrast-enhanced MRI study showed evidence of a giant intraosseous synovial cyst at the lower end of the tibia and other evidence of destructive changes in the ankle joint in the form of erosive bone changes and hypertrophic synovial membrane.

**Keywords:** Giant Intraosseous Synovial Cyst; Rheumatoid Arthritis.

### 270. Plasma Concentrations of Growth Arrest Specific Protein 6 and the Soluble Form of Its Tyrosine Kinase Receptor Axl in Patients with Systemic Lupus Erythematosus and Behçets Disease

Tamer A. Gheita, Iman H. Bassyouni and Rasha H. Bassyouni

*J. Clin Immunol*, 32: 1279-1286 (2012) IF: 3.077

Purpose the aim of the present study was to investigate plasma concentrations of Gas6 and its soluble tyrosine kinase receptor sAxl in Systemic lupus erythematosus (SLE) and Behçets disease

(BD) patients and to correlate those levels with clinical and laboratory manifestations of the diseases. Methods the study included 89 female SLE and 49 male BD patients. Twenty-seven age and sex matched healthy volunteers served as controls. All patients were subjected to full clinical examination, laboratory investigations and assessment of disease activity. Plasma concentrations of Gas6 and sAxl were quantified using ELISA technique. Results the level of Gas6 and Axl were significantly altered in the SLE patients ( $p < 0.001$ ) and in the BD patients ( $p = 0.001$  and  $0.04$  respectively) compared to those of the control. In SLE, the Gas6 was remarkably lower in those with class 1 lupus nephritis and in those with neuropsychiatric manifestations. In the BD patients, the level of Axl was significantly increased in those with neurological disease activity. The number of lymphocytes significantly negatively correlated with the Gas6 and Axl levels significantly correlated with the number of neutrophils and negatively with the lymphocytic count in the BD patients. Conclusion the plasma concentrations of Gas6 and Axl were significantly altered in SLE and BD patients, suggesting that the Axl receptor shedding is an active process affected by and influences Gas6-mediated Axl signaling in both diseases. Special attention is required in SLE patients with early lupus nephritis and neuropsychiatric manifestations and BD patients presenting with neurological disease activity. The relation with lymphocytes and neutrophils in BD throws light on the role of Gas6 and Axl on their known resistance to cell death. Although the mechanisms responsible for the initiation of BD remain to be clarified, the role of the apoptotic process seems critical throughout the disease.

**Keywords:** Growth arrest specific protein 6 (Gas6); Tyrosine kinase receptor axl; Systemic lupus erythematosus (Sle); Behçets disease.

### 271. Elevated Serum Osteopontin Levels in Chronic Hepatitis C Virus Infection: Association with Autoimmune Rheumatologic Manifestations

Iman H. Bassyouni, Rasha H. Bassyouni, Nermin H. Ibrahim and Ahmed F. Soliman

*J. Clin Immunol*, 32: 1262-1269 (2012) IF: 3.077

Owing to the suggested role of osteopontin (OPN) in inflammation, autoimmunity and fibrosis, we investigated their serum concentrations in chronic hepatitis C virus (HCV) infected patients with and without autoimmune manifestations and correlated those levels to clinical manifestations and the histological severity of hepatic fibrosis. A total of 70 chronic HCV-infected patients (35 with and 35 without autoimmune rheumatic manifestations) were compared with 35 healthy volunteers matched for age and gender. Epidemiological, clinical, immunochemical and virological data were prospectively collected. OPN serum levels were assessed by an Enzyme Linked Immunosorbant Assay.

The mean serum OPN levels were higher in HCV patients with autoimmune rheumatologic manifestations and in patients without; than that for the normal controls ( $p = 0.000$ ). The mean OPN values progressively increased by increasing severity of liver fibrosis ( $p = 0.009$ ). Multivariate analysis revealed that the presence of rheumatologic manifestations had the highest predictive value ( $b = 7.141$ ,  $\text{Beta} = 0.414$ ,  $p = 0.000$ ) followed by liver fibrosis ( $b = 4.522$ ,  $\text{Beta} = 0.444$ ,  $p = 0.000$ ) on the variation of OPN levels in our HCV patients. Among the group of patients with HCV and rheumatologic involvement, OPN serum levels were higher in patients with positive cryoglobulin and rheumatoid

factor than in those without, and with systemic vasculitis than in those without. Correlation analysis didn't reveal any statistical significance of OPN with age, serum albumin, aminotransferases and viral load. Our data suggests OPN as a promising marker for HCV associated autoimmune rheumatologic involvement, particularly with regard to development of vasculitis and cryoglobulinemia. In addition, it could serve as a biomarker to evaluate the severity of liver damages in HCV infected subjects.

**Keywords:** Osteopontin; Autoimmunity; Hepatitis C Virus; Liver fibrosis.

### 272. Clinical Significance of Soluble-Endoglin Levels in Systemic Lupus Erythematosus: Possible Association with Anti-Phospholipid Syndrome

H Bassyouni, R El-Shazly, GS Azkalany, A Zakaria and RH Bassyouni

*Lupus*, 21: 1565-1570 (2012) IF: 2.337

**Aim:** the pathogenic role of soluble endoglin (s-Eng), as an anti-angiogenic protein, has largely been demonstrated in various vascular disorders. Our aim was to assess, in a cross sectional study, plasma levels of s-Eng in systemic lupus erythematosus (SLE) patients and its relation with the disease characteristics'.

**Patients and methods:** Plasma from 86 patients with SLE and 36 normal healthy subjects were assayed for s-Eng levels by Enzyme Linked Immunosorbant Assay (ELISA). Demographic, clinical, autoantibodies and serological data were prospectively assessed. Disease activity was assessed by total SLE disease activity index score.

**Results:** in our SLE patients, the levels of s-Eng were comparable between SLE patients and the control group. However, these levels were significantly associated with anti-phospholipid syndrome (APS). In addition, s-Eng levels were significantly associated with anti-phospholipids antibodies in our studied population. On the other hand, we did not find significant differences in mean plasma s-Eng levels in relation to disease activity, other organ system involvement or the presence of anti-dsDNA.

**Conclusion:** Our preliminary data indicated the importance of s-Eng in a special subgroup of SLE patients associated with secondary APS. An additional prospective large scale, longitudinal study should be carried out to support these findings.

**Keywords:** Angiogenesis; Anti-Phospholipid Syndrome; Endoglin; Pulmonary Artery Hypertension; Systemic Lupus Erythematosus.

### 273. Evaluation of Microalbuminuria in Patients with Systemic Sclerosis as an Indicator of Early Renal Damage and Increased Morbidity

Somaya A. Hussien, Doaa Abbas Eid, Manal M. Kamal and Doaa H. Sayed

*The Egyptian Rheumatologist*, 34: 19-25 (2012) IF: 2

Renal involvement and systemic vascular damage have been shown to be significantly affecting prognosis in systemic sclerosis.

**Aim of work:** Microalbuminuria detection in SSc patients as an indicator of early renal involvement and its correlation with various SSc clinical, laboratory parameters and severity of organ

systems' damage assessed by Scleroderma Assessment Questionnaire.

**Patients and methods:** Forty SSc patients (33 females and 7 males) with mean age of  $27.48 \pm 12.56$  years and mean disease duration of  $6.2 \pm 4.14$  years were included. Twenty-four (60%) had ISSc; 13 (32.5%) had dSSc and 3 (7.5%) patients had SSc sine scleroderma.

**Results:** Eight (20%) had microalbuminuria and 9 (22.5%) patients had decreased creatinine clearance. Albumin/creatinine ratio was significantly higher among dSSc patients compared to those with ISSc and SSc sine scleroderma ( $X^2 = 9.077$ ;  $p = 0.01$ ). Albumin/creatinine ratio showed significant positive correlations with telangiectasia ( $r = 0.322$ ;  $p = 0.04$ ) and mRodnan's skin score.

**Keywords:** Scleroderma; Renal involvement; Microalbuminuria; Creatinine clearance; Scleroderma assessment questionnaire.

### 274. Interleukin-27 and its Relation to Disease Parameters in SLE Patients

Wafaa Gaber, Safaa Sayed, Hanaa M. Rady and Abeer M. Mohey

*Egyptian Rheumatologist*, 34: 99-105 (2012) IF: 2

**Introduction:** IL-27 exerts profound anti-inflammatory effects in several experimental autoimmune models, suggesting that it may be therapeutically relevant in SLE.

**Aim of the work:** to evaluate IL-27 level in SLE patients and its association to clinical manifestations, disease activity parameters and management strategy.

**Patients and methods:** We studied 80 SLE patients and 50 controls in a cross sectional study. Demographic, clinical and serological data were evaluated. Systemic lupus erythematosus disease activity index (SLEDAI) and Systemic Lupus International Collaboration Clinics/ACR damage index (SLICC) were assessed. Serum IL-27 was measured by ELISA.

**Results:** There was statistically significant difference in IL-27 level in SLE patients and healthy controls ( $9.7 \pm 21.9$  pg/ml vs  $20.2 \pm 47.3$  pg/ml in SLE vs controls, respectively) ( $p = 0.04$ ), also it was found that IL-27 level was statistically significantly lower in SLE patients with lupus nephritis ( $p = 0.02$ ) and cerebritis ( $p = 0.03$ ). Interleukin 27 level had a statistically significant negative correlation with the cumulative dose of hydroxychloroquine and azathioprine ( $r = -0.3$ ,  $p = 0.03$  and  $r = -0.3$  and  $p = 0.04$ , respectively).

**Conclusion:** IL-27 has anti-inflammatory effect in SLE patients especially those without nephritis or cerebritis and can be therapeutically relevant in SLE. To confirm our results we propose larger scale, multicentre studies with longer evaluation periods

**Keywords:** Interleukin-27; Lupus nephritis; Lupus cerebritis.

### 275. Comparative Study of Kidney Affection in SLE Patients with and Without Antiphospholipid Syndrome

Wafaa Gaber, Safaa Sayed, Yasser Ezzat, Tamer Wahid Kassem and Haytham Khalil

*Egyptian Rheumatologist*, 34: 51-57 (2012) IF: 2

**Aim of the work:** to evaluate the incidence, clinical associations and outcome of APS nephropathy in SLE patients with 2ry APS

**Patients and methods:** We studied 64 female SLE patients with nephritis; 32 of them had 2ry APS (group 1) and the rest without

2ry APS (group 2). Demographic, clinical and serological data were prospectively evaluated. Systemic lupus erythematosus disease activity index (SLEDAI) and Systemic Lupus International Collaboration Clinics/ACR damage index (SLICC) were assessed. Renal duplex, renal 99mTc-dimercaptosuccinic scan (DMSA scan) and renal magnetic resonance angiography (MRA) were all used to detect renal vascular affection.

**Results:** There were statistically significant differences between the two examined groups regarding damage index ( $p=0.000$ ), hypertension ( $p=0.02$ ), thrombocytopenia ( $p=0.000$ ), LDL ( $p=0.008$ ), C3 ( $p=0.01$ ) and TMA ( $p=0.04$ ). In group 1: MR angiography detected 7 patients with RAS: 5 patients with renal artery thrombosis that showed a significant association with TMA and proteinuria ( $p=0.002$ ,  $p=0.004$ ;  $p<0.001$ ,  $p=0.02$ , respectively). Patients with RAS had  $\uparrow$ DBP,  $\uparrow$ s.creatinine and  $\uparrow$ TGs ( $p=0.004$ ,  $p=0.005$  and  $p=0.0003$ , respectively). Renal DMSA detected 6 patients with cortical scar which showed a significant association with TMA, proteinuria, livedoreticularis and arthritis ( $p=0.001$ ,  $p=0.01$ ,  $p=0.04$  and  $p=0.03$ , respectively) those patients had  $\uparrow$ DBP and  $\uparrow$ RI ( $p=0.000$  and  $p=0.006$ , respectively).

**Conclusion:** aPL testing should become a routine investigation in patients evaluated for RAS or renal infarctions especially with hypertension and unexplainable deteriorating renal function. To confirm our results we propose that larger scale, multicentre studies with longer evaluation periods.

**Keywords:** Renal dmsa; Renal mra; Aps nephropathy; Systemic lupus erythematosus.

### 276. Thrombotic Thrombocytopenic Purpura Associated with Chronic HCV Infection

Ayman El Garf, Wafaa Gaber, Tamer Elbaz and Kamal El Garf

*The Egyptian Rheumatologist*, 34: 107-110 (2012) IF: 2

Thrombotic thrombocytopenic purpura is a potentially lethal microvascular thrombotic disorder.

**Case presentation:** in this study, we report a 32 years old woman who suffered from undifferentiated vasculitis with marked improvement on steroids and cyclophosphamide. Two years later, hepatitis C virus infection was discovered. Decision for interferon therapy was not recommended at this stage and the patient remained stable for the following 7 years. In January 2009, pegylated interferon and ribavirin were started due to worsening of her hepatitis; the treatment was stopped after 12 weeks due to the absence of any virologic response. Fourteen months later, she developed severe uncontrolled thrombotic thrombocytopenic purpura that led eventually to her death.

**Conclusion:** We report this rare case of thrombotic thrombocytopenic purpura that may directly be related to chronic HCV infection rather than to interferon therapy.

**Keywords:** Thrombotic thrombocytopenic purpura; Vasculitis; Hcv; Interferon.

### 277. Shrinking Lung Syndrome in Systemic Lupus Erythematosus Patients with Dyspnea

Tamer A. Gheita, Sherine El-Mofty, Samar M. Fawzy and Hussein El-Fishawy

*The Egyptian Rheumatologist*, 34: 179-183 (2012) IF: 2

**Aim of the work:** to identify the frequency of shrinking lung syndrome (SLS) in systemic lupus erythematosus (SLE) with

dyspnea and study the clinical characteristics and differences in disease activity and damage.

**Patients and methods:** the study included 47 SLE patients complaining of dyspnea. SLS was considered in those with exertional dyspnea, restrictive pulmonary function tests (PFTs) and elevated copula of the diaphragm.

Full history taking, thorough clinical examination, laboratory and relevant radiological investigations were performed for all the patients. Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and Systemic Lupus International Collaborating Clinics (SLICC) indices were compared. High resolution CT chest was performed for patients with radiological findings consistent with SLS.

**Results:** the mean age of the patients was  $29.43 \pm 7.45$  years, mean disease duration  $5.18 \pm 3.62$  years. The SLS was present in 8 patients (17.02%). There was bilateral elevation of the diaphragm copulae in 25% of SLS patients and two had associated basal atelectatic bands. The serum uric acid was significantly higher in those with SLS while the 24 h urine protein was significantly lower and C4 normalized. The levels of SLEDAI and SLICC tended to be lower in those with SLS, yet there was no significant difference from those without. The demographic features, clinical and laboratory manifestations, disease activity and damage scores, PFTs and radiological findings of the SLE patients are presented.

**Conclusion:** in SLE patients with dyspnea, SLS should be looked for as it is present in a high proportion of cases.

**Keywords:** Systemic lupus erythematosus (Sle); Shrinking lung syndrome; Dyspnea; Sledai.

### 278. Clinical Significance of Serum TNF $\alpha$ and -308 G/A Promoter Polymorphism and Serum IL-6 and -174 G/C Promoter Polymorphism in Systemic Lupus Erythematosus Patients

Ghada S. Azkalany, Tamer A. Gheita, Wafaa Gaber and Abeer Mohey

*The Egyptian Rheumatologist*, 34: 119-125 (2012) IF: 2

**Introduction:** Systemic lupus erythematosus (SLE) is a disorder of immune regulation where cytokine imbalance and genetic factors are implicated in its pathogenesis.

**Aim of the work:** to evaluate the clinical significance of serum levels of tumor necrosis factor alpha (TNF $\alpha$ ) and its -308 G/A promoter polymorphism as well as the IL-6 and -174 promoter polymorphism in SLE patients and find any association to the clinical and laboratory features as well as to the disease activity and severity.

**Patients and methods:** We studied 37 female SLE patients and age and gender matched healthy control. Demographic, clinical and serological data were evaluated and the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and the Systemic Lupus International Collaboration Clinics/ACR Damage Index (SLICC) were assessed. Serum TNF- $\alpha$  and IL-6 levels were measured using enzyme-linked immunosorbent assay (ELISA) and DNA genotyped for TNF- $\alpha$  promoter (-308 G/A) and IL-6 promoter (-174 G/C) by polymerase-chain reaction-restriction fragment-length polymorphism (PCR-RFLP) analysis

**Keywords:** Tnf-A; Il-6; Tnf- $\alpha$  (-308 G/A); (-174 G/C) Promoter Polymorphism; Systemic lupus erythematosus.

### 279. High-Sensitivity C-Reactive Protein (Hs-Crp) in Systemic Lupus Erythematosus Patients Without Cardiac Involvement; Relation to Disease Activity, Damage and Intima-Media Thickness

Tamer A. Gheita, Iman I. El-Gazzar and Ghada Azkalany

*The Egyptian Rheumatologist*, 34: 147-152 (2012) IF: 2

**Aim of the work:** to assess the high sensitivity C-reactive protein (hs-CRP level) in systemic lupus erythematosus (SLE) patients without cardiac involvement and find its relation with clinical and laboratory findings, disease activity, damage index and intima-media thickness (IMT).

**Patients and methods:** Forty-five female SLE patients were recruited in the present study without any cardiac involvement. History taking, examination and laboratory investigations were performed for patients. Disease activity was evaluated by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and damage by the Systemic Lupus International Collaborating Clinics (SLICC) index. Thirty age matched female healthy subjects were considered as a control group. hs-CRP was measured quantitatively by microplate immunoenzymometric assay and the IMT measured by ultrasonography.

**Results:** the hs-CRP in the patients was significantly higher ( $4.84 \pm 3.91$  mg/l) compared to the control ( $1.74 \pm 0.61$  mg/l) ( $p < 0.001$ ). the IMT in the patients was significantly increased ( $0.72 \pm 0.37$  mm) compared to the control ( $0.54 \pm 0.15$  mm) ( $p = 0.004$ ). There was no difference in the level of hs-CRP according to the presence or absence of clinical manifestations. However, it was significantly higher in those with positive DNA ( $5.71 \pm 4.36$  mg/L) compared to those with negative results ( $3.12 \pm 1.97$  mg/L) ( $p = 0.009$ ). There was a significant correlation of the hs-CRP level with the IMT ( $r = 0.49$ ,  $p = 0.001$ ) and SLEDAI ( $r = 0.67$ ,  $p < 0.001$ ).

**Conclusions:** These findings suggest that SLE patients without traditional major cardiovascular risk factors may have increased risk of future cardiac events. Measuring hs-CRP may be useful as a marker of disease activity, increased IMT and subclinical atherosclerosis in SLE especially those with positive ds-DNA.

**Keywords:** High Sensitivity C-Reactive; Protein (Hs-Crp); Systemic Lupus Erythematosus (Sle); Sledai; Slicc; Intima-Media Thickness (Imt).

### 280. Elevated Serum Trail Levels in Scleroderma Patients and Its Possible Association with Pulmonary Involvement

Noha A. Azab, Hanaa M. Rady and Samar A. Marzouk

*Clin Rheumatol*, 31 (9): 1359-1364 (2012) IF: 1.996

Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) has been reported to be involved in the pathophysiology of some autoimmune diseases as systemic lupus erythematosus, ankylosing spondylitis, and multiple sclerosis. the aim of this study was to assess serum TRAIL concentration in systemic sclerosis (SSc) patients and to investigate its possible association with various disease parameters.

Thirty SSc patients as well as 25 rheumatoid arthritis (RA) patients and 25 healthy volunteers were included in the present study.

Organ system involvement in SSc patients was investigated. Pulmonary function tests as well as chest high-resolution

computed tomography (HRCT) were done to detect pulmonary involvement in our patients.

TRAIL concentrations were measured in the sera of SSc patients, RA patients and healthy controls by enzymelinked immunosorbent assay. Mean serum TRAIL levels were significantly higher in SSc patients than in the control RA patients and in healthy controls ( $p < 0.001$ ) while they were not significantly different between patients with diffuse cutaneous SSc and patients with limited cutaneous scleroderma.

Serum TRAIL levels were significantly higher in SSc patients with pulmonary involvement and were significantly correlated with HRCT scores.

Serum TRAIL levels are significantly elevated in SSc patients and are associated with SSc-associated pulmonary involvement denoting a possible role of TRAIL in the pathogenesis of SSc. Further studies may be needed to confirm these findings and the possible use of TRAIL in detection and possibly treatment of SSc-associated pulmonary disease.

**Keywords:** Pulmonary involvement; Systemic sclerosis; Tumor necrosis factor-related apoptosis-inducing ligand (Trail).

### 281. The Practical Value of Biologics Registries in Africa and Middle East: Challenges and Opportunities

Najia Hajjaj-Hassouni, Marzooq Al-Badi, Ala' Al-Heresh, Samar Al-Emadi, Ahmed El Bawendi, Ayman El Garf, Khaled El Hadidi, Hussein Halabi, Mohammed Hammoudeh, Selma El Hassani, Mustafa Al Maaini, Ibrahim Nahar, Aïcha Ladjouze Rezig, Slaheddine Sellami, Wafaa Sweiri, Ramiz Alswailem, Beverly Traub, Imad Uthman, Elsa van Duuren, Leith Zakraoui, Bassel El Zorkany, Loreto Carmona and Maxime Dougados

*Clin Rheumatol*, 31: 407-416 (2012) IF: 1.996

Biologics, including tumor necrosis factor (TNF) inhibitors, are increasingly used for the treatment of inflammatory conditions such as rheumatoid arthritis (RA), psoriatic arthritis, and ankylosing spondylitis. the efficacy of these drugs has been demonstrated in randomized controlled trials (RCTs). However, these studies are conducted in controlled environments, and the results may not necessarily reflect clinical outcomes in daily clinical practice. in Europe and other western countries, numerous biologics registries that enroll and monitor patients receiving biologics have been established.

These registries follow patients irrespective of whether they continue with the initial biologic drug. Thus, real-life efficacy data from these registries can be used to assess the long-term safety of biologics through longitudinal studies.

In Africa and Middle East (AFME), such registries currently exist only in Morocco and South Africa. in light of the increasing availability of biologics and scarcity of long-term safety data of these agents in the AFME population, there is a need to establish biologics registries in other countries across the region.

This review discusses the value of biologics registries versus RCTs as well as safety and efficacy data from observational studies presented as lessons from well-established biologics registries. in addition, the rationale for establishing such registries in the AFME region is also presented.

**Keywords:** Africa and middle east; Biologics; Registries; Rheumatoid arthritis; Safety; Tumor necrosis factor inhibitors.

### 282. Early Diagnosis and Treatment of Ankylosing Spondylitis in Africa and the Middle East

Bahiri Rachid, Bassel El Zorkany, Ehab Youseif and Mohammed Tikly

*Clin Rheumatol*, (2012) IF: 1.996

Ankylosing spondylitis (AS) is the prototype for spondyloarthritis primarily affecting young men. Geographic and ethnic variations exist in the prevalence and severity of AS and relate to the wide disparity in the frequency of human leukocyte antigen (HLA)-B27, a major genetic risk factor. The strength of the disease association with HLA-B27 is lower in most Arab populations (25–75 %) than in Western European populations (>90 %), and there is no association in sub-Saharan Africa, where the prevalence of HLA-B27 is <1 %. Other epidemiologic differences between European and African populations are the apparent later age at presentation in sub-Saharan Africa, and the high rate of spondyloarthropathies associated with human immunodeficiency virus infection.

Diagnosis of AS is often delayed 8–10 years; potential reasons for the delay in Africa and the Middle East include low awareness among physicians and patients, the requirement for radiographic evidence of sacroiliitis for diagnosis, and limited access to magnetic resonance imaging in some countries. Treatment should be initiated early to prevent or reduce skeletal deformity and physical disability. Nonsteroidal anti-inflammatory drugs are effective first-line treatment and anti-tumor necrosis factor- $\alpha$  drugs are indicated for patients who have an inadequate response to first-line therapy. In Africa and the Middle East, such treatments may be precluded either by cost or contraindicated because of the high prevalence of latent tuberculosis infection. Research is sorely needed to develop cost-effective tools to diagnose AS early as well as effective, inexpensive, and safe treatments for these developing regions.

**Keywords:** Africa; Ankylosing spondylitis; Diagnosis; Hla-B27; Middle east.

### 283. Transient Osteoporosis of the Hip, Complete Resolution after Treatment with Alendronate as Observed by Mri Description of Eight Cases and Review of the Literature

Yasser Emad, Yasser Ragab, Nashwa El-Shaarawy and Johannes J. Rasker

*Clinical Rheumatology*, 31: 1641-1647 (2012) IF: 1.996

Transient osteoporosis of the hip (TOH), also referred to as transient bone marrow edema syndrome, is most common in middle-aged men and often after trivial trauma or sport-related injuries. Diagnosis is usually made by eliminating other possible causes of hip pain. Magnetic resonance imaging (MRI) plays an important role in diagnosis and demonstrates a typical pattern of bone marrow edema (BME) in the form of diffuse low signal on T1-weighted images and high signal on T2 fat-suppressed or short T1 inversion recovery images. No consensus exists about the management of TOH, as it may progress to avascular necrosis. We describe eight cases of TOH treated with alendronate resulting in improvement of pain and function and complete resolution of BME on MRI. The literature is reviewed regarding TOH and the relationship with bone marrow edema syndrome, avascular necrosis of the hip and regional migratory osteoporosis.

to our knowledge, this is the first report describing the improvement of this condition after use of alendronate with documented radiological improvement on follow-up MRI.

**Keywords:** Alendronate; Bone marrow edema syndrome; Magnetic resonance imaging (Mri); Transient osteoporosis of the hip.

### 284. Prevalence and Clinical Presentations of Hepatitis C Virus Among Patients Admitted to the Rheumatology Ward

Ayman El Garf, Bassel El Zorkany, Rasha Gheith, Hala Sheba, Geilan Abdel Moneim and Kamal El Garf

*Rheumatol Int*, 32 ( 9 ): 2691-2695 (2012) IF: 1.885

To study the prevalence of anti-HCV antibodies among patients admitted to the rheumatology department, Cairo University hospitals, in 6-month period as well as to determine whether chronic HCV infection was the primary cause of their admission or just a concomitant association with the rheumatic disease. One hundred and fifty-seven patients were included in this study. They represent all patients admitted to the rheumatology inpatient department of Cairo University hospitals during the study period. Preset questionnaire including detailed demographic data, cause of admission and clinical manifestations of their disease was obtained for every patient. All patients were screened for HCV antibodies using ELISA technique. Other laboratory and imaging investigations were done according to the patient's diagnosis. Twenty-nine patients (18.5%) were positive for HCV antibody. Eleven patients of them (38%) were admitted due to rheumatic manifestations directly related to chronic HCV infection, which represent 7% of all admitted patients (11/157). HCV antibodies were found in 17.6 and 6.7% among patients with rheumatoid and systemic lupus erythematosus. Arthritis, palpable purpura, digital gangrene and mononeuritis multiplex were the most common causes of admission related to chronic HCV infection. HCV antibodies were found in 18.5% among admitted patients to the rheumatology ward. The rheumatic manifestations of chronic HCV represent the primary cause of admission in 7% of all admitted patients. HCV screening should be included in the routine investigations for patients presenting to rheumatology departments in countries with high prevalence of chronic HCV infection.

**Keywords:** Hcv; Prevalence; Rheumatology wards; Clinical presentations; Egypt.

### 285. The TIE2 Receptor Antagonist Angiopoietin-2 in Systemic Lupus Erythematosus: its Correlation with Various Disease Activity Parameters

Maysa K. Salama, Fatma M. Taha, Miriam Safwat, Hanan E.A. Darweesh and Mohamed El Basel

*Immunological Investigations*, 1-12: (2012) IF: 1.164

Systemic lupus erythematosus is one of the autoimmune diseases characterized by multisystem involvement associated with autoantibody and immune complex vasculitis along with endothelial cell damage.

**Objective:** to study the possible role of Angiopoietin-2 (Ang-2) as a recently highlighted inflammatory and angiogenic mediator in the pathogenesis of SLE and its correlation with the state of

another inflammatory marker, P-Selectin, as well as with various markers of the disease activity. Patients and

**Methods:** the present study included 3 main groups: active SLE patients (group I), inactive SLE patients (group II) and healthy normal control subjects (group III). Groups I and II were subjected to disease activity assessment using the SLEDAI scoring system and measurement of plasma Ang-2 and P-Selectin by ELISA in addition to various laboratory investigations to assess disease activity as: Complete blood count, ESR, serum creatinine, C3, C4 and 24-h urinary proteins.

**Results:** the mean level of Plasma Ang-2 and P-selectin showed a high significant increase in active group compared to inactive SLE patients and control subjects ( $p < 0.001$ ). There was a significant positive correlation between Ang-2, P-Selectin, and each of SLEDAI score and 24-h urinary proteins in all SLE patients as well as in the active group, and Ang-2 was a significant independent marker for proteinuria. A significant negative correlation was found between Ang-2, P-Selectin and each of C3, C4. Ang-2 and P-Selectin showed a high sensitivity and specificity in the patients with SLE.

**Conclusion:** Our study suggests that Ang-2 may be a more useful marker than P-Selectin, C3 and C4 in the assessment of disease activity.

**Keywords:** Angiopoietin (Ang-2); Systemic lupus erythematosus (Sle); Systemic lupus.

### 286. Insulin Resistance and Metabolic Syndrome in Primary Gout: Relation to Punched-Out Erosions

Tamer A. Gheita, Hussein S. El-Fishawy, Mohamed M. Nasrallah and Hani Hussein

*Int J Rheum Dis*, 15: 521-525 (2012) IF: 0.807

**Objectives:** to verify the relation of gout to insulin resistance (IR) and metabolic syndrome (MetS) and find any association of metatarsophalangeal (MTP) joint erosions to the features of MetS and IR.

**Methods:** Forty-six primary gout male patients with a mean age of  $41.96 \pm 5.77$  years were grouped according to the presence of MetS. Twenty-seven age and sex matched healthy volunteers served as controls. Insulin sensitivity was estimated using the homeostatic model assessment index (HOMA-B) for beta cell function and HOMA-IR for peripheral tissue IR.

**Results:** Gout patients had significantly higher HOMA-IR and HOMA-B compared to controls. Those with MetS ( $n = 27$ ) had significantly higher serum uric acid (SUA) than those without ( $n = 19$ ;  $11.51 \pm 3.72$  mg/dL vs.  $9.15 \pm 2.34$  mg/dL;  $P = 0.012$ ). Gout patients with MTP erosions had notable higher insulin levels and more IR as shown by the higher levels of HOMA-IR and HOMA-B compared to those without. HOMA-IR and HOMA-B significantly correlated with the presence of erosions. Moreover, the presence of erosions significantly correlated with SUA ( $r = 0.64$ ,  $P < 0.0001$ ).

**Conclusions:** the level of SUA is closely related to IR in patients with and without MetS. There is an association of the severity of gout and presence of MTP erosions to IR. Metabolic syndrome forms an important marker for those who develop more punched-out erosions.

**Keywords:** Erosions; Gout; Homa-B; Homa-IR; Insulin resistance; Metabolic syndrome.

### 287. Metabolic Syndrome and Insulin Resistance Comorbidity in Systemic Lupus Erythematosus: Effect on Carotid Intima-Media Thickness

T. A. Gheita, H.A. Raafat, S. Sayed, H. El-Fishawy, M.M. Nasrallah and E.Abdel-Rasheed

*Z Rheumatol*, 62 (11): 1071-1077 (2012) IF: 0.458

**Objective:** the aim of the present study was to assess the effect of metabolic syndrome (MetS) and insulin resistance comorbidity on the carotid intima-media thickness (IMT) in SLE patients and their relation to clinical manifestations, disease activity and damage.

**Methods:** the study included 92 SLE patients (mean age  $30.18 \pm 8.27$  years) and 30 matched control. Disease activity and damage were assessed by the SLEDAI and SLICC Indices respectively. The Health assessment questionnaire II (HAQII) and Quality of life (QoL) index were assessed in the patients. Levels of insulin, glucose, creatinine and lipid profile were measured in patients and control. Insulin sensitivity was estimated using the homeostatic model assessment index (HOMA-B) for beta cell function and (HOMA-IR) for peripheral tissue insulin resistance. the carotid IMT was measured by ultrasonography.

**Results:** the SLE patients had high HOMA-IR and HOMA-B. the IMT was significantly increased ( $0.82 \pm 0.29$  mm) compared to the control ( $0.45 \pm 0.2$  mm), the HOMA-IR, SLEDAI, SLICC, HAQII and IMT were significantly higher and the QoL lower in those with MetS ( $n = 34$ ) compared to those without ( $n = 58$ ) while the HOMAB was comparable. There was a significant correlation between the IMT and the SLEDAI, SLICC and WHR. **Conclusion:** Insulin sensitivity and IMT are altered in SLE patients especially those with MetS co-morbidity with an associated increase in disease activity and damage. Effective management of MetS would aid in controlling SLE activity, damage and future development of cardiovascular events especially in the absence of symptoms of cardiovascular disease.

**Keywords:** Sle; Metabolic syndrome; Homa-ir; Homa-B; Imt.

### 288. Anti-Annexin V Antibodies In Neuro-Behc Et Patients: Clinical Significance And Relation To Disease Activity

Tamer A. Gheita, Hatem Samir and Hani Hussein

*International Journal Of Rheumatic Diseases*, 15:124 -126 (2012) IF: 0.205

Behc,et's disease (BD) is a chronic, relapsing vasculitis of unknown etiology and involvement of parenchymal central nervous system (CNS) (neuro-BD) is a serious complication and leading cause of mortality. Treatment of neuro-BD remains largely empirical, and may not adequately control the disease.<sup>1</sup> Annexins are a group of highly conserved proteins which exert several regulatory functions on cell biology.

They are involved in numerous cell processes, including vesicle trafficking, calcium signaling, cell growth, division and apoptosis. Auto-antibodies directed toward annexin I, II, V and XI have been reported, but their roles and their clinical correlates are controversial.<sup>2</sup> It has been suggested that lymphocytes in patients with BD are relatively resistant to apoptosis mediated by anti-Fas antibody. These apoptosis-resistant, or long-lived, lymphocytes may be involved in the



chronic and recurrent intraocular inflammation seen in these patients.<sup>3</sup> Annexin V has a high affinity for phospholipids, playing a pivotal role in the regulation of coagulation cascade and its antibodies were found in patients with arterial or venous thrombosis, especially those with autoimmune rheumatic diseases.<sup>2</sup> The aim of this study was to measure the level of serum anti-annexin V antibodies in BD patients and to study their significance in relation to neurological manifestations.

### 289. Subclinical Atherosclerosis in Behçet's Disease

Samia Hassan, Tamer Gheita, Shada Ghoneim and Loi Nasr

*Turk J Rheumatol*, 27(2): 109-114 (2012) IF: 0.191

**Objectives:** This study aims to assess the carotid intima-media thickness (IMT) and plaque formation in patients with Behçet's disease (BD) by Doppler ultrasonography (US) and to correlate it with disease activity, and clinical and laboratory parameters.

**Patients and methods:** Thirty BD patients (25 males and 5 females; mean age 35.8±8.7 years; 22 to 54 years) diagnosed according to the new set of diagnostic criteria published by the International Study Group for Behçet's Disease, were recruited from the Rheumatology Department, Cairo University Hospitals. The mean disease duration was 8.7±5.9 years. Subjects with diabetes mellitus, hypertension or evidence of myocardial infarction were excluded. Full history taking, clinical examination and skin pathology test were carried out for all patients. Laboratory measurements including lipid profile were also performed for both patients and controls. Disease activity was assessed using the Behçet's Disease Current Activity Form (BDCAF). Carotid artery ultrasonography was carried out.

**Results:** the mean IMT was significantly different in the patient group, compared to controls ( $p=0.003$ ). The mean IMT was significantly correlated with urea, creatinine, cholesterol, triglycerides and the BDCAF, while it was inversely associated with HDL level. Atherosclerotic plaque was found in five patients (16.7%).

**Conclusion:** A morphologic evidence of subclinical atherosclerosis in patients with BD is verified. Renal function in these patients may indicate possible risks and BDCAF score may significantly suggest cardiovascular involvement.

**Keywords:** Behçet disease; Behçet's disease current activity form; Intima-media thickness; Subclinical atherosclerosis.

### 290. Using Clinical and Multislice Computer Tomographic Features to Assess Temporomandibular Joint Osseous Involvement in Rheumatoid Arthritis: A Preliminary Study

Tamer Gheita, Moushira Dahaba, Eman Ahmed, Shorouk Khalifa and Ayman Basmay

*Turk J Rheumatol*, 27(1): 47-55 (2012) IF: 0.191

**Objectives:** In this study, we aimed to assess the osseous involvement of temporomandibular joint (TMJ) in rheumatoid arthritis (RA) patients by multislice computed tomography (MSCT) scanning with multiplanar reconstruction (MPR), and to find any relation to the clinical, laboratory and radiological disease parameters.

**Patients and methods:** Twenty-four female patients (mean age 35.5±6.6 years; range 38.3 to 42 years) with definite diagnosis of

RA were recruited in the study. Assessment was conducted through medical history, physical examination and clinical investigation. Disease Activity Scores in 28 Joints (DAS28) was calculated and Health Assessment Questionnaire-II (HAQ-II) used. The TMJs were assessed according to the TMJ clinical dysfunction score. Radiological grading of hands and feet was performed according to the modified Larsen score. Findings of the MSCT were assessed using the TMJ CT score.

**Results:** Temporomandibular joint involvement was present in 70.83% of patients. The most commonly seen clinical TMJ dysfunction manifestations were difficult manipulation and pain, tenderness (45.83%) clicking (29.17%), locking (16.67%), followed by altered mouth opening (8.33%). The TMJ osseous involvement became more frequent (83.33%) after using bilateral MPR scan. The most frequent findings were mandibular condyle erosions, altered condyle position, mandibular subchondral sclerosis, articular eminence flattening, altered condyle shape and articular fossa erosion, osteophytes, articular eminence erosion, followed by mandibular subcondral cysts. The mouth opening was obviously reduced in 41.67% of patients. The TMJ CT score showed a trend to correlate with DAS28 and modified Larsen score.

**Conclusion:** the MSCT MPR is a diagnostically reliable modality for the estimation of TMJ involvement in relation to the clinical manifestations and disease activity in RA patients. Early assessment is of utmost importance for the RA patients with symptomatic TMJ.

**Keywords:** Multiplanar reconstruction; Multislice computed tomography; Rheumatoid arthritis; Temporomandibular joint.

### 291. Cxcr4 Expression on Peripheral Blood T-Lymphocytes in Patients with Systemic Lupus Erythematosus and its Relation to Disease Activity

Dina S. Al-Zifzaf, Abir M. Nabil, Rasha Mamdouh and Reem A K Khattab

*Life Science Journal*, 9 (4): 3073-3079 (2012) IF: 0.073

In this study, we evaluated the expression of CXCR4 on peripheral blood T cells from SLE patients and studied the association between these levels and various clinical and laboratory parameters in order to find out whether SLE patients demonstrated expression abnormalities of CXCR4 to establish if there is a relation between its expression and disease activity in SLE.

**Patients and Methods:** This study was conducted on thirty two patients with SLE. All patients were diagnosed according to the 1997 updated American College of Rheumatology (ACR) revised Criteria for diagnosis of SLE. The study also included ten ages and sex matched apparently healthy controls. All patients were subjected to full history taking, thorough clinical examination, assessment of the disease activity according to the modified SLE disease activity index (SLEDAI), SLE cumulative organ damage was scored using the Systemic Lupus International Collaborating Clinics (SLICC) damage index. Routine laboratory investigations were done as well as estimation of CXCR4 expression by flow cytometry on Total Lymphocytes and T lymphocytes.

**Results:** There was a significant increase in CXCR4 expression on Lymphocytes in general and specifically on T-lymphocytes among SLE patients compared to healthy controls. SLE patients with joint manifestations had significantly lower frequency of expression of CXCR4 on their T cells. On the other hand, patients with serositis had significantly higher levels of expression of



CXCR4 on their lymphocytes. Patients with nephritis did not show a significant difference in their chemokine receptor expression as compared to patients without nephritis. Also, no such difference was found regarding the any other clinical or lab characteristic of the patients. A positive significant correlation between T lymphocytes expressing CXCR4 and disease activity measured by the SLEDAI was found. the test validity characters of CXCR4 expression on T lymphocytes for discrimination of SLE at the best cutoff value of 34.6% showed 100% specificity, 87.5% sensitivity and 90.5% efficacy.

**Conclusion:** CXCR4 expression levels are elevated on total lymphocytes as well as T cells from SLE patients. This increase in cell expression of CXCR4 correlates positively with disease activity. These findings suggest that CXCR4 hyperexpression may play a vital role in the pathogenesis of SLE, and may after further studies be used as an indicator of disease activity. This also suggests CXCR4 antagonists may halt the role of these cells in the pathogenesis of the disease and improve prognosis for SLE patients.

**Keywords:** Systemic lupus erythematosus; Lymphocytes; T lymphocytes; Cxcr4.

## 292. Implication Rénale Subclinique Dans La Vasculrite Cryoglobulinémique Essentielle Et La Périartérite Nouvelle Classique

Tamer A. Gheita, Nermeen A. Khairy, Mohamed Nasr-Allah and Hani Hussein

*Revue Du Rhumatisme*, 79: 215-221 (2012)

**Objectif:** La vasculrite rénale est habituellement associée à des auto-anticorps anti-cytoplasme des neutrophiles (ANCA). Cependant, les patients ne présentant pas d'ANCA constituent une catégorie de vasculrite rénale rarement étudiée. L'objectif de cette étude était de mettre en évidence des implications rénales caractéristiques chez des patients atteints de vasculrites systémiques primaires non associées à des ANCA (VNAA) et parmi eux, de comparer les vasculrites cryoglobulinémiques essentielles (VCE) avec les périartérites nouvelles (PAN) classiques.

**Méthodes:** L'étude incluait trente patients atteints de VNAA. Quinze patients étaient atteints de VCE et les quinze autres étaient atteints de PAN classiques. Les patients ont été recrutés dans les départements de rhumatologie, de médecine interne et du service des consultations externes des hôpitaux universitaires du Caire. Les patients n'avaient pas ou peu d'implications rénales à l'entrée, et les ANCA étaient négatives lors de test Elisa ou par immunofluorescence. Une biopsie rénale a été réalisée chez tous les patients avec une analyse histopathologique.

**Résultats:** Des anomalies rénales ont été observées dans les biopsies de six femmes. Une patiente atteinte de PAN montrait une vasculrite rénale et une glomérulonéphrite membrano-proliférative (GNMP). Elle avait des anticorps anti-nucléaire (ANA) et était positive pour le virus de l'hépatite B (VHB), mais n'avait pas de cryoglobulines et était négative pour le virus de l'hépatite C (VHC). Les cinq autres patientes, atteintes de VCE associées à une infection par le VHC, avaient également des anomalies rénales. L'une avait une néphrite interstitielle chronique et était positive pour le VHB, les quatre autres patientes étaient négatives pour le VHB. Parmi les quatre patientes, deux d'entre elles étaient atteintes d'une GNMP, les deux autres étant atteintes d'une glomérulonéphrite proliférative focale ou d'une glomérulonéphrite à croissants épithéliaux.

**Conclusions:** Une meilleure compréhension des manifestations des vasculrites systémiques est susceptible de servir de base pour l'usage de thérapies immunomodulatrices plus sélectives dans le futur. Nous espérons que cette étude fera prendre conscience des implications rénales dans les vasculrites non associées aux ANCA.

**Keywords:** Rénale; Non anca; Pan; Cryoglobulinémie; Vasculrites.

## 293. Assessment of Glucocorticoids Induced Preclinical Atherosclerosis

Amr Amin and Zeinab Nawito

*Glucocorticoids- New Recognition of our Familiar Friend*, (2012)

In 1948, the US rheumatologist Philip Hench and his associates at the Mayo Clinic first administered hydrocortisone to a patient with rheumatoid arthritis and discovered its clinical benefits. Two years later, Hench, together with biochemists Edward Kendall and Tadeus Reichstein, shared the Nobel Prize in Medicine. Today, glucocorticoids are among the most frequently prescribed class of anti-inflammatory medications. They are part of the standard treatment for a wide range of disorders which feature inflammation and/or immune activation, such as asthma, chronic obstructive pulmonary disease, hypersensitivity reactions, autoimmune diseases, and in organ transplantation.

*Dept. of Surgery*

## 294. Mass Casualties in Tahrir Square at the Climax of the Egyptian Uprising. Evidence of an Emerging Pattern of Regime's Organized Escalating Violence During 10 Hours on the Night of January 28, 2011

Mohamed D. Sarhan, Ashraf A. Dahaba, Michael Marco and Ayman Salah.

*Annals of Surgery*, 256 ( 6): 1093-1097 (2012) IF: 7.492

Documentation of the management of mass casualties in Tahrir Square.

**Background:** We documented the sequences of our medical response to mass casualties in Tahrir Square between January 28, 2011, and February 4, 2011, at "Kasr El-Ainy" Cairo University Hospital, the largest hospital in the Middle East and the tertiary referral center for all hospitals in Egypt that happened to be the closest to Tahrir Square.

**Methods:** at the peak of Tahrir Square demonstrations, injured protesters received first aid in amakeshift clinic inside Tahrir Square, manned by volunteer doctors and nurses, before they were evacuated to the Cairo University Hospital Surgical Casualty Department. General surgeons, orthopedic surgeons, anesthesiologists, and critical care nurses from multidisciplinary teams hastily triaged and treated the incoming casualties. Thousands of casualties were seen at the peak of the uprising. This article provides a detailed review of mass casualties seen between January 28, 2011, and February 4, 2011.

**Results:** of 3012 casualties, 453 were triaged as "immediate care" patients. on arrival, 339 of 453 patients (74.8%) needed surgical intervention within 6 hours of arrival whereas 74 of 453 patients (16.3%) were managed conservatively. Forty of 453 (8.8%) of patients did not survive their injuries. Most of the inpatients (302/453, 66.6%) were admitted within 10 hours on January 28,

2011, during which evidence of a pattern of regime's organized escalating violence emerged.

**Conclusions:** We describe the pattern of injuries and our management of Tahrir Square mass casualties. We believe that forming multidisciplinary teams of surgeons, anesthesiologists, and nurses was the key to our effective management of such a huge event.

**Keywords:** Arab spring; Egyptian uprising; Lessons learned; Mass casualties.

### 295. Single-Port Transumbilical Laparoscopic Appendectomy: A Preliminary multicentric Comparative Study in 87 Patients with Acute Appendicitis

Ramon Vilallonga, Umut Barbaros, Ahmed Nada, Aziz Sümer, Tuğrul Demire, José Manuel Fort, Oscar González and Manuel Armengol

*Minimally Invasive Surgery*, (2012)

**Introduction:** Laparoscopic appendectomy (LA) has been performed in many approaches such as open, laparoscopic and recently Single Port Access (SPAA). in order to elucidate its potential advantages, we compared the two laparoscopic approaches.

**Methods:** 87 patients were included in a multicentric study for suspected appendicitis in order to perform (SPAA) appendectomy or laparoscopic appendectomy (LA). All outcomes, including blood loss, operative time, complications, and length of stay and pain were recorded prospectively.

**Results:** There were 46 patients in the SPAA group and 41 in the LAG with a mean operative time of 40,4 minutes in the SPAA group and 35,0 minutes in the LA group. Only one patient was converted to an open approach. We described only 2 complications. Pain was graded 2,8 in the SPAA group and 2,9 in the LA group, according to the AVS after 24 hours. Patients in the SPAA Group were more satisfied (7,5 versus 6,9) ( $P < 0.05$ ). Same results were found for the cosmetic result (8,6 versus 7,4) ( $P < 0.05$ ).

**Conclusion:** Using the single port approach feasible and safe. the true benefit of the technique should be assessed by new randomised controlled trials.

**Keywords:** Single-port; Laparoscope; Appendectomy.

#### Dept. of Urology Dept

### 296. Effect of Extracorporeal Shock Wave Lithotripsy on Kidney Growth in Children

A. Fayad, M. G. El-Sheikh, H. El-Fayoumy, R. El-Sergany and A. Abd El Bary

*J Urology*, 188: 928-931 (2012) IF: 3.746

**Purpose:** We investigated whether shock wave lithotripsy affects kidney growth in children.

**Materials and Methods:** This prospective controlled study included 150 children with renal stones who presented for shock wave lithotripsy between March 2005 and February 2010 (group A). the control arm included 100 children without any urological problems who were enrolled in the study after obtaining written maternal consent (group B). All children in both groups underwent abdominal ultrasound to assess renal size (bipolar

renal length), which was repeated after 6 months for group A and after 1 year for both groups.

**Results:** Bipolar renal size in group A increased significantly at 6 months and 1 year after shock wave lithotripsy. Renal growth did not differ based on patient age at shock wave lithotripsy ( $p = 0.472$ ), number of shock wave lithotripsy sessions ( $p = 0.65$ ) or number of stones ( $p = 0.405$ ). There was no significant difference between the rate of kidney growth in children who underwent shock wave lithotripsy during the year of the study and normal controls.

**Conclusions:** Shock wave lithotripsy has no deleterious effect on the normal rate of renal growth in children. This outcome is not affected by either the number of stones or the age of the child at shock wave lithotripsy.

**Keywords:** Cicatrix; Kidney calculi; Lithotripsy; Radionuclide imaging; Ultrasonography.

### 297. Long-Term Follow-Up (18–35 Years) of Male Patients with History of Bladder Exstrophy (Be) Repair in Childhood: Erectile Function and Fertility Potential Outcome

Hosni Khairy Salem and Mohammed Eisa,

*J Sex Med*, 9: 1466-1472 (2012) IF: 3.552

**Introduction:** Bladder exstrophy is a rare condition that may lead to severe psychosexual malformation and require a lifelong follow-up.

**Aim:** We describe the long-term sexual outcome of patients with bladder exstrophy treated at our institution at early stage.

**Methods:** Thirty patients with mean age of 26 years (range 18–35 years) were included in the study. Fifteen patients underwent staged primary reconstruction, five patients underwent complete primary repair, and 10 patients underwent primary or secondary ureterosigmoidostomy. Main Outcome Measures. Evaluation consisted of pediatric medical records, interview questionnaire including the psychosexual history, International Index of Erectile Function (IIEF), and semen analysis.

**Results:** Erectile functions were maintained in 28 patients based on IIEF domain score. in all cases, penile length was objectively less than average (mean 7.65 cm). Seven patients were not satisfied with their penile length, and four cases complained of slight curvature. Ten patients were married (33%), of whom four patients had children (after normal conception in three, and after assisted reproductive technique in one). the remaining 20 patients were not married because of the feeling of sexual inadequacy to be able to engage in sexual intercourse (six patients), afraid of the cosmetic appearance of the genitalia (10 patients), and incontinence (four patients). Retrograde ejaculation was documented in 16 cases (53.5%), low volume ejaculate in eight cases (26.5%), and anejaculation in six cases (20%).

Cosmetic outcome was considered satisfactory by 50% of the patients. Sixteen patients voided per urethra, four performed clean intermittent catheterization, and 10 patients had ureterosigmoidostomy diversion. Urinary tract infection was documented in 20% of the cases, and recurrent attacks of pyelonephritis in 10% of the cases.

**Conclusion:** Long-term outcome of bladder exstrophy repair in male patients showed fair results with respect to sexual function with more or less stable sexual relationship. We should do our best to solve the problem of those with restricted sexual lives. Salem HK and Eisa M. Long-term follow-up (18–35 years) of male

patients with history of bladder exstrophy (BE) repair in childhood: Erectile function and fertility potential outcome

**Keywords:** Bladder exstrophy; Male; Erectile function; Penile length.

### 298. Changing Patterns (Age, Incidence, and Pathologic Types) of Schistosoma-Associated Bladder Cancer in Egypt in the Past Decade

Hosni Khairy Salem and Soheir Mahfouz

*Urology*, 79 (2): 0-0 (2012) IF: 2.428

**Objective** to assess the patterns of schistosomiasis-associated bladder cancer in Egypt from 2001 to 2010 in a retrospective study. Bilharzial bladder carcinoma is the most common cancer, particularly in Egyptian men. Classically, carcinoma in a bilharzial bladder is most commonly of the squamous cell type. During the past decade, certain changes have occurred in the features in Schistosomiasis-associated carcinoma in Egypt with a decline in the frequency of squamous cell carcinoma and increase in the frequency of transitional cell carcinoma.

**Methods** This was a retrospective study of 1932 patients treated at Kasr Al Aini Hospital, Cairo University, from 2001 to 2010. Two groups were selected: group 1 included 1002 patients from 2001 to 2005 and group 2 included 930 patients from 2006 to 2010.

**Results** the mean patient age increased from 41.12 years to 52.86 years, and the male/female ratio changed from 5.6:1 to 4.2:1. The incidence of associated bilharziasis decreased from 80% to 50%. A significant increase occurred in transitional cell carcinoma from 20% to 66%, with a significant decrease in squamous cell carcinoma from 73% to 25%. No difference was observed in the tumor stage or grade or incidence of lymph node metastases between the 2 groups.

**Conclusion** the pattern of incidence of the various histologic types of bladder cancer have changed, with most cases now transitional cell carcinoma, in contrast to the findings in the earlier Egyptian series. Additional studies are encouraged to explain the factors explaining these changes.

**Keywords:** Changing patterns; Schistosoma; Bladder cancer; Egypt.

### 299. Rehabilitation of the Cavernous Smooth Muscle in Patients with Organic Erectile Dysfunction

H. Salem and T. Mostafa

*Andrologia*, 44: 125-129 (2012) IF: 1.546

This study aimed at assessing the effect of regular use of intracorporeal injection (ICI), sildenafil citrate and vacuum constriction device (VCD) on cavernous smooth muscle and erectile activity. One hundred and sixty-five patients with organic erectile dysfunction were investigated for 3 months. The patient and his partner were classified prospectively after proper counselling: group I (n = 56) received ICI twice per week; group II (n = 55) received sildenafil 100 mg twice per week; and group III (n = 54) used VCD twice per week. Duplex ultrasound was carried out before and after treatment, and then, the patients were followed up for a month to assess the resumption of unaided erection. The results showed that there was significant improvement in mean peak systolic velocity (PSV) and mean cavernosal artery diameter (CAD) at the end of the treatment in

all groups, being higher in the ICI group than in the other two groups. Also, the percentage of patients who resumed unaided intercourse were higher in the ICI group compared with the other two groups (17.9%, 9.1% and 3.7% respectively). It is concluded that repeated regular use of ICI, sildenafil or VCD by patients with organic erectile dysfunction has a positive impact on their cavernous blood flow and erectile activity.

**Keywords:** Cavernous tissue; Erectile dysfunction; Erection; ICI—sildenafil citrate; Vacuum device.

### 300. Primary and Secondary Malignant Involvement of Gynaecological Organs at Radical Cystectomy for Bladder Cancer: Review of Literature and Retrospective Analysis of 360 Cases

H. Salem and A. El-Mazny

*Journal of Obstetrics and Gynaecology*, 590-593: (2012)

IF: 0.542

The pathological analysis of cystectomy specimens from 360 female patients who underwent radical cystectomy for bladder cancer was retrospectively reported. The uterus was not available in 29 specimens, while one ovary was absent in 18 specimens and the two ovaries were absent in 20 specimens. Uterine involvement was observed in one case of transitional cell carcinoma, and benign uterine pathology was detected in 37 cases. All patients had normal ovaries, while the vagina was involved in 13 cases. A total of 12% of the patients had urethral involvement. None of the 29 patients, in whom the internal genitalia were totally or partially preserved, had late ovarian, vaginal or uterine recurrence at the last follow-up.

Thus, the preservation of female internal genitalia in young patients undergoing radical cystectomy should be considered under strict criteria (low-grade, low-stage tumours away from the bladder neck). This will improve the quality-of-life (QoL) and the functional outcome without compromising cancer control.

**Keywords:** Bladder cancer; Gynaecological organs; Pelvic exenteration; Radical cystectomy.

### 301. Islam and Circumcision

Mohamed S. El-Sheemy

*Surgical Guide To Circumcision*, (2012)

Circumcision is a universal practice that is greatly influenced by cultural and religious traditions. It is the most frequent operation on males not only in Islamic countries, but also other parts of the world [1, 2]. For example, in the USA more than one million male infants are circumcised each year [3]. It is estimated that one-third of the global male population is circumcised.

### 302. Merits and Arguments Related To Circumcision

Hosni Khairy Salem

*Complementary Pediatrics*, (2012)

Christians and non-believers perform Circumcision for health and hygienic reasons especially in U.S.A. and some countries of the Middle East. It is uncommon in Northern Europe, Central and South America and Asia (Leitch, 1970). It is one of the "oldest operations but it has not received enough consideration or progress in the Middle East. It is always regarded as a minor

outpatient procedure often performed by primitive clamps by barbers, Mohels, medical students and house officers (Kaplan, 1977).in hospitals, male circumcision is perform a review of the literature regarding the different aspects of male circumcision and discussing the following points; history of circumcision, urgent indications of circumcision.

## Faculty of Nursing

### Dept. of Community Health Nursing

#### 303. Improvements in the Status of Women and Increased Use of Maternal Health Services in Rural Egypt

Chifa Chiang, Inass Helmy Hassan Elshair, Leo Kawaguchi, Nawal Abdel Moneim Fouad, Nagah Mahmoud Abdou, Michiyo Higuchi, Saneya Rizk El Banna and Atsuko Aoyama

*Nagoya Journal of Medical Science*, 74: 233-240 (2012)

This research investigated the association between the household status of women and their use of maternal health services in rural Egypt. Face-to-face interviews with a structured questionnaire to 201 married women were carried out in a village, posing questions about their health service utilization and their household socio-economic status. the association between service utilization and other variables was statistically analysed. Older ages at first marriage and higher education levels showed significant positive associations with the three outcome variables—regular antenatal care (ANC), deliveries attended by skilled health professionals, and deliveries at health facilities—of the use of maternal health services. Women who had not experienced physical assaults by husbands and had knowledge of community activities were more likely to receive ANC regularly; however, there were no significant association with the other two outcome variables. Participation in household decision-making and availability of assistance with household chores had no significant linkage to the use of maternal health services. Marriages to husbands with secondary or higher levels of education and residence in extended families were significantly associated with greater maternal health service usage. Our results suggest that the improved status of women in the household and moral support from family members contributes to an increase in the use of maternal health services.

**Keywords:** Maternal health services; Women'S status; Family support; Egypt.

### Dept. of Maternal and Newborn Health Nursing

#### 304. Prenatal Attachment and Fetal Health Locus of Control Among Low Risk and High Risk Pregnant Women

Abeer Eswi and Amal Khalil

*World Applied Sciences Journal*, 18 (4): 462-471 (2012)

The present study was carried out to assess prenatal attachment and fetal health locus of control among low risk and high risk Egyptian pregnant women. A descriptive correlational design was utilized for the study. A total of 100 pregnant women, both low (N=55) and high (N= 45) risk pregnant women were recruited for the study. Prenatal attachment inventory and fetal health locus of

control scale (FHLC) were used for data collection Results indicated that participants experienced more positive feelings of attachment towards their fetuses, the mean prenatal attachment was 50.7 (SD± 9.9). Participants also reported high levels of fetal health locus of control, with the mean of 119.3 (SD ±15.0). Prenatal attachment was positively associated with fetal health locus of control, age and number of living children. Fetal health locus of control was positively associated with number of deliveries, number of abortions and marital status. Both prenatal attachment and fetal health locus of control differed by high/low risk pregnancy. in Conclusion, Egyptian pregnant women experienced more positive feeling of attachment toward their fetuses. Prenatal attachment differed by high/low risk pregnancy.

**Keywords:** Prenatal attachment; Locus of control; High risk and Low risk pregnancy.

### Dept. of Medical-Surgical Nursing

#### 305. Psychological Stress Among Gaza War Amputees: Impact of A Designed Training Counseling Program

Atef Ismail (Author), Warda Morsy (Author), Nefissa Abd El kader

*Book Published by Lap Lambert Academic Publishing*, (2012)

Wounded amputees are faced with myriad issues involving mutilation, pain, multiple surgeries, body image issues, depression, anxiety, and post traumatic stress disorder symptoms. All are common and must be addressed rapidly with ongoing counseling and pharmacologic management and along period of rehabilitation.the aim of this study was to investigate the effect of a designed training-counseling program on psychological stress among Gaza War amputees in Gaza Governorates. Quasi-experimental design (pre-test/post-test) was used in this study.the study was conducted on the 24 subjects who have the highest stress level scores. the training counseling program was designed on Albert Ellis theory for rational emotive behavior therapy. Results revealed that the designed training counseling program was having an effective impact on reducing psychological stress level among Gaza war amputees. the study concluded that Gaza war amputees were exposed to a higher stress level that could negatively affect all their life aspects.However,the training counseling program showed a positive impact on reducing their psychological stress level and promoting their abilities to function productively.

## Faculty of Oral Dental Medicine

### Dept. of Endodontics

#### 306. The Effect of Prior Calcium Hydroxide Intracanal Placement on the Bond Strength of Two Calcium Silicate-Based and Epoxy Resin-Based Endodontic Sealers

Suzan Abdul Wanees Amin, Reham Saeed Seyam and Mohammed Abbas El-Samman

*J. Endodont*, 696-699: (2012) IF: 2.88

**Introduction:** the aim of this study was to investigate the effect of prior calcium hydroxide (Ca[OH]2) intracanal placement on

the bond strength of AH Plus (Dentsply DeTrey GmbH, Konstanz, Germany), iRoot SP (Innovative Bioceramics, Vancouver, BC, Canada), and MTA Fillapex (Angelus Soluções Odontológicas, Londrina, PR, Brazil).

**Methods:** the root canals of 90 human incisor teeth were prepared with the ProTaper System (Dentsply Maillefer, Ballaigues, Switzerland) up to a master apical file size of F5. Canals were filled using the single-cone technique either immediately (the control group, n = 30) or after a 7-day Ca(OH)<sub>2</sub> placement. Ca(OH)<sub>2</sub> removal was performed either manually using F5 with distilled water irrigation (the Ca [OH]<sub>2</sub> group, n = 30) or manually using Protaper F5 followed by passive ultrasonic irrigation with 2.5%Na OCl with a final flush of 17 % EDTA and then distilled water (the PUI group, n = 30).

After obturation, a 2-mm-thick middle section of each root was then subjected to push-out testing. Results: Using one-way analysis of variance, AH Plus showed a higher bond strength than iRoot SP and MTA Fillapex in the control group (P < .05). with prior Ca(OH)<sub>2</sub> placement, AH Plus and iRoot SP showed a similar bond strength (P > .05), which was higher than MTA Fillapex (P < .05). Conclusions: Prior Ca (OH)<sub>2</sub> placement seemed to improve the dislodgment resistance of iRoot SP but did not affect AH Plus and MTA Fillapex.

**Keywords:** Calcium hydroxide; Iroot sp; Mta fillapex; Push-out Bond.

### 307. The Effect of Acidity on Dislodgment Resistance of Mineral Trioxide Aggregate and Bioaggregate in Furcation Perforations: an in Vitro Comparative Study

Ahmed Abdel Rahman Hashem and Suzan AbdulWanees Amin

*J. Endodont.* 245-249: (2012) IF: 2.88

**Introduction:** the aim of this study was to compare the effect of acidic environment on the dislodgment resistance of mineral trioxide aggregate (MTA) and Bioaggregate (Innovative BioCeramics, Vancouver, Canada) when used as perforation repair materials.

**Methods:** Eighty, human, mandibular molars were used. Perforations were made in the furcation of each molar and enlarged to #4 Pessio drills. After perforation repair, specimens of each material were randomly divided into 4 groups (n = 10) according to storage media and time: group A: phosphate-buffered saline (PBS) (pH = 7.4) for 4 days, group B: acetic acid (pH = 5.4) for 4 days, group C: PBS for 34 days, and group D: acetic acid (pH = 5.4) for 4 days followed by exposure to PBS for 30 days. Dislodgment resistance was then measured using a universal testing machine, and then the specimens were vertically split to examine the perforated dentin wall using scanning electron microscopy.

**Results:** MTA resisted dislodgment more efficiently than BA after 4 days in PBS (P < .05). the dislodgment resistance of MTA was significantly reduced (P < .05) after exposure to acetic acid, whereas BA was not affected (P > .05). There was an increase in the dislodgment resistance with the increase in the storage time to 34 days (P < .01). After 34 days, there was a statistically significant difference among groups; the MTA D group had significantly the highest bond strength, and the BA D group D had the lowest (P < .05).

**Conclusions:** MTA is more influenced by acidic pH than BA. Storage for 30 days in PBS can reverse the affected bond of MTA by the acidic environment.

**Keywords:** Bioaggregate; Furcation perforation; Mineral trioxide aggregate; Ph; Scanning electron microscopy.

### Dept. of Operative Dentistry

#### 308. Effect of Surface Roughness and Adhesive System on Repair Potential of Silorane-Based Resin Composite

Enas H. Mobarak

*Journal of Advanced Research*, 3: 279-286 (2012) IF: 3

This study was performed to evaluate the influence of surface roughness and adhesive system on the repair strength of silorane-based resin composite. Twenty-four substrate discs from silorane-based FiltekP90 were made and stored for 24 h. Half of the discs were roughened against 320 grit SiC paper while the other half was polished against 4000 grit SiC paper. All discs were etched with phosphoric acid. Repair resin composite, FiltekP90 or Filtek Z250, was bonded to the treated surfaces using their corresponding adhesive; P90 System Adhesive (SA) or Adper Scotchbond Multipurpose (SBMP) ending up with four repair groups. the groups were as follows:

G1: Smooth +SA + Filtek P90; G2: Roughened + SA +Filtek P90; G3: Smooth +

SBMP +Filtek Z250; G4: Roughened + SBMP+ Filtek Z250. Additional six unrepaired discs from each resin composite (G5 and G6) were prepared to test the cohesive strength. After 24 h, discs (n= 6/group) were serially sectioned to obtain sticks (n= 30/group) for microtensile bond strength (ITBS) testing. Scanning electron microscopic (SEM) evaluation of substrates that received different treatments as well as representative substrate-repair sticks from each group were performed.

Modes of failure were also determined. Two-way ANOVA with Repeated-Measures revealed that surface treatment and repair material had no significant effect on repair bond strength of siloranebased composite material. Paired t-test showed that all repair strength values were significantly lower than the cohesive strength of Filtek P90. Adhesive failure was the predominant mode of failure which was confirmed by SEM. Surface treated FiltekP90 composite showed different textures under SEM whereas phosphoric acid did not produce clear changes. an interaction layer between.

**Keywords:** Low shrinkage composite; Repair; Methacrylate based resin composite; Acid etching.

### Dept. of Oral and Maxillofacial Surgery

#### 309. Role of Intra-Articular Ozone Gas Injection in the Management of Internal Derangement of the Temporomandibular Joint

Emad T. Daif

*Oral Surgery Oral Medicine Oral Pathology Oral Radiology*, 113: 10-14 (2012) IF: 1.457

**Objectives:** This study was carried out to compare intra-articular ozone gas injection and drug therapy as conservative treatment modalities for internal derangement of the temporomandibular joint (TMJ).

**Study Design:** Sixty patients (49 female and 11 male) with bilateral internal derangement of the TMJs, disc displacement with reduction, were included in this study. They were divided

randomly into 2 equal groups. the first group was treated by a direct injection of ozone gas into the superior joint space. Each joint received 2 mL ozone-oxygen mixture (ozone gas concentration 10 µg/mL). the injections were repeated 2 times per week for 3 weeks. the second group received nonsteroidal antiinflammatory drugs and muscles relaxants. the clinical signs and symptoms before and after the treatment were assessed according to Helkimos clinical dysfunction index.

**Results:** the results showed that 87% of the patients who received ozone gas injections into the superior joint space (n = 26) either completely recovered (37%; n = 11) or improved (50%; n = 15). in the second group, 33% of the patients who were treated with nonsteroidal antiinflammatory drugs and muscle relaxants (n = 10) showed only an improvement in their clinical dysfunction indexes.

**Conclusions:** Based on the findings of the present study, we can consider that intra-articular ozone gas injection is a promising new treatment modality for internal derangement of the TMJ. However, further clinical and experimental studies are required to provide direct evidence for its mechanism of action and to substantiate our results.

### 310. Correlation of Splint Therapy Outcome with the Electromyography of Masticatory Muscles in Temporomandibular Disorder with Myofascial Pain

Emad T. Daif

*Acta Odontologica Scandinavica*, 70: 72-77 (2012) IF: 1.066

**Objectives:** the aim of this study was to assess the effect of occlusal splint therapy on the electromyographic amplitude records (µV) of masticatory muscles in temporomandibular disorder (TMD) with myofascial pain and to detect a possible existence of a relationship between this effect and the treatment outcome.

**Materials and methods:** Forty patients (23 females and 17 males) having TMD with myofascial pain were included in this study. They were randomly divided into two equal groups (20 of each). the first group (A) was treated by occlusal splints for 6 months while the second group (B) acted as a control. A clinical assessment and surface electromyography (EMG) for the masticatory muscles were performed at the beginning of the study, then 6 months later. the collected data were statistically analyzed using paired t-test. the differences were considered significant at  $p < 0.05$ .

**Results:** the results showed that 85% of group A either completely recovered (35%) or clinically improved (50%) while only 20% of group B had a spontaneous improvement. in group A, the means of the electromyographic amplitude records (µV) of the monitored muscles have decreased after 6 months. However, the decrease was statistically insignificant ( $p > 0.05$ ) in the patients (15%) who had no clinical changes. in group B, the means of the muscles records (µV) in the left side slightly increased while those of the right side slightly decreased. These changes were statistically insignificant ( $p > 0.05$ ).

**Conclusions:** Occlusal splint could eliminate or improve the signs and symptoms of TMD patients with myofascial pain. It reduces the electromyographic amplitude records (µV) of the masticatory muscles. the splint therapy outcome has a correlation with the electromyographic amplitude changes of the masticatory muscles.

**Keywords:** Tmd disorder with myofascial pain; Splint; Electromyography.

### Dept. of Oral Biology

### 311. The Relationship Between Receptor for Advanced Glycation End Products Expression and the Severity of Periodontal Disease in the Gingiva of Diabetic and Non Diabetic Periodontitis Patients

Marwa Magdy Abbass, Nahed Sedky Korany, Ahmed Helmy Salama, John J. Dmytryk and Barbara Safiejko-Mroccka

*Arch Oral Biol*, 57: 1342-1354 (2012) IF: 1.603

Activation of receptor for advanced glycation end products (RAGE) has been implicated in many chronic diseases, including diabetic complications. in this study we examined the relationship between RAGE expression and the morphological changes seen in the gingiva of diabetic and periodontitis patients.

**Design:** Gingival biopsies from 15 diabetic patients with periodontitis, 25 non diabetic patients with periodontitis and 10 healthy individuals were collected. Sections were stained with haematoxylin and eosin, and immunohistochemically to detect RAGE. Samples were examined in light and fluorescence microscopes and histomorphometric analysis was performed.

**Results:** Increased number of inflammatory cells and changes in collagen and vasculature were observed in diabetic and non diabetic patients with periodontitis. RAGE was weakly expressed in healthy gingiva. the strongest reaction with anti-RAGE antibody was found in the gingiva of diabetic patients with periodontitis followed by the severe periodontitis patients. RAGE expression in inflammatory cells was stronger than in the epithelium. the number of inflammatory cells in the gingiva was higher in the diabetic periodontitis patients than in the non diabetic severe periodontitis patients.

**Conclusions:** RAGE is strongly expressed in the gingiva of diabetic patients with periodontitis and with severe periodontitis alone, the latter indicating RAGE activation even in the absence of hyperglycemia. However our findings are based on relatively small sample size. with a larger patient population, some of our other findings may have reached statistical significance.

**Keywords:** Receptor for advanced glycation end products (Rage); Diabetes; Periodontitis; Gingiva; Immunohistochemistry; Immunofluorescence.

### 312. Evaluation of Socket Healing in Irradiated Rats After Diode Laser Exposure (Histological and Morphometric Studies)

Nahed S. Korany, Samah S. Mehanni, Heba M. Hakam and Eman M.F. El-Maghraby

*Arch Oral Biol*, 57 (7): 884-891 (2012) IF: 1.603

**Objective:** the purpose of this study is to evaluate the effect of low-level laser therapy (LLLT) in enhancing bone repair in irradiated sockets of albino rats.

**Design:** Thirty male Swiss Albino rats ranging from 120 to 150 g were used in this study. The animals were subjected 6 gray gamma radiations. Three days post irradiation, right and left mandibular first molars were extracted. the sockets of the left sides were irradiated by (GaAIA) diode laser device immediately after extraction, while the sockets of the right side were not exposed to the laser and served as control. the rats were randomly assigned into three groups (10 rats each) according to the date of sacrifice, 3, 7 and 10 days into groups I, II and III, respectively.

the two sides of each mandible were separated. Each group was further subdivided into subgroups A and B (10 specimens each), where A represents the right side of the mandible and B represents the left side. The specimens were stained with hematoxylin and eosin, and Masson's trichrome.

**Results:** LLLT accelerated bone healing, while, radiotherapy induced delay of bone healing along the three experimental groups. This acceleration was assessed histologically by the presence of mature collagen fibre bundles and early new bone formation in the lased groups. Histomorphometric analysis revealed an increase in the area percentage of bone trabeculae in the lased sockets compared to the control ones in group II. This increase was statistically significant ( $p = 0.0274$ ). The increase in the area percentage of bone trabeculae between the lased and control sockets of group III was statistically insignificant ( $p = 0.1903$ ).

**Conclusions:** in a rat model application of LLLT with a GaAlAs diode laser device can enhance bone healing and mineralisation in sockets subjected to gamma radiation.

**Keywords:** Preoperative irradiation; Bone repair; Low-level laser therapy (LLT); Rats.

### 313. Histomorphological Study of Dentine Pulp Complex of Continuously Growing Teeth in the Rabbits

Zoba H. Ali and Rabab Mubarak

*Life Science Journal*, 9 (3): 1554-1564 (2012) IF: 0.073

Rabbits have a diphyodont dentition (permanent and deciduous sets of teeth). Rabbit teeth are also heterodont (of different types). Incisors as well as posterior cheek teeth are aradicular hypsodont, indicating that the teeth have a long anatomic crown and do not have true roots. These teeth erupt continuously, and remain openrooted.

**Aim:** the present study aims to clarify the morphological and histological features of the dentine pulp complex of continuously growing incisors & molars teeth of rabbits.

**Methods:** Ten New Zealand white rabbits in the age of three months old were used in this study. After scarification, the lower jaws were dissected out and hemisected in sagittal direction into two halves (right and left sides of the mandible), Then prepared for Morphological examination using stereo microscopy and histological examination of decalcified and ground sections using light microscopy.

**Results:** stereo microscopic examination revealed that molar teeth consist of two laminae with double apical openings. Histological examination showed dentine precipitation along the side of the pulp and complete obliteration of the coronal portion of the pulp by osteodentine.

**Conclusion:** different types of dentine are precipitated within the pulp chamber of continuously growing teeth as a compensatory mechanism for continuous teeth wear out.

**Keywords:** Rabbit cheek molar teeth; Dentine pulp complex; Osteodentine.

### 314. Propolis Versus Daktarin® in Mucosal Wound Healing

Zoba H. Ali and Heba Mahmoud Dahmouh

*Life Science*, 9 (2): 624-636 (2012) IF: 0.073

The aim of this study was to compare the effect of propolis versus daktarin on mucosal wound healing. Fifty two albino rats were

randomly divided into three groups; G 1 (propolis), G 2 (daktarin) and control group. Following the induction of a surgical mucosal wound in the labial mucosa by means of a 1-mm punch-biopsy instrument, biopsy specimens were taken on days 1, 3, 7 and 14 from groups of sacrificed rats and stained with haematoxylin-eosin stains, Mallory's trichrome stain as well as CD68 immunohistochemical stain. Data were analyzed statistically. Histological evaluation of each specimen was done and scoring criteria were used to compare the healing status of wounds. There was no statistical significance between different groups, on day 1. However there was statistically significant difference between G1 and both G2 and control group on day 3. on day 7, statistically significant difference was found between G1 and control group, but there was no statistically significant difference between G1 and G2. Conclusion: Propolis has an enhancing effect on the healing of oral mucosal wounds compared to daktarin.

**Keywords:** Propolis; Daktarin; Labial mucosa; Cd68 immunohistochemical stain.

### Dept. of Oral Medicine and Periodontology

#### 315. Expression Levels of Microrna-21 and Microrna-146A in Patients with Oral Lichen Planus

Gihane Gharib Madkour, Hani EL Nahass and Wesam Abd El Moneim Mohamad

*Life Science Journal*, 9 (4): 4666-4670 (2012) IF: 0.073

Increasing evidence indicates that microRNAs (miRNAs) play a critical role in the pathogenesis of inflammatory diseases. Oral lichen planus (OLP) is a chronic inflammatory disease involving the oral mucosal tissues. The role of miRNAs in the pathogenesis of OLP has not been investigated. Therefore, the aim of this study was to investigate the expression levels of miRNA-21 and miRNA-146a in oral tissue samples from patients with OLP and matched healthy controls using real-time quantitative reverse transcriptase polymerase chain reaction (qRT-PCR). Our results showed a significant over-expression of miRNA-21 (3.2-fold) and miRNA-146a (5.6-fold) in OLP patients compared to healthy controls. These results indicate that miRNAs may be the novel candidate biomarkers for the implication of miRNAs in the pathogenesis of OLP.

**Keywords:** Oral lichen planus; Mirna-21; Mirna; 146A.

#### 316. Receptor Activator of Nuclear Factor-Kappa B Ligand, Osteoprotegerin and Interleukin-17 Levels in Gcf of Chronic, Aggressive Periodontitis and Type 2 Diabetes

Riham Omar Ibrahim

*Life Science Journal*, 9 (4): 2895-2903 (2012) IF: 0.073

The aim of this study is to compare the levels of osteoclastogenesis-related factors sRANKL and OPG and their ratios as well as the level of IL-17 in gingival crevicular fluid (GCF) from subjects with chronic periodontitis, generalized aggressive periodontitis and controlled type 2 DM patients with chronic periodontitis.

**Methods:** GCF samples and clinical periodontal parameters were randomly obtained from sixteen patients with chronic periodontitis, 16 patients with aggressive periodontitis, 16 patients with controlled diabetes type II and 12 healthy controls.

Concentrations of sRANKL, OPG, and IL-17 in GCF were analyzed by enzyme-linked immunosorbent assay (ELISA).

**Results:** Higher concentration levels of sRANKL, OPG, RANKL/OPG ratios and IL-17 in the three diseased (experimental) periodontitis groups compared to the control group. Aggressive periodontitis group showed higher concentration level of GCF IL-17 in GCF significantly higher than both chronic periodontitis and diabetic groups. Significant There was positive correlation of sRANKL, IL-17, and sRANKL/OPG ratio in GCF with the clinical parameters ( $P < 0.01$ ).

**Conclusion:** GCF total amount of sRANKL, OPG were significantly increased in periodontal disease, supporting its role in the alveolar bone changes developed in this disease. Th17 responses may be characteristic of AgP, and IL-17 may play a role in the pathogenesis of aggressive periodontitis.

**Keywords:** Periodontitis; Diabetes Type 2; Rankl; Opg; Il-17; Gcf; Elisa.

#### Dept. of Oral Pathology

### 317. The Adverse Effects of Nano-Bond Adhesive Systems used as Direct Pulp Capping Materials

Sahar A. M. Abd El Halim and Dalia H. El-Rouby

*European Journal of Dentistry and Medicine*, 4 (2): 14-25: (2012)

**Objective:** the purpose of this study was to evaluate the histopathological changes in mechanically exposed dog's pulps capped with Nano Bond®, Clearfil SE Bond Self-etching adhesive systems in comparison to Dycal.

**Methods:** Six dogs were used in this study. Class V cavities were prepared on the buccal surface of 15 intact teeth in each dog. Pulps were then mechanically exposed, then capped according to each group:

Group (1): Control, pulp capped with CH Dycal (lower right side);

Group (2): Pulp capped with Nanobond®;

Group(3): Pulp capped with Clearfil SE Bond (SE). the cavities were restored with Nano composite Filtek Supreme XT. Dogs were sacrificed at 7,14,30 days postoperatively.

Teeth were fixed, decalcified, processed and stained with hematoxylin and eosin. the histo-pathological features were examined and graded using light microscopy. the data were statistically analyzed using Kruskal-Wallis test.

**Results:** for both adhesive systems, the pulp tissue exhibited moderate to severe inflammatory infiltrate involving the coronal pulp. Dycal induced a less severe inflammatory response and more consistent formation of reparative dentine. Statistically significant differences in inflammatory response, tissue disorganization, and hard tissue formation were observed among teeth treated with adhesive systems and Dycal.

**Conclusion:** A less favorable pulpal response was noted in the experimental groups in comparison to the control.

**Keywords:** Nanobond adhesive; Direct pulp capping; Histopathology; Pulp reaction.

#### Dept. of Orthodontics

### 318. Deep Overbite Malocclusion: Analysis of the Underlying Components

Mostafa M. El-Dawlatly, Mona M. Salah Fayed and Yehya A. Mostafa

*Am J Orthod Dentofac*, 473-480: (2012) IF: 1.381

**Introduction:** A deepbite malocclusion should not be approached as a disease entity; instead, it should be viewed as a clinical manifestation of underlying discrepancies. the aim of this study was to investigate the various skeletal and dental components of deep bite malocclusion, the significance of the contribution of each, and whether there are certain correlations between them.

**Methods:** Dental and skeletal measurements were made on lateral cephalometric radiographs and study models of 124 patients with deepbite. These measurements were statistically analyzed.

**Results:** an exaggerated curve of Spee was the greatest shared dental component (78%), significantly higher than any other component ( $P = 0.0335$ ). A decreased gonial angle was the greatest shared skeletal component (37.1%), highly significant compared with the other components ( $P = 0.0019$ ). A strong positive correlation was found between the ramus/Frankfort horizontal angle and the gonial angle; weaker correlations were found between various components.

**Conclusions:** an exaggerated curve of Spee and a decreased gonial angle were the greatest contributing components. This analysis of deepbite components could help clinicians design individualized mechanotherapies based on the underlying cause, rather than being biased toward predetermined mechanics when treating patients with a deepbite malocclusion.

**Keywords:** Deep over-bite; Diagnosis; Components.

### 319. Insulin-Like Growth Factor I: A Biologic Maturation Indicator

Ramy Abdul Rahman Ishaq, Sanaa Abou Zeid Soliman, Manal Yehya Foda and Mona Mohamed Salah Fayed

*Am J. Orthod Dentofac*, 142: 654-661 (2012) IF: 1.381

Determination of the maturation level and the subsequent evaluation of growth potential during preadolescence and adolescence are important for optimal orthodontic treatment planning and timing. This study was undertaken to evaluate the applicability of insulin-like growth factor I (IGF-I) blood level as a maturation indicator by correlating it to the cervical vertebral maturation index. Methods: the study was conducted with 120 subjects, equally divided into 60 males (ages, 10-18 years) and 60 females (ages, 8-16 years). A lateral cephalometric radiograph and a blood sample were taken from each subject. for each subject, cervical vertebral maturation and IGF-I serum level were assessed. Mean values of IGF-I in each stage of cervical vertebral maturation were calculated, and the means in each stage were statistically compared with those of the other stages. Results: the IGF-I mean value at each cervical vertebral maturation stage was statistically different from the mean values at the other stages. the highest mean values were observed in stage 4, followed by stage 5 in males and stage 3 in females. Conclusions: IGF-I serum level is a reliable maturation indicator that could be applied in orthodontic diagnosis

**Keywords:** Insulin; Growth; Factor; Maturation; Index.



## Faculty of Pharmacy

### Dept. of Analytical Chemistry

#### 320. New Spectrofluorimetric Methods for Determination of Melatonin in the Presence of N-{2-[1-({3-[2-(Acetylamino)Ethyl]-5-Methoxy-1H-Indol-2-Yl}Methyl)-5-Methoxy-1H-Indol-3-Yl]-Ethyl}Acetamide: A Contaminant in Commercial Melatonin Preparations

Hany W Darwish and Mohamed I Attia

*Chem Cent J*, 36: 1-11 (2012) IF: 3.281

**Background:** Melatonin (MLT) has many health implications, therefore it is of valuable importance to develop specific analytical methods for determination of MLT in the presence of its main contaminant, N-{2-[1-({3-[2-(acetylamino)ethyl]-5-methoxy-1H-indol-2-yl}methyl)-5-methoxy-1H-indol-3-yl]ethyl}acetamide (10). for development of these analytical methods, compound 10 had to be prepared in an adequate amount.

**Results:** Compound 10 was synthesized in six steps starting from 5-methoxyindole-2-carboxylic acid (1). Analytical performance of the proposed spectrofluorimetric methods was statistically validated with respect to linearity, accuracy, precision and specificity. the proposed methods were successfully applied for the assay of MLT in laboratory prepared mixtures containing up to 60 % of compound 10 and in commercial MLT tablets with recoveries not less than 99.00 %. No interference was observed from common pharmaceutical additives and the results were favorably compared with those obtained by a reference method.

**Conclusions:** This work describes simple, sensitive, and reliable second derivative spectrofluorimetric method in addition to two multivariate calibration methods, principal component regression (PCR) and partial least square (PLS), for the determination of MLT in the presence of compound 10.

**Keywords:** Melatonin; Contaminants; Synthesis; Spectrofluorimetry; Commercial Preparations.

#### 321. Combining the Isoabsorptive Point in the Ratio Spectrum and the Smart Ratio Difference Methods for A Single Step Determination of Compounds with Overlapped Spectra

Eman S. Elzanfaly, Ahmed S. Saad and Abd-Elaziz B. Abd-Elaleem

*Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 95: 188-192 (2012) IF: 2.098

A new method significantly advantageous over the conventional spectrophotometric methods regarding simplicity, minimal data processing and applicability was developed. the new method is based on the fact that isoabsorptive points whenever present in an absorption spectrum will be retained even after division by a one component as a divisor in the ratio spectrum, in addition to a smart modification of the conventional ratio derivative and ratio subtraction methods.

This modified method though simpler, enabled wider range of applications. the proposed method was applied for the analysis of brimonidine and timolol in laboratory prepared mixtures with mean percentage recoveries  $100.64 \pm 1.10$  and  $100.96 \pm 1.16$ , respectively, and in their pharmaceutical formulation with mean

percentage recoveries  $100.88 \pm 0.34$  and  $100.84 \pm 0.72$ , respectively. the suggested method was validated according to USP guidelines and can be applied for routine analysis in quality control laboratories.

**Keywords:** Spectrophotometry; Binary mixtures; Brimonidine; Timolol; Ratio difference method; Isoabsorptive point; Dpiso.

#### 322. Comparative Study of Novel Spectrophotometric Methods Manipulating 3 Ratio Spectra: an Application on Pharmaceutical Ternary Mixture of Omeprazole, Tinidazole and Clarithromycin

Hayam Mahmoud Lotfy and Maha Abdel-Monem Hagazy

*Spectrochimica Acta*, 96: 259-270 (2012) IF: 2.098

Three simple, specific, accurate and precise spectrophotometric methods manipulating ratio spectra are developed for simultaneous determination of omeprazole (OM), tinidazole (TN) and clarithromycin (CL) in tablets.

Method A, is an extended ratio subtraction one (EXRSM). Method B is a ratio difference spectrophotometric one (RDSM), while method C is mean centering of ratio spectra (MCR). the calibration curves are linear over the concentration range of 1–20 lg/mL, 10–60 lg/mL and 0.25–1.0 mg/mL for OM, TN and CL, respectively. the specificity of the developed methods is investigated by analyzing laboratory prepared mixtures of the three drugs and their combined dosage form.

Standard deviation values are less than 1.5 in the assay of raw materials and tablets. the three methods are validated as per ICH guidelines and accuracy, precision, repeatability and robustness are found to be within the acceptable limits.

**Keywords:** Ternary Mixture; Extended Ratio Subtraction; Ratio Difference; Mean Centering; Spectrophotometry.

#### 323. New Developed Spectrophotometric Method for Simultaneous Determination of Salmeterol Xinafoate and Fluticasone Propionate in Bulk Powder and Seritide Diskus Inhalation

Ahmed Samir, Hesham Salem and Mohammad Abdelkawy

*Bulletin of Faculty of Pharmacy, Cairo University*, 50: 121-126 (2012) IF: 2

A new simple, accurate, precise, rapid and economical method was developed for the simultaneous determination of Salmeterol xinafoate and Fluticasone propionate in their binary mixture in bulk powder and Seritide diskus inhalation.

The new method depends on new calculations using the mixture's absorbance at 225 and 256.5 nm where the absorptivity of Salmeterol xinafoate is double the absorptivity of Fluticasone propionate, while the content of Salmeterol xinafoate was determined by measuring the absolute value of the first derivative ultraviolet curves at 352 nm, without interference from Fluticasone propionate. the proposed method was validated and the results obtained by adopting the proposed method were statistically analyzed and compared with those obtained by reported methods.

**Keywords:** Salmeterol Xinafoate.

### 324. Stability Indicating Hplc and Spectrophotometric Methods for the Determination of Bupropion Hydrochloride in the Presence of Its Alkaline Degradates and Related Impurity

Samah S. Abbas, Mohamed R. Elghobashy, Rafeek F. Shokry and Lories I. Bebawy

*Bulletin of Faculty of Pharmacy, Cairo University*, 50: 49-59 (2012) IF: 2

Four sensitive and selective stability-indicating methods for the determination of bupropion hydrochloride in the presence of its alkaline degradates, related impurity, 3-chlorobenzoic acid, and in its pharmaceutical formulation were developed.

Method A is an isocratic reversed phase HPLC, good separation between bupropion hydrochloride, its alkaline degradates and related impurity was achieved using a mobile phase of 1.2% w/v ammonium dihydrogen phosphate pH 4.5 and acetonitrile (80:20, v/v) and detection at 210 nm.

Method B is based on the first derivative (D1) measurement of the drug at 259 nm, zero contribution point of its alkaline degradates and related impurity.

Method C is based on the resolution of the drug, its alkaline degradates and related impurity by first derivative ratio spectra (DD1).

Method D is based on the determination of bupropion hydrochloride and its impurity by the Q value method at 248 nm, 227 nm and at isoabsorptive point 237 nm.

These methods are successfully applied for the determination of bupropion hydrochloride in bulk powder, pharmaceutical formulation and in the presence of its alkaline degradates and related impurity. The results obtained are statistically analyzed and there are no significant differences between the four methods and the official one with respect to accuracy and precision.

**Keywords:** Bupropion hydrochloride; Reversed phase-hplc; First derivative spectrophotometry; First derivative of ratio spectra; Q value.

### 325. Miniaturized Membrane Sensors for Potentiometric Determination of Metoprolol Tartrate and Hydrochlorothiazide

Nesrin K. Ramadan, Heba M. Mohamed and Azza A. Mostafa

*Acta Chimica Slovenica*, 59: 344-352 (2012) IF: 1.328

Four micro-sized graphite and platinum wire poly(vinyl chloride) matrix membrane electrodes responsive to some drugs affecting cardiovascular system, Metoprolol tartrate (MT) and Hydrochlorothiazide (HZ) were developed, described and characterized.

These sensors were constructed by using (2-Hydroxypropyl)- $\beta$ -cyclodextrin (2HP  $\beta$ -CD) as an ionophore which has a significant influence on increasing both membrane sensitivity and selectivity. The four sensors were fabricated in a polymeric matrix of carboxylated polyvinyl chloride (PVC-COOH) and dioctylphthalate (DOP) as a plasticizer, based on the interaction between the drugs and the dissociated COOH groups in the PVC-COOH. Fast and stable Nernstian responses of  $1.0 \times 10^{-6}$ – $1.0 \times 10^{-2}$  M for MT (sensors 1 and 2) and of  $1.0 \times 10^{-7}$ – $1.0 \times 10^{-3}$  M for HZ (sensors 3 and 4) over pH range 3.0–9.0 and 3.0–7.0 for the MT and HZ sensors respectively were obtained. Nernstian slopes of 56.2, 54.6, 19.0 and 20.8 mV/decade for

electrodes 1–4 respectively were observed. The proposed method displayed useful analytical characteristics for the determination of MT and HZ in their pure powder forms with average recoveries of  $99.11 \pm 0.357$ ,  $99.21 \pm 0.389$ ,  $100.08 \pm 0.459$  and  $100.28 \pm 0.438\%$  for sensors 1–4 respectively. The lower limit of detection (LOD) were  $5.5 \times 10^{-6}$ ,  $4.5 \times 10^{-6}$ ,  $4.8 \times 10^{-8}$  and  $5.0 \times 10^{-8}$  M for sensors 1–4 respectively indicated high sensitivity.

The four sensors displayed a good stability over a period of 6 weeks. The selectivity coefficients of the developed sensors indicated excellent selectivity. Results obtained by the four electrodes revealed the performance characteristics of these electrodes which evaluated according to IUPAC recommendations. The method was successively applied for the determination of MT and HZ in presence of each other, in presence of Salamide (SA), the main degradation product of HZ, in their pharmaceutical formulations and in human plasma samples. Statistical comparison between the results obtained by this method and those obtained by the official methods of the drugs was done and no significant difference was found.

**Keywords:** Metoprolol tartrate; Hydrochlorothiazide; Microsized electrodes; Cyclodextrin; Human plasma.

### 326. Ion-Selective Electrodes for the Potentiometric Determination of Pramoxine HCl Using Different Ionophores

Nesrin K. Ramadan and Hanan A. Mery

*Acta Chim. Slov.*, 59: 870-878 (2012) IF: 1.328

Four novel pramoxine HCl (PAM) selective electrodes were investigated with 2-nitrophenyl octylether as a plasticiser in a polymeric matrix of polyvinyl chloride (PVC). Sensor 1 was fabricated using sodium-tetraphenylborate (TPB) as an anionic exchanger without incorporation of an ionophore. Sensor 2 used 2-hydroxy propyl -cyclodextrin as an ionophore, while sensors 3 and 4 were constructed using 4-sulfocalix-6-arene and 4-sulfocalix-8-arene respectively as ionophores. Linear responses of PAM within the concentration ranges of  $10 \times 10^{-4}$  to  $10 \times 10^{-2}$  mol L<sup>-1</sup> and  $10 \times 10^{-5}$  to  $10 \times 10^{-2}$  mol L<sup>-1</sup> were obtained using sensors 1 and 2, respectively and  $10 \times 10^{-5}$  to  $10 \times 10^{-2}$  mol L<sup>-1</sup> were obtained using sensors 3 and 4. Nernstian slopes of  $50.4 \pm 0.6$ ,  $54.3 \pm 0.8$ ,  $56.3 \pm 0.3$  and  $59.1 \pm 0.5$  mV/decade over the pH range of 3–6 were observed. The selectivity coefficients of the developed sensors indicated excellent selectivity for PAM. The utility of 2-hydroxy-propylcyclodextrin (2HP- $\beta$ -CD) and 4-sulfocalix [6, 8] arene (SC 6, 8) as ionophores had a significant influence on increasing the membrane sensitivity and selectivity of sensors 2, 3 and 4 compared to sensor 1. The proposed sensors displayed useful analytical characteristics for the determination of PAM in bulk powder, pharmaceutical formulation, and in biological fluid. Validation of the method showed the suitability of the proposed electrodes for the use in the quality control assessment of the drug. Furthermore, statistical comparison between the results obtained by the proposed method and the official method of the drug was performed and no significant difference was found.

**Keywords:** Pramoxine HCl; Pramocaine HCl; 2-Hydroxy Propyl- $\beta$ -Cyclodextrin; Calixarene; Potentiometry; Plasma.

### 327. New Spectrofluorimetric Methods for the Simultaneous Determination of Olmesartan Medoxamil and Amlodipine Besylate in Their Combined Tablets

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*Digest Journal of Nanomaterials and Biostructures*, 1599-1607 (2012) IF: 1.2

Olmesartan medoxamil (OLM, an angiotensin II receptor blocker) and amlodipine besylate (AML, a dihydropyridine calcium channel blocker), are co-formulated in a single-dose combination for the treatment of hypertensive patients whose blood pressure is not adequately controlled on either component monotherapy. In this work, two simple, sensitive, and reliable spectrofluorimetric methods have been developed and validated for the simultaneous determination of OLM and AML in their combined tablets. These methods are first derivative and ratio subtraction methods for OLM and AML, respectively. The optimum assay conditions were established and the methods were validated with respect to linearity, sensitivity, accuracy, precision and specificity.

Regression analysis showed excellent correlation between the peak amplitude or fluorescence intensity with the concentration over the concentration ranges of 0.08-1 and 0.25-2  $\mu\text{g mL}^{-1}$  for OLM and AML, respectively. The proposed methods were successfully applied for the assay of the two drugs in their laboratory prepared mixtures and combined pharmaceutical tablets with recoveries not less than 99.0%. No interference was observed from common pharmaceutical additives. The results were favourably compared with those obtained by a reference method.

**Keywords:** Olmesartan medoxamil; Amlodipine besylate; Spectrofluorimetry; Simultaneous determination; Pharmaceutical tablets.

### 328. Simultaneous Determination of Sumatriptan and Naproxen in Dosage Forms and Human Plasma Using LC/MS

M. Michael, Adel; M. Lotfy, Hayam; R. Reda, Mamdouh; Michail, Karim; Somayaji, Vishwa; G. Siraki, Arno; O.S. El-Kadi, Ayman and A. Shehata, Mostafa

*Current Analytical Chemistry*, 8: 512-519 (2012) IF: 1

This work describes a simple and sensitive method for the concurrent determination of sumatriptan (SUM) and naproxen (NAP) in dosage forms and human plasma using LC/MS and internal standardization. The drugs were separated isocratically on a C18 column using a binary mobile phase composed of water and acetonitrile at 0.05% acetic acid. The method was validated over a linearity range of 10-100 ng/mL and 0.1-10  $\mu\text{g/mL}$  for SUM and NAP, respectively. The LOQ for SUM and NAP were 10 and 100 ng/mL, respectively. The proposed method was successfully used for the determination of SUM and NAP in plasma after a double liquid-liquid extraction (LLE). The assay was successfully applied to the determination of both drugs in pharmaceutical dosage form without interference from tablet excipients. Results obtained by the proposed method were satisfactory compared to those of a reported method, and no significant difference was observed.

**Keywords:** LC/MS; Naproxen; Plasma; Pharmaceutical dosage forms; Sumatriptan.

### 329. Simultaneous Determination of Methocarbamol and Ibuprofen or Diclofenac Potassium Using Mean Centering of the Ratio Spectra Method

Nouruddin Wageih Ali, Maha Ahamd Hegazy, Mohamed Abdelkawy and Eglal Abdelahamid Abdelaleem

*Acta Pharmaceut*, 62: 191-200 (2012) IF: 0.912

Accurate and sensitive methods were developed for simultaneous determination of methocarbamol and ibuprofen or diclofenac potassium in their binary mixtures, and in the presence of a methocarbamol related substance (guaifenesin) using mean centering of the ratio spectra method. The results obtained were statistically compared with the reported HPLC methods; no significant difference between the proposed methods and the reported methods was found regarding either accuracy or precision.

**Keywords:** Methocarbamol; Diclofenac potassium; Ibuprofen; Mean centering of ratio spectra; Guaifenesin.

### 330. On-Line Sample Cleanup and Enrichment Chromatographic Technique for the Determination of Ambroxol in Human Serum

Emara S, Kamal M and Abdel Kawi M.

*J Chromatogr Sci*, 50: 91-96 (2012) IF: 0.884

A sensitive and efficient on-line clean up and pre-concentration method has been developed using column-switching technique and protein-coated m-Bondapak CN silica pre-column for quantification of ambroxol (AM) in human serum. The method is performed by direct injection of serum sample onto a protein-coated m-Bondapak CN silica pre-column, where AM is pre-concentrated and retained, while proteins and very polar constituents are washed to waste using a phosphate buffer saline (pH 7.4). The retained analyte on the pre-column is directed onto a C18 analytical column for separation, with a mobile phase consisting of a mixture of methanol and distilled deionized water (containing 1% triethylamine adjusted to pH 3.5 with orthophosphoric acid) in the ratio of 50:50 (v/v).

Detection is performed at 254 nm. The calibration curve is linear over the concentration range of 12–120 ng/mL ( $r^2 = 0.9995$ ). The recovery, selectivity, linearity, precision, and accuracy of the method are convenient for pharmacokinetic studies or routine assays.

**Keywords:** Ambroxol; Enrichment chromatographic.

### 331. Simultaneous Determination of Methocarbamol and Its Related Substance (Guaifenesin) in Two Ternary Mixtures with Ibuprofen and Diclofenac Potassium by HPTLC Spectrodensitometric Method

Nouruddin W. Ali, Maha A. Hegazy, Mohammed Abdelkawy, and Eglal A. Abdelaleem

*Jpc-J Planar Chromat*, 25: 150-155 (2012) IF: 0.767

Accurate, sensitive, and precise high-performance thin-layer chromatographic (HPTLC) method was developed and validated for the determination of Methocarbamol (ME) and its related substance (guaifenesin (GU)) in two ternary mixtures with ibuprofen (IB) and diclofenac potassium. The method depends on separation and quantification of the studied drugs on TLC silica

gel 60 F254 plates using ethyl acetate–acetone–triethylamine–formic acid (62:35:6:0.3, by volume) as the developing system followed by densitometric measurement of the bands at 222 nm for the first mixture containing methocarbamol, IB, and GU and at 278 nm for the second mixture containing methocarbamol, diclofenac potassium, and GU. the proposed methods were successfully applied for the determination of ME, IB, and diclofenac potassium in the presence of ME-related substance (GU) either in bulk powder or in their pharmaceutical formulations.

**Keywords:** Methocarbamol; Ibuprofen; Diclofenac potassium; Guaifenesin; Hptlc spectrodensitometry.

### 332. Simultaneous Determination of Methocarbamol and Its Related Substance (Guaifenesin) in Two Ternary Mixtures with Ibuprofen and Diclofenac Potassium by Rphplc Method

Nouruddin W. Ali, Maha A. Hegazy, M. Abdelkawy and Eglal A. Abdelaleem

*J. Liq Chromatogr R T*, 35: 2229-2242 (2012) IF: 0.706

Accurate, sensitive, and precise RP-HPLC methods were developed and validated for determination of Methocarbamol and its related substance (Guaifenesin) in two ternary mixtures with Ibuprofen and Diclofenac potassium. the first mixture containing Methocarbamol, Ibuprofen, and Guaifenesin was separated using Isocratic elution on a Phenomenex C18 column using 0.05M KH<sub>2</sub>PO<sub>4</sub> (pH/47): acetonitrile methanol (90:25:15, by volume) as a mobile phase at a flow rate of 1.2 mL.min<sup>-1</sup> and UV detection at 220 nm. the second mixture containing Methocarbamol, Diclofenac potassium, and Guaifenesin was separated using Isocratic elution on a Phenomenex C18 column using 0.05M KH<sub>2</sub>PO<sub>4</sub> (pH/47): acetonitrile (80:30, v=v) as a mobile phase at a flow rate of 1.5 mL.min<sup>-1</sup> and UV detection at 278 nm. the proposed methods were successfully applied for determination of Methocarbamol, Ibuprofen, and Diclofenac potassium in presence of Methocarbamol related substance (Guaifenesin) either in bulk powder or in its pharmaceutical formulation.

**Keywords:** Diclofenac potassium; Guaifenesin; Ibuprofen; Methocarbamol; Rp-Hplc.

### 333. Back-Flush Column-Switching Technique for on-Line Sample Cleanup and Enrichment to Determine Guaiphenesin in Human Serum

Samy Emaraa, Maha Kamala, Ghada Hadadb, Hala ZaaZaac and Mohamed Abdel Kawia

*J Liq Chromatogr R T*, 35: 15-27 (2012) IF: 0.706

A direct injection high-performance liquid chromatographic (HPLC) method, with column-switching, for the determination of guaiphenesin (GP) in human serum has been developed. Serum samples were directly injected onto protein-coated RP-8 silica precolumn, where GP was preconcentrated and retained while proteins and very polar components were washed to waste using phosphate buffer saline, pH 7.4. GP was back-flushed from the precolumn by a column-switching technique and separated on a ZORBAX Eclipse XDB-C18 analytical column with a mobile phase consisting of methanol-0.01M phosphate buffer (containing 1% triethylamine adjusted to pH 3.5 with ortho-phosphoric acid) in the ratio of 45:55 (v=v). the analyte was detected by its UV

absorbance at 254 nm. the calibration curve was linear over the concentration range of 25–4000 ng=mL ( $r^2/0.9994$ ). the method was validated for linearity, accuracy, precision, selectivity, and robustness.

**Keywords:** Column-Switching; guaiphenesin; Hplc; Protein-Coated Rp-8 silica precolumn; Zorbax eclipse Xdb-C18 column.

### 334. Water Hyacinth Roots as Economic Potential Biomass for the Removal of Organic Pollutants in Wastewater Via Application of Coated Wire Electrodes

Safa'a M. Riad and Nouruddin W. Ali

*Analytical & Bioanalytical Electrochemistry*, 480-497: (2012) IF: 0.67

The applicability of Water Hyacinth (*Eichhornia crassipes*) as an important aquatic weed plant in sub-tropical regions of the world makes it a useful bio-accumulator and biosorbent for some organic pollutants including phenolic pollutants and some nitrogenous organic pollutants from wastewater. the experimental conditions upon using the investigated biomass were optimized to achieve a reduction of the chemical oxygen demand (COD) and the total organic carbon (TOC) by about 90%. Also the sorption of the reported pollutants was examined as a function of its initial concentration in wastewater, pH, weight of roots and contact time. the concentration of phenolic pollutants and nitrogenous organic compounds in influent and effluent of wastewater and in the collected water samples were monitored using several coated wire ion selective electrodes (ISEs). Each ion selective electrode is designed specifically to monitor one type of pollutants. the results obtained using the dried roots of water hyacinth is compared to that obtained when a granular activated carbon (GAC) is used.

Preliminary results show that the outlet of the purification biomass meets most of the regulator's limits for discharge of treated wastewater in Egypt. Therefore, the treated effluents can be used safely in different applications such as irrigation of golf course, green way or park. If it is sufficiently clean it can also be used for ground water recharge, in recharging of batteries or in some industrial use. Moreover, such water hyacinth roots can be used as an effective tool for the treatment and reuse of wastewater as they have been shown to adsorb and accumulate toxic elements.

**Keywords:** Keywords-water hyacinth roots; Ion-selective electrodes; Phenolic pollutants; Nitrogenous organic pollutants.

### 335. Simultaneous Determination of Retinoic Acid and Hydroquinone in Skin Ointment Using Spectrophotometric Technique (Ratio Difference Method)

Eman S. Elzanfaly, Ahmed S. Saad and Abd-Elaziz B. Abd-Elaleem

*Saudi Pharmaceutical Journal*, 20: 249-253 (2012) IF: 0.662

An innovative spectrophotometric method was developed for simultaneous determination of compounds with interfering spectra in binary mixtures without previous separation, showing significant advantages over the conventional methods regarding minimal data manipulation and applicability. the proposed

method was applied for the determination of retinoic acid and hydroquinone in laboratory-prepared mixtures with mean percentage recoveries  $100.13 \pm 0.31$  and  $99.99 \pm 0.04$ , respectively, and in their pharmaceutical formulation with mean percentage recoveries  $100.13 \pm 0.86$  and  $100.07 \pm 0.58$ , respectively. the method was validated according to USP guidelines and can be applied for routine quality control testing.

**Keywords:** Spectrophotometry; Binary mixtures; Retinoic acid; Hydroquinone and ratio difference method.

### 336. Novel Spectrophotometric Methods for the Determination of Fluconazole in the Presence of Its Oxidative Degradation Product

Hayam Mahmoud Lotfy, Hany Hunter Monir and Abd El-Aziz El-Bayoumi Abd El-Aleem

*J. Chilean Chem. Soc.*, 57: 1199-1207 (2012) IF: 0.448

Five sensitive, selective and precise spectrophotometric stability-indicating methods for the determination of fluconazole in the presence of its oxidative degradation product and in pharmaceutical formulations are developed and validated. Method A is a newly developed spectrophotometric one that is called ratio difference method by measuring the difference in amplitudes between 261.5 and 266.5 nm of ratio spectrum. Method B is a third derivative spectrophotometric one, which determines peak amplitudes from 265.5-268nm (peak-peak). Method C is ratio subtraction method. Method D is the first derivative of the ratio spectra by measuring the peak amplitude at 269 nm. Finally, method E is the mean centering of ratio spectra method by measuring the peak amplitude at 266.5 nm. the proposed methods allow the determination of fluconazole in the presence of its oxidative degradation product over a concentration range of 50-400  $\mu\text{g.mL}^{-1}$  with mean percentage recoveries of  $100.24 \pm 0.91$ ,  $99.91 \pm 0.52$ ,  $100.20 \pm 1.26$ ,  $99.79 \pm 0.69$ , and  $100.77 \pm 0.72$  respectively. the selectivity of the proposed methods is checked using laboratory prepared mixtures. the proposed methods have been successfully applied to the analysis of fluconazole in pharmaceutical dosage forms without interference from other dosage form additives and the results have been statistically compared with a reported method.

**Keywords:** Fluconazole; Spectrophotometry; Ratio difference spectrophotometry; Stability-indicating analysis.

### 337. Determination of Diniconazole Fungicide Residues in Grapes and Zucchini by Capillary Gas Chromatography

Hayam M.Lotfy, Abdel-Aziz A.Abdel-Aleem and Hany H.Monir

*Analytical Chemistry - an Indian Journal*, 11: (2012)

A sensitive gas chromatographic method using an electron-capture detector (ECD) has been developed for the determination of diniconazole fungicide residues in grapes and zucchini. the developed method consists of extraction with ethyl acetate, and column chromatographic clean-up, followed by capillary gas chromatographic determination. the recoveries of diniconazole were greater than 90% for both plant samples.

The limit of determination of the method was 0.0001 ppm. the method was applied to determine residues and the rate of disappearance of diniconazole from grapes and zucchini [open

field treatment, 35 cc of Sumi-eight 5%EC (emulsifiable concentrate) for 100 L of water].

The fungicide incorporated into the plants decreased rapidly with a half-life time around 6 days in grapes and 2 days for zucchini. It is recommended not to apply diniconazole on grapes after maturation stage No residues could be detected in zucchini 16 days after field application. Hence, the plant could be used safely after that period of time. Four market samples were chosen from different regions from A.R.E. and all of them showed no residues of diniconazole.

**Keywords:** Diniconazole; Grapes; Zucchini; Gas chromatography.

### 338. Application of Spectrophotometric and Chromatographic Methods for Stability Indicating Determination of Leflunomide

D.S. Shokry, M. Abdel Kawy and S.A. Weshahy

*Journal of Applied Sciences Research*, 8: 1547-1557 (2012)

Leflunomide, an amide containing compound, pyrimidine synthesis inhibitor a leading drug in treatment of moderate to severe rheumatoid arthritis.

Four stability indicating methods are presented in this paper for the selective determination of leflunomide in presence of its alkaline degradate. the resolution of the drug and its alkaline degradate has been achieved using derivative spectrophotometry including second-, third- and fourth derivatives.

The derivative amplitudes are measured at 256.4 nm, 269.8 nm, 226.6 nm for D2, D3 and D4 respectively. the proposed methods were found to be linear over the range of (2.0-24.0  $\mu\text{g.mL}^{-1}$ ). the fourth method is based on the chromatographic separation on a C18 column using a mobile phase of 0.01 M aqueous potassium dihydrogen phosphate adjusted at pH 3.5 with orthophosphoric acid, acetonitrile in a ratio of [30:70], a flow rate of 1 ml/min and UV detection at 262 nm. the proposed methods were validated with regard to accuracy, precision, selectivity, robustness, application to pharmaceutical preparation and further validated by applying standard addition technique.

**Keywords:** Derivative spectrophotometry (Ds); Hplc; Leflunomide; Alkaline degradate.

### 339. Validated Stability Indicating Assay of Linezolid by Spectrophotometric and High Performance Liquid Chromatographic Methods

M. Abdel Kawy, S.A.Weshahy and Dina S. Shokry

*Australian Journal of Basic and Applied Sciences*, 6: 767-778 (2012)

Simple, precise and sensitive methods have been used for the determination of linezolid and its alkaline induced degradation product and in pharmaceutical dosage form. the first method depends on differential derivative spectrophotometry that is based on inducing spectral changes upon changing pH of the medium. in this method,  $\Delta A$  values have been measured at 227.2 nm and Beer's law was obeyed in concentration range of 2.0-14.0  $\mu\text{g.mL}^{-1}$ . Another three methods based on derivative spectrophotometry including D<sup>2</sup>, D<sup>3</sup> and D<sup>4</sup> were proposed in which the derivative amplitudes were measured at 260.9 nm, 252.0 nm, 245.6 nm respectively. the calibration curve was linear over the concentration range of 1.0-14.0  $\mu\text{g.mL}^{-1}$  for these methods. the

fifth method depends on reversed phase high performance liquid chromatographic method (RP-HPLC) that was successful in the resolution of linezolid and its alkaline induced degradate using ZORBAX- C18 column and a mobile phase of KH<sub>2</sub>PO<sub>4</sub> buffer adjusted at pH 3.0 : methanol: acetonitrile in the ratio of 60:20:20 (v/v/v). A linear response ( $r^2=0.9998$ ) was observed over the range of 2.0-24.0  $\mu\text{g mL}^{-1}$ . the retention times of linezolid and its degradate were  $2.973\pm 0.008$  &  $1.464\pm 0.118$  respectively. All methods were successfully applied to the commercial pharmaceutical preparation without interference from common ingredients accompanying the drug.

**Keywords:** Derivative Differential Spectrophotometry; Hplc; Linezolid; Alkaline Degradate.

#### 340. Validation of Selective Electrochemical Method for Determination of Sumatriptan in Combined Dosage Form

Mamdouh R. Rezk, Adel M. Michael, Hayam M. Lotfy and Mostafa A. Shehata

*Analytical and Bioanalytical Electrochemistry*, 4: 553-563 (2012)

A novel sumatriptan (SUM) selective electrode was investigated with dioctyl phthalate as a plasticizer in a polymeric matrix of carboxylated polyvinyl chloride (PVCCOOH), based on the interaction between the drug solution and the dissociated COOH groups in the PVC-COOH. the sensor was fabricated by using PVC-COOH only as anionic site without incorporation of an ionophore. Linear response of SUM within a concentration range of  $10^{-6}$ - $10^{-3}$  M with a slope of  $34\pm 1$  mV/decade over pH range of 6-8 was observed. the measurement was characterized by a fast stable response within about 45 seconds. the proposed sensor was successfully applied for the selective determination of sumatriptan in the pure powder form and in its pharmaceutical formulation with naproxen without any interference. the results obtained by the proposed procedure were statistically analyzed and compared with those obtained by the U.S. Pharmacopeia method. No significant difference for either accuracy or precision was observed.

**Keywords:** Sumatriptan; Ion selective electrode; Carboxylated Pvc; Pharmaceutical formulation.

#### 341. Selective Determination of Itraconazole in the Presence of Its Oxidative Degradation Product

Amr M. Badawey, Nesrine T. Lamie and Abd El-Aziz B. Abd El-Aleem

*International Journal of Drug Development and Technology*, 2: 71-80 (2012)

Stability-indicative determination of itraconazole (in the presence of its oxidative degradation product, is investigated. the degradation product has been isolated, via oxidative-degradation, characterized and elucidated. Selective quantification of itraconazole, singly in bulk form, pharmaceutical formulations and/or in the presence of its oxidative degradation product is demonstrated. the indication of stability has been undertaken under conditions likely to be expected at normal storage conditions. Among the spectrophotometric methods adopted for quantification are second derivative (2D), first derivative of ratio spectra (1DD), Difference spectrophotometry and bivariate analysis.

**Keywords:** Itraconazole; Second derivative spectrophotometry; Derivative ratio; Bivariate.

#### 342. Different Stability-Indicating Chromatographic Techniques for the Determination of Netobimin

Nesrin K. Ramadan, Afaf O. Mohamed, Sara E. Shawky and Maissa Y. Salem

*Journal of Analytical Methods in Chemistry*, 1-8 (2012)

Two simple, accurate, and sensitive methods were developed for the determination of netobimin in the presence of its degradation product. Method (A) was an HPLC method, performed on C18 column using acetonitrile/methanol/0.01M potassium dihydrogen phosphate (56 : 14 : 30 by volume) as a mobile phase with a flow rate of 0.5 mL/min. Detection was performed at 254 nm. Method (B) was a TLC method, using silica gel 60 F254 plates; the optimized mobile phase was toluene/methanol/chloroform/ ammonium hydroxide (5 : 4 : 6 : 0.1 by volume). the spots were scanned densitometrically at 346 nm. Linearity ranges were 1–10  $\mu\text{g/mL}$  for method (A) and 0.5–5  $\mu\text{g/band}$  for method (B), and the mean percentage recoveries were  $99.3\pm 0.7\%$  and  $99.7\pm 0.7\%$  for methods (A) and (B), respectively. the proposed methods were found to be specific for netobimin in the presence of up to 90% of its degradation product. Statistical comparison between the results obtained by these methods and the manufacturer method was done, and no significance difference was obtained.

**Keywords:** Netobimin; Hplc; Tlc; Stability; Degradate.

#### 343. Application of Membrane-Selective Electrodes for the Determination of Naftidrofuryl Oxalate in the Presence of its Alkaline Degradant in Tablets and Plasma

Samah S. Abbas, Hala E. Zaazaa, Mohamed R. El-Ghobashy, Yasmin M. Fayed and Soheir A. Fattah

*Portugaliae Electrochimica Acta*, 177-188: (2012)

Membrane selective electrodes were used to determine Naftidrofuryl Oxalate (NFL) in presence of its alkaline degradate (I). the membrane selective electrodes include construction of water insoluble ion-association complexes. These are NFL-tetraphenyl borate (NFL-TPB), NFL- reinikate (NFL-R). These complexes are used as electroactive materials, in poly-vinyl chloride (PVC) matrix membrane sensors, for the determination of NFL. the performance characteristics of these sensors, evaluated according to IUPAC recommendations, reveal fast, stable and linear response for NFL. the sensors are used for determination of NFL in plasma. the suggested method was used to determine NFL in synthetic mixtures and in commercial tablets. the obtained results were statistically compared with official HPLC method, showing no significant difference with respect to accuracy and precision.

**Keywords:** Naftidrofuryl oxalate; Pvc membranes; Ion selective electrode.

#### 344. Stability Indicating Methods for Determination of Naftidrofuryl Oxalate

Samah S.Abbas, Hala E.Zaazaa, Mohamed R.El-Ghobashy, Yasmin M.Fayez and Soheir A.Fattah

*Analytical Chemistry an Indian Journal*, 11: 0-334 (2012)

First derivative ratio and densitometry were used to determine Naftidrofuryl Oxalate (NFL) in presence of its alkaline degradate (I). for first derivative ratio, the peak amplitude at 249.2 nm was used for selective determination of NFL in presence of I in the range of 10-90  $\mu\text{g mL}^{-1}$ , while utilizing densitometric technique allows selective determination of NFL in presence of I in range of 0.6-8  $\mu\text{g spot}^{-1}$ . the suggested methods were used to determine NFL in synthetic mixtures and in commercial tablets. the validity of the proposed methods was further assessed by applying standard addition technique. the obtained results were statistically compared with official HPLC method, showing no significant difference with respect to accuracy and precision.

**Keywords:** Naftidrofuryl oxalate; First derivative ratio spectrophotometry; Thin layer chromatography and densitometry.

#### 345. Ion Selective Membrane Electrodes for Stability- Indicating Determination of Amisulpride

Ghada AbdElHamid, Mohamed Refaat ElGhobashy, Eman Saad ElZanfaly, Sawsan Mohamed Amer and Sonia Zaki ElKhateeb

*Analytical & Bioanalytical Electrochemistry*, 4: 579-592 (2012)

This work describes the construction and electrochemical response characteristics for three different polyvinyl chloride (PVC) membrane sensors for determination of amisulpride in presence of its degradation products and commonly used excipients. the first two sensors are based on the ion association complexes of amisulpride cation with sodium tetraphenyl borate (TPB) [sensor 1] or ammonium reineckate (R) [sensor 2] counter anions as ion exchange sites in PVC matrix.  $\beta$ -cyclodextrin ( $\beta$ -CD)-based technique with TPB as a fixed anionic site in PVC matrix was used for fabrication of the third membrane sensor [sensor 3]. the performance characteristics, sensitivity and selectivity of these electrodes in presence of amisulpride degradation products were evaluated according to IUPAC recommendations. Fast, stable and linear response was obtained for amisulpride over the concentration range  $1 \times 10^{-6}$ - $1 \times 10^{-2}$  M for sensors 1 and 3 while for sensor 2 it was found to be  $1 \times 10^{-5}$ - $1 \times 10^2$  M. the proposed sensors showed stable Nernstian responses of 29.1, 28.2 and 31.1 mV per concentration decade with sensors 1, 2 and 3, respectively. These sensors exhibit fast response time (10-20 s) and good stability (4-6 weeks). the direct potentiometric determination of amisulpride in its pure form using the proposed sensors gave average recoveries of  $99.93 \pm 0.72$ ,  $100.01 \pm 0.93$  and  $99.94 \pm 0.87$  for sensors 1, 2 and 3, respectively. the sensors were used for determination of amisulpride, in pure form, in presence of its degradation products, in tablets and in plasma. Validation of the method shows suitability of the proposed sensors for use in the quality control assessment of amisulpride and for routine analysis as stability indicating method. the developed method was found to be simple, accurate and precise when compared with a reported RP-HPLC method.

**Keywords:** Amisulpride; Ion selective electrodes; Potentiometry; Pharmaceutical analysis; Stability indicating methods.

#### 346. Stability-Indicating Methods for the Determination of Rosuvastatin in the Presence of Its Oxidative Degradation Products

Nadia M. Mostafa, Amr M. Badawey, Nesrine T. Lamie and Abd El-Aziz B. Abd El-Aleem

*International Journal of Pharmacy and Biomedical Science*, 3: 193-202 (2012)

Four different accurate, sensitive and reproducible stability-indicating methods for the determination of rosuvastatin calcium in the presence of its oxidative degradation products are presented. the first method is Second-derivative (2D) method at 243.6 nm in a concentration range of 5-30  $\mu\text{g mL}^{-1}$  with mean percentage recovery of  $99.94 \pm 1.171$ .

The second method is based on ratio-spectra 1st derivative (1DD) spectrophotometry of the drug at 240 nm, over a concentration range of 5-35  $\mu\text{g mL}^{-1}$  with mean percentage recovery of  $99.77 \pm 0.974$ .

The third method utilizes quantitative densitometric evaluation of thin-layer chromatography of rosuvastatin calcium in the presence of its oxidative degradation products, using ethyl acetate: methanol: ammonia (7:3:0.01, v/v/v) as a mobile phase. Chromatograms are scanned at 245 nm. This method analyses rosuvastatin calcium in a concentration range of 0.6-3.4  $\mu\text{g spot}^{-1}$  with mean percentage recovery of  $99.78 \pm 1.419$ . the fourth method is an HPLC method for the simultaneous determination of rosuvastatin calcium in the presence of its oxidative degradation products. the mobile phase consists of water: acetonitrile: methanol (40: 40: 20 by volume).

The standard curve of rosuvastatin calcium shows a good linearity over a concentration range of 10-60  $\mu\text{g mL}^{-1}$  with mean percentage recovery of  $100.22 \pm 0.859$ . These methods were successfully applied to the determination of rosuvastatin calcium in bulk powder, laboratory-prepared mixtures containing different percentages of the degradation products and pharmaceutical dosage forms. the validity of results was assessed by applying standard addition technique. the results obtained were found to agree statistically with those obtained by a reported method, showing no significant difference with respect to accuracy and precision.

**Keywords:** Rosuvastatin calcium; Stability-indicating; Ratio-spectra; Derivative; Densitometry; Hplc technique.

#### 347. Simultaneous Determination of Valsartan and Hydrochlorothiazide in Their Pharmaceutical Formulations

Mamdouh R. Rezk, NaemaM. El Remali and Abdel-Aziz El Bayoumi Abdel Aleem

*Der Pharma Chemica*, 4: 529-537 (2012)

Four methods namely, first-derivative of ratio spectra, bivariate, thin layer chromatography and high performance liquid chromatography were used to determine valsartan and hydrochlorothiazide simultaneously in their pharmaceutical dosage forms. the derivative ratio spectra method was based on measuring the peak amplitudes for valsartan at 233 nm and 253 nm using 0.4  $\mu\text{g mL}^{-1}$  hydrochlorothiazide as a divisor. Bivariate method is used for simultaneous determination of both drugs by measuring the absorbance at the selected wavelengths. A TLC separation with densitometric detection of both drugs was achieved using chloroform: methanol: ammonia [8:2:0.1, v/v/v]

as developing solvent. Furthermore, a high performance liquid chromatographic procedure with ultraviolet detection at 225 nm was developed for the separation and determination of the studied drugs using a C18 column. the mobile phase is composed of 0.02 M phosphate buffer (pH 2.9): acetonitrile: methanol [50: 40: 10, v/v/v]. the proposed methods were successfully applied for the determination of the studied drugs in their mixtures and in pharmaceutical formulations containing them.

**Keywords:** Valsartan; Hydrochlorothiazide; Ratio spectra; Bivariate; Tlc; Hplc.

#### 348. Simultaneous Determination of Pioglitazone and Glimepiride in their Pharmaceutical Formulations

Mamdouh R. Rezk, Safaa M. Riad, Ghada Y. Mahmoud and Abdel-Aziz El Bayoumi Abdel Aleem.

*Journal of Applied Pharmaceutical Science*, 2: 177-184 (2012)

Four sensitive and precise spectrophotometric methods were developed and validated for the simultaneous determination of pioglitazone hydrochloride (PGZ) and glimepiride (GLM) in their pharmaceutical formulations.

Among the methods adopted were direct absorbance, first derivative (1D), second-derivative (2D) and first-derivative of ratio spectra (1DD). the selectivity of the proposed methods was checked using laboratory prepared mixtures. the proposed methods were successfully applied to the analysis of GLM and PGZ in their mixture and in pharmaceutical dosage forms without interference from other additives.

**Keywords:** Derivative-Ratio; Derivative spectrophotometry; Glimepiride; Pioglitazone.

#### 349. Chromatographic Determination of Ezitimibe and Simvastatin in their Pharmaceutical Formulation

Mamdouh R. Rezk, Naema M. El Remali and Abdel-Aziz E. Abdel Aleem

*Analytical Chemistry an Indian Journal*, 11: 264-268 (2012)

Two accurate and precise methods were developed for the Simultaneous determination of Ezitimibe and Simvastatin in their pharmaceutical formulations.

A high performance liquid chromatographic method with ultraviolet detection at 240 nm was developed for the separation and determination of the studied drugs using a C18 column. the mobile phase was composed of 0.1 M ammonium acetate buffer (pH 4.5): acetonitrile: methanol [35: 55: 10, by volumes]. ATLC separation with densitometric detection of both drugs was achieved using toluene: n-butanol: triethylamine (8.5:2.5:0.5, by volumes) as a developing solvent. the proposed methods were validated according to the ICH guidelines.

The developed methods were found to be accurate, precise and suitable for the quantitative determination of both the drugs in their pure form, mixtures and in pharmaceutical formulations containing them.

**Keywords:** Ezitimibe; Simvastatin; Hplc; Tlc-Densitometry.

#### 350. Potentiometric Determination of Amlodipine Besilate and Valsartan Using Microsized and Polymeric Matrix Membrane Sensors Matrix Membrane Sensors

Nesrin K. Ramadan, Heba M. Mohamed and Azza A. Mostafa

*Portugaliae Electrochimica Acta*, 30: 15-29 (2012)

Two poly (vinyl chloride) matrix membrane electrodes responsive to some drugs affecting the cardiovascular system, Amlodipine besilate (AM) and Valsartan (VL), were developed, described and characterized. A microsized graphite selective sensor was investigated with dibutylsebacate (DBS) as a plasticizer in a polymeric matrix of carboxylated polyvinyl chloride (PVC-COOH) in case of (sensor 1). This sensor 1 was prepared using 2-hydroxy propyl  $\beta$ -cyclodextrin (2HP  $\beta$ -CD) as an ionophore. While sensor 2 preparation was based on precipitation technique with bathophenanthroline iron (II) as electroactive materials in poly(vinyl chloride) (PVC) matrix. Fast and stable Nernstian responses near  $1 \times 10^{-5}$ - $1 \times 10^{-3}$  M for the two drugs over the pH range 3-6 and 7-9 for the two sensors, respectively, were obtained. the method was successively applied for the determination of AM and VL in presence of each others, in their pharmaceutical formulations and in human plasma samples. the percentages recoveries for the determination of the drugs by the proposed selective electrodes were  $99.78 \pm 0.382$  %,  $100.23 \pm 0.440$  %, for sensors 1 and 2, respectively. Statistical comparison between the results obtained by this method and those obtained by the official method and the reported method of the drugs was done and no significant difference was found.

**Keywords:** Amlodipine besilate; Valsartan; Micro sensors; Human plasma.

#### 351. Development and Validation of Spectrophotometric and Spectrofluorimetric Methods for Simultaneous Determination of Tofisopam

Ramadan, Nesrin K., Osman, Afaf, Foad, Roaida, Moustafa and Azza A.

*Journal of Applied Pharmaceutical Science*, 2: 112-0 (2012)

Two simple, rapid and accurate spectrophotometric and spectrofluorimetric methods developed for the determination of Tofisopam (TF) in pure form and in pharmaceutical formulation. the spectrophotometric method (A) is based on the reduction of ferric into ferrous in presence of 1, 10-phenanthroline to give an orange-red colored ferrous complex measured at 510 nm. Method (B) spectrofluorimetric method is based on the oxidative coupling reaction of TF with 3-methylbenzothiazolin-2-one hydrazone (MBTH) hydrochloride in presence of cerium (IV) ammonium sulfate in an acidic medium. the quenching effect of TF on the fluorescence of excess cerous ions is measured at the emission  $\lambda_{em}$  345 nm with excitation  $\lambda_{ex}$  at 296 nm. The factors affecting the reactions were carefully studied and optimized. Beer's law is obeyed in the range of 2-12  $\mu\text{g ml}^{-1}$  for both methods with the mean percentages recovery of  $100.04 \pm 0.445$  and  $99.29 \pm 0.563$  for method (A) and (B), respectively. the two proposed methods were successfully applied for the determination of TF in Nodoprine tablets. Statistical comparison between the results obtained by these methods and that obtained by the official



method for the determination of the drug was done, and it was found that there was no significant differences between them.

**Keywords:** Spectrophotometry; Spectrofluorimetry; Tofisopam; O-Phenanthroline; Mbth.

### 352. Analytical Study of Two Commercial Sex Pheromone Lures for Monitoring Males of Cotton Leafworm (Clw) and Spiny Bollworm (Sbw) in Egypt

Ezzat M. Abdel-Moety, Hayam M. Lotfy, Nasr S. Khalil and Yasmin Rostom

*Arpn Journal of Agricultural and Biological Science*, 7: 912-926 (2012)

A simple and reliable GC-FID method was applied for the determination of the of the synthetic sex pheromone components of the Egyptian armyworm *Spodoptera littoralis* (Cotton leafworm, CLW) (I) pheromone isomers *cis*-9, *trans*-11-tetradecadienyl acetate (major) is the active pheromone while *cis*-9, *trans*-12-tetradecadienyl acetate (minor) is the synergist in ratio 9:1, w/w, and *Earias insulana* (Spiny bollworm, SBW) (II) pheromone isomers (10E, 12E)-10, 12-hexadecadienal (major) is the active pheromone while (Z)-11-hexadecenal (minor) is the synergist in ratio 99:1, w/w in their pure form. the proposed method showed high sensitivity with good linearity over the concentration range of 12.5-400 µg / ml of major, 5-80µg / ml of minor in case of I and 25-400 µg / ml of major and 1-32µg / ml of minor in case of II. the method is successfully applied to the analysis of commercial lures containing (I) and (II) with excellent recovery. the kinetics investigation are carried out in Egyptian environmental condition by monitoring the ratio of the pheromone isomers in order to achieve optimum biological activity and follow up longetivity of the lure in the trap under field conditions. GC-FID is considered to be the most promising method for this purpose because of its sensitivity, specificity and versatility. Moreover uncertainty of measurement for the pheromone components of CLW and SBW was calculated.

**Keywords:** Pheromone; Cotton leafworm (Clw; *Spodoptera littoralis*); Spiny bollworm (Sbw; *Earias Insulana*); Gc analysis.

### 353. Trace Determination of Red Palm Weevil, *Rhynchophorus Ferrugineus*, Pheromone at Traping Locations under Egyptian Climate

Ezzat M. Abdel-Moety, Hayam M. Lotfy and Yasmine Rostom

*Int. J. of Agricultural and Food Science*, 2: 44-50 (2012)

A simple and reliable methodology was developed for the determination of the release rate and profile of red palm weevil (RPW) pheromone from its commercial lures, in order to evaluate their longetivity. Analysis were performed on a narrow bore (0.25 µm) GC-column [30 m x 0.25 mm ID coated with DB-5ms (Phenyl Arylene polymer virtually equivalent to a (5%-Phenyl)-methylpolysiloxane] utilizing flame ionization detection (FID, temp.: 250 °C), with sample-splitting injection (50%, temp.: 230 °C). Pure N2 was used as carrier gas at a flow rate of 1 mL min<sup>-1</sup>. Initial column temperature was kept at 40 °C for 1 min., and then programmed at a rate of 15 °C min. up to 120 °C (2 min.), 20 °C min<sup>-1</sup> to 250 °C (4 min.), with a total analysis time of ~ 17.5 min. per run. Moreover, residues have been detected in the surrounding environment, including the plants in the nearby area of the trapping.

**Keywords:** Pheromone; 4-Methyl-5-Nonanol; 4-Methyl-5-Nonanone; Red palm weevil (Rpw; *rhynchophorus ferrugineus*); Gc Analysis.

### 354. Spectrophotometric Determination of Triclabendazole by Acid-Dye Complexation Method in Bulk and Pharmaceutical Formulation

Nesrin K. Ramadan, Afaf O. Mohamed, Sara E. Shawky and Maissa Y. Salem

*Journal of Applied Pharmaceutical Science*, 2: 128-133 (2012)

Two simple, accurate and sensitive spectrophotometric methods were developed for the determination of ticlabendazole in bulk and pharmaceutical formulation. These methods were based on the formation of ion-pair association complex (1:1) with bromocresol purple (BCP) and bromophenol blue (BPB). the coloured products were extracted into chloroform and measured spectrophotometrically at 420 nm. Linearity ranges were 20 – 100 µg/ml for BCP and 10 – 100 µg/ml for BPB, the mean percentage recoveries were 99.61±1.152% and 99.60±0.986% for BCP and BPB respectively. Statistical comparison between the results obtained by these methods and the manufacturer's method was done, and no significance difference was obtained.

**Keywords:** Triclabendazole; Spectrophotometry; Bromocresol Purple; Bromophenol Blue.

### 355. Potentiometric Membrane Sensors for Determination of Memantine Hydrochloride and Pramipexole Dihydrochloride Monohydrate

Hanan A. Mery, Marwa I. Helmy, Shereen M. Tawakkol, Safaa S. Toubar and Mohamed S. Risk

*Portugaliae Electrochimica Acta*, 1: 31-43 (2012)

Five solid membrane sensors responsive to memantine hydrochloride (MEM) and pramipexole dihydrochloride monohydrate (PXL) are described for simple and fast determination of these drugs in pharmaceutical preparation and human plasma. the first three sensors are based on the formation of an ion association complex between cationic drug (MEM or PXL) and Na tetra phenyl borate or Ammonium reineckate (as anionic exchanger). the produced electroactive material is dispersed in PVC matrix. While the other two sensors are based on using functionalized lipophilic cyclodextrin derivative (2-hydroxypropyl-?-cyclodextrin) as sensor ionophore for the determination of MEM and PXL. the performance characteristics of these sensors - evaluated according to IUPAC recommendations - reveal fast, stable and near Nernstian response for 1x10<sup>-4</sup>-10<sup>-1</sup> M and 1x10<sup>-6</sup>-10<sup>-2</sup> M for (MEM) and (PXL), respectively. Many inorganic and organic substances such as drug excipients and diluents normally used in drug formulations do not interfere with drugs response.

Statistical comparison between the results obtained by applying the proposed potentiometric method for the determination of the (MEM) and (PXL) in their pure powder forms and those obtained by applying the reported methods was done and no significant difference was found at p=0.05.

Validation of the method according to ICH guidelines shows the suitability of the sensors for quality control analysis of the cited drugs in pharmaceutical formulations and human plasma. the proposed sensors can also be used as a detector for HPLC.

**Keywords:** Memantine hydrochloride; Pramipexol dihydrochloride; Membrane sensors; Potentiometry.

### 356. Validated Stability Indicating Methods for Determination of Nitazoxanide in Presence of its Degradation Products

Nouruddin W. Ali, Samah Sayed Abbas, Hala El-Sayed Zaazaa, Maha Mohamed Abdelrahman and Mohamed Abdelkawy

*Journal of Pharmaceutical Analysis*, 2: 104-115 (2012)

Three sensitive, selective and reproducible stability-indicating methods are presented for determination of Nitazoxanide (NTZ), a new anti-protozoal drug, in presence of its degradation products. Method A utilizes the first derivative of ratio spectra spectrophotometry by measurement of the amplitude at 364.4 nm using one of the degradation products as a divisor. Method B is a chemometric-assisted spectrophotometry, where principal component regression (PCR) and partial least squares (PLS) were applied. These two approaches were successfully applied to quantify NTZ in presence of degradation products using the information included in the absorption spectra in the range 260–360 nm. Method C is based on the separation of NTZ from its degradation products followed by densitometric measurement of the bands at 254 nm. This separation was carried out on silicage 160F254, using chloroform–methanol–ammonium solution–glacial acetic acid (95:5:1:1 by volume, pH 4.80) as a developing system. These methods are suitable as stability-indicating methods for the determination of NTZ in presence of its degradation products either in bulk powder or in pharmaceutical formulations. Statistical analysis of the results has been carried out revealing high accuracy and good precision.

**Keywords:** Nitazoxanide; Stability Indicating.

### 357. Novel Validated Potentiometric Methods for the Determination of Torasemide in Bulk Drug, in Formulations and in Plasma

Safa'a M. Riad

*Analytical & Bioanalytical Electrochemistry*, 417-430: (2012)

Three novel techniques for the selective determination of torasemide (TOS) in bulk powder, in formulations and in plasma were described. The three techniques were the construction and electrochemical response characteristics of novel poly (vinyl chloride) matrix membrane sensors for torasemide cation based on the use of the ion-association complexes of this cation with tetraphenyl borate, phosphotungstic acid and ammonium reineckate counter anions as ion exchange sites in a plasticized PVC matrix, either as ion selective membranes, microcoated wire or as micro-sized graphite selective sensors. All these sensors were prepared and fully characterized in terms of composition, life span, usable pH range, response time and temperature. The electrodes were selectively applied for the potentiometric determination of torasemide in pure form, pharmaceutical preparations and in plasma. These sensors showed near Nernstian responses with slopes of 28.3, 28.9, 27.9, 28.0, 30.0, 27.7, 28.5, 29.2 and 27.5 mV over the concentration ranges of  $1.0 \times 10^{-6}$ – $1.0 \times 10^{-2}$  M for all sensors. The electrodes exhibit good selectivity for (TOS) with respect to a large number of inorganic cations, organic cations, sugars and amino acids. The proposed electrodes offer the advantages of simplicity, accuracy and applicability to turbid and colored samples. The behavior of the three sensors in presence of human plasma was also studied and reasonable results

were obtained. All the fabricated sensors were validated according to the International Conference on Harmonization (ICH) guidelines and successfully applied for the determination of the studied drug in pure form, pharmaceutical preparations and in plasma without any interference.

**Keywords:** Torasemide; Sodium tetraphenyl borate (Natpb); Phosphotungstic acid (Pta); Ammonium reineckate (Arnc); Potentiometry and plasma.

### 358. Simultaneous Determination of Metronidazole and Diiodohydroxyquin in Bulk Powder and Paramibe Compound Tablets by TLC-Densitometry and HPLC

Hesham Salem, Safaa M. Riad, Mamdouh R. Rezk and Kholoud Ahmed

*Pharmaceutica Analytica Acta*, 3: 1-4 (2012)

Two sensitive and precise chromatographic methods were developed and validated for simultaneous determination of metronidazole (MTR) and diiodohydroxyquin (DIQ) in pharmaceutical preparation. The techniques adopted for quantification are coupled TLC-densitometry and HPLC. A mixture of chloroform, toluene, ethanol and acetic acid (9:9:1:1, v/v/v/v) was used as the developing solvent for TLC-densitometry. A mixture of methanol and acetonitrile, (96:4, v/v) was used as a mobile phase for HPLC at 0.6 mL min<sup>-1</sup> flow rate and UV detection at 254 nm. Linearity was obtained in concentration range of 0.5–10 µg spot<sup>-1</sup> for DIQ and 1–20 µg spot<sup>-1</sup> for MTR applying TLC-densitometry and 0.005–0.5 mg mL<sup>-1</sup> for DIQ and 0.01–0.5 mg mL<sup>-1</sup> for MTR applying HPLC. The selectivity of the proposed methods was checked using laboratory prepared mixtures. The proposed methods were successfully applied to the analysis of MTR and DIQ in their mixture and in pharmaceutical dosage forms without interference from other additives.

**Keywords:** Metronidazole; Diiodohydroxyquinoline; Tlc-Densitometry; Hplc; Tablets dosage form.

### 359. Spectrophotometric Determination of Sitagliptin and Metformin in their Pharmaceutical Formulation

Safaa M Riad, Mamdouh R Rezk, Ghada Y Mahmoud and Abdel-Aziz El Bayoumi Abdel Aleem

*International Journal of Comprehensive Pharmacy*, 3: 1-4 (2012)

Two simple, accurate and precise spectrophotometric methods were developed and validated for the determination of sitagliptin phosphate monohydrate (STA) and metformin hydrochloride (MTF). The first method was based on measuring the absorbance of STA at 268 nm in the range of 25–500 µg mL<sup>-1</sup>. The second method was the isosbestic point method. The total mixture concentration was calculated by measuring the absorbance at 257 nm. The proposed methods used to determine each drug in binary mixture. The results were statistically compared using one-way analysis of variance (ANOVA). The developed methods were satisfactorily applied to the analysis of the pharmaceutical formulation and proved to be selective and accurate for the quality control of the cited drugs in their pharmaceutical formulation.

**Keywords:** Metformin; Sitagliptin phosphate; Spectrophotometry.

### 360. Novel Conductometric Procedures for Cilostazol Determination in Pharmaceutical Formulations, Its Degradation Product and Plasma

Safa'a M. Riad and Nouruddin W. Ali

*Inte. J. of Chemical and Analytical Science*, 1629-1633 (2012)

Three simple and sensitive conductometric methods for the determination of Cilostazol using phosphotungestic acid, potassium tetraphenyl borate and ammonium reineckate were described. Optimized conditions including temperature, solvent and reagent concentration were studied. The suggested methods were used for conductometric determination of Cilostazol in its pharmaceutical preparations. Precision, measured as relative standard deviation was less than 1% and accuracy was in the range 98.86-100.40%. The obtained results comparable were with data using reported method. The proposed procedures were successfully adapted for the determination of Cilostazol in plasma. For comparison, some interference was also determined by the conductometric titrations. At equimolar concentration levels, some molecules of similar structure interfere with the original drug. A reduction in interferent concentration by a factor of 10 negated the interference. The suggested conductometric titration were also used as a stability indicating one for the determination of intact drug in presence of its oxidative degradation product. It has no effect on the proposed procedures.

**Keywords:** Cilostazol; Conductometry; Phosphotungestic acid; Potassium tetraphenyl borate and ammonium reineckate.

### 361. A Smart Simple Spectrophotometric Method for Simultaneous Determination of Binary Mixtures

Eman S. Elzanfaly, Ahmed S. Saad and Abd Elaziz B. Abd Elaleem

*Journal of Pharmaceutical Analysis*, 2: 382-385 (2012)

A new simple spectrophotometric method was developed for the simultaneous determination of drugs with interfering spectra in binary mixtures without previous separation. The new method is based on a simple modification for the ratio subtraction method. This modification enabled wider range of application. The proposed ratio difference method was applied for the determination of brimonidine and timolol in laboratory prepared mixtures with mean percentage recoveries 100.4072.29 and 101.2371.30 respectively, and in their pharmaceutical formulation with mean percentage recoveries 101.0870.44 and 100.6670.52 respectively. The suggested ratio difference method was validated according to USP guidelines and can be applied for routine quality control testing.

**Keywords:** Spectrophotometry; Binary mixtures; Brimonidine; Timolol.

### 362. A Novel Simple Method for Resolving Overlapped Spectral Data with A Wide Range of Applicability, and its Application as A Stability Indicating Method for Determination of Tazarotene

Eman S Elzanfaly, Ahmed S Saad and Abd-Elaziz B Abd-Elaleem

*Pharmaceutica Analytica Acta*, 3: 1-4 (2012)

Smart simple spectrophotometric method was developed for simultaneous determination of compounds with interfering

spectra in binary mixtures without previous separation. The proposed method showed significant advantages over the conventional methods regarding minimal data manipulation and applicability. The new method is based on a modification for the ratio subtraction and derivative ratio methods. This modification enabled wider range of application. The proposed method was applied for the determination of tazarotene and its alkaline degradation product in laboratory prepared mixtures with mean percentage recoveries  $99.68 \pm 1.36$  and  $100.86 \pm 1.09$  respectively. The suggested method was validated according to USP guidelines and can be applied for routine quality control testing.

**Keywords:** Spectrophotometry; Binary mixtures; Tazarotene.

### 363. Stability-Indicating Methods for the Determination of Ornidazole in the Presence of its Degradate According to ICH Guidelines

Fatma I Khattab, Nesrin K Ramadan, Maha A Hegazy and Nermine S Ghoniem

*Pharmaceutica Analytica Acta*, 3: 1-8 (2012)

Four simple, sensitive, selective and precise methods were developed for the determination of Ornidazole (OZ) in presence of its degradation product. The first method was based on first derivative spectrophotometry D1 and measuring the peak amplitude of D1 spectra at 290.4 and 332 nm. The second method was depended on measuring the peak amplitude of the first derivative of the ratio spectra DD1 at 288.5 and 328 nm. The third method was the mean centering of the ratio spectra one (MCR), which allowed the determination of OZ in presence of its degradate and the concentration of OZ was determined by measuring the amplitude at 312.8 nm. Separation and determination of OZ by HPLC in the fourth method was achieved using Lichrosorb RP-18 column and acetonitrile: water, (50:50 v/v), 0.2% triethylamine, the pH was adjusted to 4 using o-phosphoric acid. The flow rate was 1 mL min<sup>-1</sup>. Beer's law was obeyed in concentration range 5–30 µg/ml for the first three methods. The linearity range in the fourth method was 2–20 µg/ml. The proposed methods were used to determine OZ in its pure powdered form with mean percentage recoveries of  $99.86 \pm 1.249\%$  and  $99.98 \pm 0.868\%$  for OZ at 290.4 and 332 nm respectively, in D1 method. In DD1 method, the mean percentage recoveries were  $100.11 \pm 1.020\%$  and  $100.15 \pm 1.043\%$  at 288.5 and 328 nm respectively. While in MCR and HPLC methods, the mean percentage recoveries were  $100.09 \pm 0.387\%$  and  $100.00 \pm 1.302\%$  respectively. The degradation product was obtained in alkaline stress condition, separated, and identified by LC-MS spectral analysis, from which the degradation product was confirmed. The four methods were validated according to International Conference on Harmonization. The four methods were found to be specific for OZ in presence of up to 80% of its degradation product in the first three methods. The four proposed methods were successfully applied for the determination of OZ in Tibezole® tablets. Statistical comparison between the results obtained by these methods and the reported method for the determination of the drug in its pharmaceutical formulation was done, and it was found that there was no significant difference between them.

**Keywords:** Ornidazole; Derivative; Ratio derivative; Mean centering spectrophotometry; Hplc.

### 364. A Comparative Study of the Novel Ratio Difference Method Versus Conventional Spectrophotometric Techniques for the Analysis of Binary Mixture with Overlapped Spectra

Hayam M. Lotfy, Sarah S. Saleh, Nagiba Y. Hassan and Samia M. Elgizawy

*American Journal of Analytical Chemistry*, 3: 761-769 (2012)

The smart novel ratio difference spectrophotometric method was developed and validated for the determination of a binary mixture of Sodium cromoglicate (SCG) and Fluorometholone (FLU) in presence of benzalkonium chloride without prior separation. the results were compared to that of the conventional methods (dual wavelength and first derivative of ratio spectra). The suggested methods were validated in compliance with the ICH guidelines and were successfully applied for determination of SCG and FLU in their laboratory prepared mixtures and commercial ophthalmic solution. the novel method showed significant advantages over the conventional methods regarding simplicity, minimal data manipulation and maximum reproducibility and robustness; which enabled the analysis of binary mixtures with overlapped spectra for routine quality control testing with quite satisfactory

**Keywords:** Ratio difference; Sodium cromoglicate; Fluorometholone; Binary mixtures; Spectrophotometry.

### 365. Determination of Simvastatin and Ezetimibe in Combined Tablet Dosage Forms by Constant Center Spectrophotometric Method

Hayam Mahmoud Lotfy

*International Journal of Pharmacy and Pharmaceutical Sciences*, 4: 673-679 (2012)

A novel, simple, specific and accurate spectrophotometric method is developed and validated for determination of simvastatin (SM) and ezetimibe (EZ) namely; constant center spectrophotometric method(CCSM).the proposed spectrophotometric method do not require any separation step. Linear correlation was obtained in range 2-16 µg/ml and 4-24 µg/ml for simvastatin and ezetimibe respectively, with mean recoveries 100.15± 1.281 for simvastatin and 100.12± 0.818 for ezetimibe. the proposed method was applied to pharmaceutical formulation and the results obtained were statistically compared with reported HPLC method. the statistical comparison showed that there is no significant differencebetween the proposed method and the reported HPLC method regarding both accuracy and precision. the method was validated according to ICH guideline

**Keywords:** Simvastatin; Ezetimibe; Constant center; Constant calculation; Amplitude difference; Ratio difference; Constant multiplication.

### 366. Novel Ion Selective Electrode for Determination of Pregabalin in Pharmaceutical Dosage Form and Plasma

Hayam M. Lotfy, Adel M. Awad and Mostafa A. Shehata

*Analytical & Bioanalytical Electrochemistry*, 4: 507-517 (2012)

Ion selective electrode technique was developed for determination of pregabalin. the key to construct such an electrode is to produce

a sensitive and selective membrane that responds to a particular ionic species. Such membrane is usually prepared by in incorporating an appropriate ion exchanger and solvent mediator into a poly (vinyl chloride) or (PVC) membrane matrix. the present work originates from the fact that pregabalin behaves as a cation in 0.1 N HCl solution and forms a precipitate with anionic potassium tetrakis p-chlorophenyl borate which used in fabrication of the membrane sensor. the potentiometric response was linear with constant slope over a drug concentration range of 10<sup>-6</sup>–10<sup>-3</sup> M with slope of 53±1 mV/decade . the developed method was applied successfully for the determination of pregabalin in the pure powder form, pharmaceutical formulation and in spiked human plasma without any interference.

**Keywords:** Pregabalin; Ion selective electrode; Pvc; Potassium tetrakis P-chlorophenyl.

### 367. Selective Determination of A Validated Hplc Method for Separation and Determination of Mefloquine Enantiomers in Pharmaceutical Formulations

Ola A. Saleh, Aida A. El-Azzouni, Amr M. Badawey and Hassan Y. Aboul-Enein

*Gazi University Journal of Science*, (2012)

A simple, rapid and validated method for separation and determination of mefloquine enantiomers was developed. Mefloquine was separated and quantitated on cyclodextrin chiral column Quest-CM carboxymethyl- BCD (250x4mm i.d., 5.µm particle size) using a mixture of acetonitrile: 1% triethylammonium acetate buffer (pH = 4.5) (20:80 v/v) as a mobile phase at 20 °C and a flow rate of 1 mL /min. the UV-detector was set at 240 nm. the applied HPLC method allowed the separation and quantification of mefloquine enantiomers with good linearity (r > 0.999) in the studied range. the relative standard deviations (RSD) were 0.865 and 0.907 for the mefloquine enantiomers with accuracy of 100.00 and 100.68. the limit of detection and limit of quantification of mefloquine enantiomers were found to be 5 and 15 µg/mL, respectively. the method was validated through the parameters of linearity, accuracy, precision and robustness. the HPLC method was applied for the quantitative determination of mefloquine in pharmaceutical formulations.

**Keywords:** Chiral separation; Antimalarials; Mefloquine; Pharmaceutical analysis.

#### Dept. of BioChemistry

### 368. Neuronal Stimulation Induces Autophagy in Hippocampal Neurons that is Involved in Ampa Receptor Degradation after Chemical Long-Term Depression

Mohammad Shehata, Hiroyuki Matsumura, Reiko Okubo-Suzuki, Noriaki Ohkawa and Kaoru Inokuchi

*J Neurosci*, 32: 10413-10422 (2012) IF: 7.115

Many studies have reported the roles played by regulated proteolysis in synaptic plasticity and memory, but the role of autophagy in neurons remains unclear. in mammalian cells, autophagy functions in the clearance of long-lived proteins and organelles and in adaptation to starvation. in neurons, although

autophagy-related proteins (ATGs) are highly expressed, autophagic activity markers, autophagosome (AP) number, and light chain protein 3-II (LC3-II) are low compared with other cell types. In contrast, conditional knock-out of ATG5 or ATG7 in mouse brain causes neurodegeneration and behavioral deficits. Therefore, this study aimed to test whether autophagy is especially regulated in neurons to adapt to brain functions. In cultured rat hippocampal neurons, we found that KCl depolarization transiently increased LC3-II and AP number, which was partially inhibited with APV, an NMDA receptor (NMDAR) inhibitor. Brief low-dose NMDA, a model of chemical long-term depression (chem-LTD), increased LC3-II with a time course coincident with Akt and mammalian target of rapamycin (mTOR) dephosphorylation and degradation of GluR1, an AMPA receptor (AMPA) subunit. Downstream of NMDAR, the protein phosphatase 1 inhibitor okadaic acid, PTEN inhibitor bpV (Hopic), autophagy inhibitor wortmannin, and short hairpin RNA-mediated knockdown of ATG7 blocked chem-LTD-induced autophagy and partially recovered GluR1 levels. After chem-LTD, GFP-LC3 puncta increased in spines and in dendrites when AP-lysosome fusion was blocked. These results indicate that neuronal stimulation induces NMDAR-dependent autophagy through PI3K-Akt-mTOR pathway inhibition, which may function in AMPA degradation, thus suggesting autophagy as a contributor to NMDAR-dependent synaptic plasticity and brain functions.

**Keywords:** Nmdar; Autophagy; Synaptic plasticity.

### 369. The Potential Role of Ozone in Ameliorating the Age-Related Biochemical Changes in Male Rat Cerebral Cortex

Nagwa Ibrahim Shehata, Hanan Mohamed Abd-Elgawad, Mohamed Nabil Mawsouf and Amira Abd-Elmonem Shaheen

*Biogerontology*, 13: 565-581 (2012) IF: 3.339

Controlled ozone (O<sub>3</sub>) administration is known to promote oxidative preconditioning and, thus, may reverse chronic oxidative stress that accompanies aging. Therefore, the present work was undertaken to study the potential role of O<sub>3</sub> in ameliorating certain age-related biochemical changes represented by impaired activities of inner mitochondrial membrane enzymes, compromised energy production and increased oxidative burden in male rat cerebral cortex. Prophylactic administration of O<sub>3</sub>-O<sub>2</sub> mixture to 3 month-old rats, at an intrarectal dose of 0.6 mg O<sub>3</sub> kg<sup>-1</sup> body weight twice/week for 3 months then once/week until the age of 15 months, normalized reduced glutathione content, adenosine triphosphate/ adenosine diphosphate ratio, mitochondrial superoxide dismutase (SOD) and complex IV (cytochrome-c oxidase) activities, improved glutathione redox index (GSHRI), complex I (NADH-ubiquinone oxidoreductase) and mitochondrial nitric oxide synthase (mtNOS) activities, and attenuated the rise in malondialdehyde (MDA) and mitochondrial protein carbonyl levels. On the other hand, therapeutic administration of the same dose of O<sub>3</sub>-O<sub>2</sub> mixture to 14 month-old rats three times/week for 1 month, reduced mitochondrial protein carbonyl level only. Other favorable effects, including normalization of Na,K-adenosine triphosphatase (Na,K-ATPase) activity and reduction in lipofuscin level in the prophylactic group, as well as improvement in mitochondrial SOD and complex I activities with a decrease in total MDA level in the therapeutic group, were comparable to the effects observed in the corresponding O<sub>2</sub>-treated control groups. In conclusion, the

present study revealed that prophylactic administration of O<sub>3</sub>-O<sub>2</sub> mixture provided better amelioration of age-related cerebrocortical alterations by combining the advantages of both O<sub>3</sub> and O<sub>2</sub> therapies.

**Keywords:** Ozone therapy; Oxidative preconditioning; Aging; Cerebral cortex; Mitochondria.

### 370. Deltamethrin-Induced Genotoxicity and Testicular Injury in Rats: Comparison with Biopesticide

Manal F. Ismail and Hanaa M. Mohamed

*Food Chem Toxicol*, 50: 3421-3425 (2012) IF: 2.999

Deltamethrin is a synthetic pyrethroid insecticide used extensively in pest control. Aim of the current study was to investigate the ability of deltamethrin-based commercial formulation to induce genotoxicity and testicular injury in rats in comparison to the use of the biopesticide; *Bacillus thuringiensis*. Rats were divided into three groups: Group I (DEL) received deltamethrin, 5 mg/kg b.w./day orally, in corn oil. Group II (Biopesticide, *B. thuringiensis*) received oral suspension of the biopesticide at daily dose of 8400 mg/kg b.w./day. Group III (Control) received appropriate volume of corn oil. After 4 weeks, deltamethrin-treated rats showed decreased serum testosterone, luteinizing and follicle-stimulating hormone levels. Testicular total oxidant capacity (TOC), poly (ADP-ribose) polymerase (PARP), lactate dehydrogenase (LDH) and DNA damage were significantly increased. Significant increase in bone marrow chromosomal aberrations, induced by deltamethrin, including chromatid breaks, deletions, fragments and gaps was also observed. RT-PCR demonstrated significant up-regulation in testicular mRNA for glutathione-S-transferase and heat-shock protein-70 (HSP-70) whereas steroidogenic acute regulatory (StAR) mRNA was down-regulated after deltamethrin exposure. Oral administration of the biopesticide, under the condition of our study, was found to be safe when compared to the deleterious effect of deltamethrin in rats.

**Keywords:** Deltamethrin; Dna damage; *Bacillus thuringiensis*; Chromosomal aberrations; Gene expression; Testes.

### 371. Camel's Milk Alleviates Alcohol-Induced Liver Injury in Rats

Hebatallah A. Darwish, Naglaa R. Abd Raboh and Amina Mahdy

*Food Chem Toxicol*, 50: 1377-1383 (2012) IF: 2.999

Alcoholic liver disease (ALD) represents a spectrum of clinical illness and morphological changes that range from fatty liver, hepatic inflammation and necrosis to progressive fibrosis. For the etiology of ALD, oxidative stress, increased expression of proinflammatory cytokines and apoptosis have been described. The present study aimed to investigate the effectiveness of camel's milk (CM) in alleviating alcohol-induced hepatotoxicity as a model of clinical liver illness. Male rats were grouped into four groups from which one group received normal saline and served as control. Groups from 2 to 4 received a daily oral dose of 56% ethanol for 4 weeks. Group 2 served as untreated control while groups 3 and 4 were, respectively, treated with CM either in a prophylactic or a curative approach. Alanine transaminase, aspartate transaminase, alkaline phosphatase, triglycerides, as well as cholesterol levels were estimated in the serum.

Malondialdehyde, total antioxidant capacity, and tumor necrosis factor- $\alpha$  levels along with caspase-3 activity were determined in liver tissue homogenate. A histopathological analysis of liver tissue was also achieved. Results showed amelioration of all tested parameters following administration of CM. Conclusively, treatment with camel's milk alleviates alcohol-associated hazards and protects hepatic tissue from alcohol-induced toxicity.

**Keywords:** Ethanol; Liver toxicity; Camel's milk; Oxidative stress; Tumor necrosis factor- $\alpha$ ; Caspase-3.

### 372. The Association of Receptor of Advanced Glycated End Products and Inflammatory Mediators Contributes to Endothelial Dysfunction in A Prospective Study of Acute Kidney Injury Patients with Sepsis

Nermin A. H. Sadik, Waleed A. Mohamed and Mohamed I. Ahmed

*Mol Cell Biochem*, 359: 73-81 (2012) IF: 2.057

The pathogenesis of acute kidney injury (AKI) occurring due to sepsis is incompletely understood. Endothelial activation, defined as up-regulation of adhesion molecules by proinflammatory cytokines, may be central to the development of sepsis-induced AKI. Our aim was to determine levels of circulating adhesion molecules endothelial (E)-selectin, intercellular adhesion molecule (ICAM), and vascular cell adhesion molecule (VCAM), inflammatory mediators; tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and transforming growth factor- $\beta$  (TGF- $\beta$ ), vasoactive mediators; endothelin-1 (ET-1) and nitric oxide (NO), soluble receptor for advanced glycated end products (sRAGE) and serum fetuin-A in septic AKI patients before and after antibiotic therapy.

Nineteen AKI patients with sepsis and fifteen healthy controls were enrolled in this prospective study. Results revealed that 12 weeks of therapy caused amelioration of endothelial and inflammatory injuries as well as renal function markers.

Moreover, the positive correlations between levels of RAGE and E-selectin ( $r = 0.88$ ), ET-1 ( $r = 0.90$ ), and TNF- $\alpha$  ( $r = 0.94$ ) and negative with NO ( $r = -0.75$ – $0.95$ ) suggest that possible interaction of RAGE and inflammation may contribute to endothelial dysfunction in septic AKI patients.

**Keywords:** Acute kidney injury endothelial damage inflammation rage.

### 373. The Significance of Serum Levels of Adiponectin, Leptin, and Hyaluronic Acid in Hepatocellular Carcinoma of Cirrhotic and Noncirrhotic Patients

N A H Sadik, A Ahmed and S Ahmed

*Hum Exp Toxicol*, 31: 311-321 (2012) IF: 1.772

It is well established that hepatocellular carcinoma (HCC) develops in a multistep process, from chronic hepatitis, cirrhosis to HCC. Adipose tissue is not simply an energy storage organ but also a secretory organ, producing a variety of bioactive molecules known as adipokines, including adiponectin and leptin. Hyaluronic acid (HA) is an extracellular matrix protein, often associated with a variety of human cancers. Our retrospective study determines serum levels of adiponectin, leptin, and HA in HCC of cirrhotic and noncirrhotic patients and compares these

levels to patients with cirrhosis and normal subjects. Noncirrhotic HCC (n ¼ 19), cirrhotic HCC (n ¼ 50), cirrhosis (n ¼ 36) patients and twenty one age-, sex-, and body mass index (BMI)-matched normal healthy controls were subjected in the present study. Serum adiponectin, leptin, and HA levels were determined using enzyme-linked immunosorbent assay technique. Levels of serum adiponectin were significantly higher in the cirrhosis and cirrhotic HCC groups than in the normal subjects, whereas serum HA levels were found to significantly increase in all three patients groups. The elevation of serum leptin in our HCC patients, regardless of being cirrhotic or noncirrhotic, but not in the patients with cirrhosis, may shed some light on the significance of serum leptin level in HCC. Further studies are recommended to evaluate the prognostic value of serum leptin level in HCC.

**Keywords:** Hepatocellular carcinoma; Adiponectin; Leptin; hyaluronic acid.

### 374. Evaluation of Oxidative Stress Markers and Vascular Risk Factors in Patients with Diabetic Peripheral Neuropathy

Noha Ahmed El Boghdady and Gamal Ali Badr

*Cell Biochem Funct*, 30: 328-334 (2012) IF: 1.771

Diabetic peripheral neuropathy (DPN) is one of the most common diabetic chronic complications. The pathogenesis of DPN is complex and involves an intertwined array of mechanisms. The purposes of this study were to evaluate the association of oxidative stress and vascular risk factors with the prevalence of DPN and to determine the role of these biochemical parameters in the prognosis of DPN. One hundred patients with type 2 diabetes mellitus and 40 clinically healthy individuals were evaluated. The patients were divided into two groups. Group 1 included 40 diabetic patients without peripheral neuropathy, and group 2 consisted of 60 patients with DPN. Erythrocytes glutathione (GSH) level, plasma malondialdehyde (MDA), nitrite/nitrate (NOx) and homocysteine (Hcy) levels as well as serum ceruloplasmin (Cp), total antioxidants (TAO), endothelin-1 (ET-1) levels and g-glutamyl transferase (GGT) activity were estimated. A significant decrease of erythrocyte GSH was observed in groups 1 and 2 relative to the controls. An increase in glycosylated haemoglobin (HbA1c), MDA, NOx, GGT, Cp, TAO, Hcy and ET-1 was noted in patients with DPN. In conclusion, oxidative stress biomarkers and vascular risk factors could be important in the pathogenesis of DPN. The measurement of serum GGT and Hcy in addition to HbA1c and disease duration could facilitate the early detection of neuropathy in diabetic patients.

**Keywords:** Ceruloplasmin; Endothelin-1; G-Glutamyl transferase; Glutathione; Homocysteine; Malondialdehyde; Nitrite/nitrate; Total.

### 375. Effects of Curcumin and Ginkgo Biloba on Matrix Metalloproteinases Gene Expression and Other Biomarkers of Inflammatory Bowel Disease

Motawi TK, Rizk SM and Shehata AH.

*J. Physiol Biochem*, 68: 529-539 (2012) IF: 1.711

Treatment of inflammatory bowel disease (IBD) by synthetic active ingredients leads to many side effects. The objective of this

study was to manage IBD using natural products as curcumin and Ginkgo biloba.

Rats were divided into four groups (control, IBD, curcumin treated, and ginkgo treated). Inflammation was assessed by determination of myeloperoxidase, matrix metalloproteinases, metalloproteinase-1 inhibitor, nitric oxide, hydroxyproline, tumor necrosis factor- $\alpha$ , ceruloplasmin, and histopathological scoring. IBD induction significantly increased all measured parameters. Treated groups had significantly lower levels when compared with the IBD group. In conclusion, curcumin and ginkgo were effective in prevention and treatment of IBD.

**Keywords:** Matrix metalloproteinases; Gene expression; Ibd; Curcumin; Ginkgo.

### 376. Modulatory Effects of Curcumin and Green Tea Extract Against Experimentally Induced Pulmonary Fibrosis: A Comparison with N-Acetyl Cysteine

Mohammed Ahmed Hamdy, Shohda A. El-Maraghy and Mona Abd El Aziz Kortam

*Journal of Biochemical and Molecular Toxicology*, 26: 461-468 (2012) IF: 1.38

The study was aimed to investigate the protective effect of green tea extract (GTE), curcumin and N-acetyl cysteine (NAC) on experimentally induced pulmonary fibrosis. Curcumin (200 mg/kg b.w), GTE (150 mg/kg b.w) and NAC (490 mg/kg b.w) were administered orally for 14 days with concomitant administration of cyclophosphamide (CP). Lung fibrosis was assessed by measuring hydroxyproline and elastin levels, and confirmed by histopathological examination. Oxidative stress was also observed in the CP group.

Lung myeloperoxidase activity was significantly decreased in animals of the CP group. N-acetyl  $\beta$ -D-glucosaminidase, leukotriene C<sub>4</sub> and protein were increased in bronchoalveolar lavage fluid (BALF). Transforming growth factor- $\beta$ , Interleukin-1 $\beta$  and histamine were increased in both serum and BALF. All modulators markedly attenuated the altered biochemical parameters as compared to CP treated rats. These results suggest the possibility of using these treatments as protective agents with chemotherapy and as protective agents for lung fibrosis.

**Keywords:** Bronchoalveolar lavage fluid; Curcumin; Cyclophosphamide; Greentea extract; Lung fibrosis.

### 377. Promising Antitumor Effect of Alpha-Tocopheryl Succinate in Human Colon and Liver Cancer Cells

Amal A. Abd-El Fattah, Hebatallah A. Darwish, Nevine Fathy, Amira Raafat and Samia A. Shouman

*Med Chem Res*, 21: 0-2743 (2012) IF: 1.271

The main strategy to treat any type of cancer is to look for the therapeutic agents which specifically induce apoptosis in the malignant cells sparing normal cells. The present study was performed to investigate the potential cytotoxicity of alpha-tocopheryl succinate ( $\alpha$ -TOS), a semisynthetic vitamin E analog, in colon and liver cancer cells.  $\alpha$ -TOS inhibited proliferation of HCT-116 and HepG-2 cells in a dose- and time-dependent manner. Here in,  $\alpha$ -TOS induced cell cycle arrest at G<sub>0</sub>/G<sub>1</sub> phase in both cell lines and triggered apoptosis via activation of caspase-9, thus initiating the caspase cascade in the intrinsic

mitochondrial pathway. On the other hand, no significant change in the level of the antiapoptotic protein, Bcl-2 was detected. DNA fragmentation, a hallmark of apoptosis, was observed in HCT-116 cells after 48 h and in HepG-2 cells after 24 h treatment. Inhibition of angiogenesis was evident by a significant reduction (P<0.001) in the VEGF protein levels after 24 and 48 h of  $\alpha$ -TOS treatment, relative to the control values. Conclusively,  $\alpha$ -TOS showed a promising anticancer activity through its apoptotic and antiangiogenic potentials in colon and liver tumor cells.

**Keywords:** Alpha-tocopheryl Succinate; Angiogenesis; Apoptosis; Colon cancer; Dna fragmentation; Liver cancer.

### 378. Chemomodulatory Effect of Nigella Sativa and Green Tea Against Fe-Nta-Mediated Renal Oxidative Damage in Rat

Noha A. El Boghdady and Hebatallah A. Darwish

*Journal of Food Biochemistry*, 2: 255-300 (2012) IF: 0.815

Ferric nitrilotriacetate (Fe-NTA) is a potent nephrotoxic agent. The present study was designed to underline the protective mechanism of Nigella sativa (NS) and green tea (GT) against Fe-NTA-induced renal damage. Fe-NTA (5 mg Fe/kg body weight, i.p.) enhanced serum urea and creatinine levels, lactate dehydrogenase and N-acetyl- $\beta$ -D-glucosaminidase activities. A depletion of renal glutathione content concomitant with a reduction in the activities of antioxidant and phase II metabolizing enzymes was detected. Lipid peroxidation,  $\gamma$ -glutamyl transpeptidase, adenosine deaminase and xanthine oxidase activities in renal tissue were markedly increased after Fe-NTA challenge. A significant deposition of iron in kidney and induction of serum prostaglandin E<sub>2</sub> level were associated with the enhanced oxidative damage.

Pretreatment of rats with either NS oil (2 mL/kg) or GT extract (100 mg/kg) by gavage for 7 consecutive days ameliorated most of the biochemical and histopathological changes induced by Fe-NTA. In conclusion, NS and GT can serve as potent chemopreventive agents to suppress oxidant-induced tissue injury and DNA damage.

**Practical Application** Various therapeutic effects, such as anti-inflammatory, anticancer, antidiabetic and antimicrobial effects have been described for Nigella sativa and green tea. The present study is an endeavor in the direction of determining their possible mechanism of protection in Fe-NTA-mediated renal oxidative damage in rats. Our study proved that they both exhibit a renoprotective potential and, hence, they can be used as value-added agents for managing renal diseases as well as conditions associated with oxidative overload.

**Keywords:** Ferric nitrilotriacetate; Oxidative stress; Nigella sativa; Green tea; Purine-catabolizing enzymes; Phase II enzymes; Prostaglandin E<sub>2</sub>.

### 379. Protective and Therapeutic Effects of Argyreia Speciosa Against Ethanol-Induced Gastric Ulcer in Rats

Tarek K. Motawi, Manal A. Hamed, Reem M. Hashem, Manal H. Shabana and Yomna R. Ahmed

*Z Naturforsch C*, 1-27: (2012) IF: 0.772

The objective of this study was to evaluate the protective and therapeutic effects of Argyreia speciosa Sweet (Convolvulaceae)

against ethanol-induced gastric ulcer in rats. Ethanolic and water extracts of the aerial plant parts (200 mg/kg body weight) were orally administered daily for seven days prior to or after ulceration with one oral dose of 1 mL absolute ethanol on 24 h empty stomachs. Rats were divided into eleven groups.

Group 1 served as control. Groups 2 and 3 were administered each extract. Groups 4 to 6 received each extract or ranitidine (100 mg/kg body weight) prior ulcer induction. Groups 7 to 9 received each extract or ranitidine post ulcer induction. Groups 10 and 11 were gastric ulcerative rats after one hour and one week of ethanol induction. The evaluation was done through measuring ulcer indices: stomach acidity and volume, lesion counts, mucus, and prostaglandin E<sub>2</sub> contents. Oxidative stress markers: malondialdehyde, glutathione, and superoxide dismutase were estimated. Certain marker enzymes for different cell organelles, i. e. succinate and lactate dehydrogenases, glucose-6-phosphatase, acid phosphatase, and 5'-nucleotidase, were evaluated. The work was extended to determine the collagen content, and the histopathological assessment of the stomach. Gastric ulcer exhibited a significant elevation of the ulcer index, antioxidant levels, collagen content, and the marker enzymes. The water extract attenuated this increment and was more potent as a protective agent, while the ethanol extract exhibited stronger therapeutic potency. In conclusion, *A. speciosa* acted as anti-ulcer agent. More detailed studies are required to identify the molecules responsible for the pharmacological effect.

**Keywords:** Gastric ulcer; Ethanol; *Argyrea speciosa*.

### 380. Serum Human Leukocyte Antigen-G and Soluble Interleukin 2 Receptor Levels in Acute Lymphoblastic Leukemia Pediatric Patients

Tarek MK Motawi, Nadia I Zakhary, Tarek M Salman and Samer A Tadros

*Asian Pacific Journal of Cancer Prevention*, 13: 5399-5403 (2012) IF: 0.659

**Aims and Background:** Human leukocyte antigen-G and interleukin-2 receptor play pivotal roles in the proliferation of lymphocytes, and thus generation of immune responses. Their overexpression has been evidenced in different malignant hematopoietic diseases. This study aimed to validate serum soluble human leukocyte antigen-G (sHLA-G) and serum soluble interleukin-2 receptor (sIL-2R) as an additional tool for the diagnosis and follow up of acute lymphoblastic leukemia (ALL).

**Subjects and Methods:** Both markers were determined by ELISA in the serum of 33 ALL pediatric patients before treatment and after intensification phase of chemotherapy as well as in the serum of 14 healthy donors that were selected as a control group.

**Results:** ALL patients showed abnormal CBC and high serum lactate dehydrogenase, which were improved after chemotherapy. Also, there was a non-significant increase in serum sHLA-G in ALL patients compared with the control group. However, after chemotherapy, sHLA-G was increased significantly compared with before treatment.

On the other hand, serum sIL-2R in ALL patients was increased significantly compared with the control group. After chemotherapy, sIL-2R decreased significantly compared with before treatment.

**Conclusions:** From these results it could be suggested that measurement of serum sHLA-G might be helpful in diagnosis of ALL, while sIL-2R might be useful in diagnosis and follow-up of ALL in pediatric patients.

**Keywords:** Soluble human leukocyte antigen-G; Soluble interleukin-2 receptor; Acute lymphoblastic leukemia.

### 381. Genetic Variations in E-Selectin and Icam-1: Relation to Atherosclerosis

Tarek Motawi, Olfat Shaker, Noha Taha and Marwa Abdel Raheem

*Medical Science Monitor*, 18: 381-389 (2012)

**Background:** This study aimed to investigate the association of both intercellular adhesion molecule-1 (ICAM-1) and endothelial cell adhesion molecule (E-selectin) polymorphisms using PCR technique and their role in the pathogenesis of atherosclerosis.

**Material/Methods:** The study enrolled 285 individuals, classified into 4 groups: 63 cerebrovascular atherosclerotic patients, 75 cardiovascular patients, 72 peripheral atherosclerotic patients and 75 normal healthy individuals.

**Results:** The frequency of the mutant AC genotype of E-selectin in peripheral, cerebral and cardiovascular atherosclerotic patients was significantly higher than in control subjects (29.17%, 28.53% and 28% vs. 8%, respectively). However, no significant difference was observed in the frequency of mutant CC allele between all atherosclerotic patients and control groups. The frequency of the mutant EE homozygotes of ICAM-1 in peripheral, cerebral and cardiovascular atherosclerotic patients was significantly higher compared to controls (45.8%, 42.9% and 36% vs. 12%, respectively).

The frequency of EK of ICAM-1 showed no significant difference between atherosclerotic patients and the control group. The frequency of the mutant E allele of ICAM-1 was significantly higher in peripheral, cerebral and cardiovascular patients compared to controls (58.3%, 54.8% and 54% vs. 26%, respectively).

**Conclusions:** Ser 128Arg of E-selectin and the K469E of ICAM-1 polymorphisms may be involved in predisposition to atherosclerosis.

**Keywords:** E-Selectin; Icam-1; Genetic predisposition; Polymorphism.

### 382. Grape Seed Proanthocyanidin Extract Attenuates DNA Fragmentation and Oxidant Damage in Various Tissues of Rats with Hyperthyroidism

Dina Abdel-Salam Elazazy, Sherine Maher Rizk, Maged Abdel-Hakeem Barakat and Rokaya Mahmoud Hussein

*Global Journal of Biochemistry*, 1-9: (2012)

The present study was designed to investigate the protective effects of grape seed proanthocyanidin extract (GSPE) on oxidative damage in rats with experimentally induced hyperthyroidism. Hyperthyroidism was induced by subcutaneous injection of 500 µg/kg/day L-thyroxine for 2 weeks. The experimental animals were divided into five groups: negative control, hyperthyroidism, hyperthyroidism + GSPE in a dose of 25 mg/kg/day for 2 weeks, hyperthyroidism + GSPE in a dose of 50 mg/kg/day for 2 weeks, and hyperthyroidism + vitamin C in a dose of 100 mg/kg/day for 2 weeks. Hyperthyroidism induced elevation in serum concentrations of triiodothyronine (T<sub>3</sub>) and thyroxine (T<sub>4</sub>) and decrease in thyroxine-stimulating hormone (TSH) levels did not significantly change in response to GSPE.



DNA fragmentation, thiobarbituric acid reactive substances (TBARS) and nitric oxide (NO) levels were higher in brain, liver and kidney of rats of the hyperthyroid group compared to controls. Glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) levels decreased significantly in the hyperthyroid group compared to control group. Treatment of hyperthyroid rats with GSPE decreased the elevated TBARS and NO levels and DNA fragmentation and increased the lowered GSH, SOD and CAT levels to control levels. In conclusion, our results indicate that GSPE is beneficial as a protective agent against oxidative stress induced by hyperthyroidism in rats.

**Keywords:** Hyperthyroidism; Grape seed proanthocyanidin extract; Dna fragmentation; Oxidative stress.

#### Dept. of Microbiology and Immunology

### 383. Monitoring the Inflammatory Response to Infection Through the Integration of Maldi Ims and Mri

Ahmed S. Attia, Kaitlin A. Schroeder, Erin H. Seeley, Kevin J. Wilson, Neal D. Hammer, Daniel C. Colvin, M. Lisa Manier, Joshua J. Nicklay, Kristie L. Rose, John C. Gore, Richard M. Caprioli and Eric P. Skaar

*Cell Host Microbe*, 664-673 (2012) IF: 13.5

Systemic bacterial infection is characterized by a robust whole-organism inflammatory response. Analysis of the immune response to infection involves technologies that typically focus on single organ systems and lack spatial information. Additionally, the analysis of individual inflammatory proteins requires antibodies specific to the protein of interest, limiting the panel of proteins that can be analyzed. Herein we describe the application of matrix-assisted laser desorption/ionization imaging mass spectrometry (MALDI IMS) to mice systemically infected with *Staphylococcus aureus* to identify inflammatory protein masses that respond to infection throughout an entire infected animal. Integrating the resolution afforded by magnetic resonance imaging (MRI) with the sensitivity of MALDI IMS provides three-dimensional spatially resolved information regarding the distribution of innate immune proteins during systemic infection, allowing comparisons to in vivo structural information and soft-tissue contrast via MRI. Thus, integrating MALDI IMS with MRI provides a systems-biology approach to study inflammation during infection.

**Keywords:** Inflammatory response; Infection; Mri; Maldi ims.

### 384. Host Hdl Biogenesis Machinery is Recruited to the Inclusion of Chlamydia Trachomatis-Infected Cells and Regulates Chlamydial Growth

John V. Cox, Nirun Naher, Yasser M. Abdelrahman and Robert J. Belland

*Cell Microbiol*, 14: 1497-1512 (2012) IF: 5.458

*Chlamydia trachomatis* is an obligate intracellular bacterial pathogen that is the most common cause of sexually transmitted bacterial infections and is the etiological agent of trachoma, the leading cause of preventable blindness. The organism infects epithelial cells of the genital tract and eyelid resulting in a damaging inflammatory response. *Chlamydia trachomatis* grows within a vacuole termed the inclusion, and its growth depends on

numerous host factors, including lipids. Although a variety of mechanisms are involved in the acquisition of host cell cholesterol and glycosphingolipids by *C. trachomatis*, none of the previously documented pathways for lipid acquisition are absolutely required for growth. Here we demonstrate that multiple components of the host high-density lipoprotein (HDL) biogenesis machinery including the lipid effluxers, ABCA1 and CLA 1, and their extracellular lipid acceptor, apoA-1, are recruited to the inclusion of *C. trachomatis*-infected cells. Furthermore, the apoA-1 that accumulates within the inclusion colocalizes with pools of phosphatidylcholine. Knockdown of ABCA1, which mediates the cellular efflux of cholesterol and phospholipids to initiate the formation of HDL in the serum, prevents the growth of *C. trachomatis* in infected HeLa cells. In addition, drugs that inhibit the lipid transport activities of ABCA1 and CLA 1 also inhibit the recruitment of phospholipids to the inclusion and prevent chlamydial growth. These results strongly suggest that *C. trachomatis* co-opts the host cell lipid transport system involved in the formation of HDL to acquire lipids, such as phosphatidylcholine, that are necessary for growth.

**Keywords:** Chlamydia Trachomatis; Lipids; Hdl; Abca1; Cla1; ApoA-1; Phosphatidylcholine; Cholesterol; Phospholipids.

### 385. Menaquinone Biosynthesis Potentiates Haem Toxicity in Staphylococcus Aureus

Catherine A. Wakeman, Neal D. Hammer, Devin L. Stauff, Ahmed S. Attia, Laura L. Anzaldi, Sergey I. Dikalov, M. Wade Calcutt and Eric P. Skaar

*Molecular Microbiology*, 86: 1376-1392 (2012) IF: 5.01

*Staphylococcus aureus* is a pathogen that infects multiple anatomical sites leading to a diverse array of diseases. Although vertebrates can restrict the growth of invading pathogens by sequestering iron within haem, *S. aureus* surmounts this challenge by employing high-affinity haem uptake systems. However, the presence of excess haem is highly toxic, necessitating tight regulation of haem levels. To overcome haem stress, *S. aureus* expresses the detoxification system HrtAB. In this work, a transposon screen was performed in the background of a haem-susceptible, HrtAB-deficient *S. aureus* strain to identify the substrate transported by this putative pump and the source of haem toxicity. While a recent report indicates that HrtAB exports haem itself, the haem-resistant mutants uncovered by the transposon selection enabled us to elucidate the cellular factors contributing to haem toxicity. All mutants identified in this screen inactivated the menaquinone (MK) biosynthesis pathway. Deletion of the final steps of this pathway revealed that quinone molecules localizing to the cell membrane potentiate haem-associated superoxide production and subsequent oxidative damage. These data suggest a model in which membrane-associated haem and quinone molecules form a redox cycle that continuously generates semiquinones and reduced haem, both of which react with atmospheric oxygen to produce superoxide.

**Keywords:** Menaquinone; Haem toxicity; *Staphylococcus aureus*.

### 386. Plasmid-Cured *Chlamydia Caviae* Activates Tlr2-Dependent Signaling and Retains Virulence in the Guinea Pig Model of Genital Tract Infection

Lauren C. Frazer, Toni Darville, Kumar Chandra-Kuntal, Charles W. Andrews Jr., Matthew Zurenski, Margaret Mintus, Yasser M. AbdelRahman, Robert J. Belland, Robin R. Ingalls and Catherine M. O'Connell

*Plos One*, 7: 1-14 (2012) IF: 4.092

Loss of the conserved "cryptic" plasmid from *C. trachomatis* and *C. muridarum* is pleiotropic, resulting in reduced innate inflammatory activation via TLR2, glycogen accumulation and infectivity.

The more genetically distant *C. caviae* GPIC is a natural pathogen of guinea pigs and induces upper genital tract pathology when inoculated intravaginally, modeling human disease. To examine the contribution of pCpGP1 to *C. caviae* pathogenesis, a cured derivative of GPIC, strain CC13, was derived and evaluated in vitro and in vivo.

Transcriptional profiling of CC13 revealed only partial conservation of previously identified plasmid-responsive chromosomal loci (PRCL) in *C. caviae*. However, 2-deoxyglucose (2DG) treatment of GPIC and CC13 resulted in reduced transcription of all identified PRCL, including *glgA*, indicating the presence of a plasmid-independent glucose response in this species. In contrast to plasmid-cured *C. muridarum* and *C. trachomatis*, plasmid-cured *C. caviae* strain CC13 signaled via TLR2 in vitro and elicited cytokine production in vivo similar to wild-type *C. caviae*. Furthermore, inflammatory pathology induced by infection of guinea pigs with CC13 was similar to that induced by GPIC, although we observed more rapid resolution of CC13 infection in estrogen-treated guinea pigs.

These data indicate that either the plasmid is not involved in expression or regulation of virulence in *C. caviae* or that redundant effectors prevent these phenotypic changes from being observed in *C. caviae* plasmid-cured strains.

**Keywords:** *Chlamydia trachomatis*; *C. muridarum*; *C. caviae* gpic; Cryptic plasmid; Tlr2; Pcpgp1; Cc13; Virulence; GlgA; Plasmid curing.

### 387. Type II Collagen Induces Peripheral Tolerance in Balb/C Mice Via the Generation of Cd8+ T Regulatory Cells

Shukkur M. Farooq and Hossam M. Ashour

*Plos One*, 7: 1-6 (2012) IF: 4.092

Antigens introduced into the anterior chamber (AC) of the eye induce a potent form of antigen-specific peripheral immune tolerance termed AC-associated immune deviation (ACAID), which prevents inflammatory immune responses and is characterized by impaired delayed-type hypersensitivity (DTH) responses. Type-II collagen (CII) is a fibrillar protein expressed exclusively in cartilage tissues. Although of its clinical relevance to Rheumatoid arthritis, aging, and osteoarthritis, there have been no studies to date to test if CII has the ability to induce ACAID. We hypothesized that ACAID could be generated via AC injection of CII in BALB/c mice. Using a DTH assay, the hypothesis was supported and led to another hypothesis that CII is capable of inducing specific immune tolerance via CD8(+) T

regulatory cells (Tregs). Thus, we performed functional local adoptive transfer (LAT) assays to examine the regulatory roles of spleen cells, T cells, and CD8(+) T cells in the specific immune regulation induced by CII injection into the AC. Results indicated that CII induced ACAID when injected into the AC. Spleen cells of mice injected with CII in the AC significantly suppressed DTH responses. The T cell compartment of the spleen was capable of expressing this suppression. CD8(+) Tregs could solely express this CII-driven suppression and even exerted more noticeable suppression than spleen cells or splenic T cells. This study suggests a crucial role for CD8(+) Tregs in mediating CII-driven ACAID-mediated immune tolerance. This could have therapeutic implications in Rheumatoid arthritis, aging, osteoarthritis, and other diseases in which CII is involved.

**Keywords:** Collagen; Tolerance; Acaid.

### 388. Nosocomial Infections in Leukemic and Solid-Tumor Cancer Patients: Distribution, Outcome and Microbial Spectrum of Anaerobes

Amany El-Sharif, Walid F Elkhatib and Hossam M Ashour

*Future Microbiology*, 7: 1423-1429 (2012) IF: 3.819

**Aims:** Nosocomial infections cause significant morbidity and mortality in cancer patients. As a result of their debilitated immune system, cancer patients are likely candidates for colonization with anaerobes. We sought to compare the distribution of nosocomial infections in neutropenic and non-neutropenic cancer patients and to calculate the associated mortality rates.

**Material & methods:** This is the first study to demonstrate a complete microbial spectrum of anaerobes in various infection sites in hospitalized cancer patients.

**Results:** Frequencies of bloodstream infections (BSI), respiratory tract infections (RTI), and GI tract infections (GITI) were significantly higher in neutropenic cancer patients ( $p < 0.01$ ). Conversely, urinary tract infection (UTI) and skin infection (SI) rates were significantly higher in non-neutropenic cancer patients ( $p < 0.01$ ). Mortalities attributed to BSI, UTI, RTI, SI, and GITI occurred at the respective percentage frequencies of 12.5%, 11.5%, 10.4%, 7.7% and 4.9%. Anaerobes constituted 4.7% of total isolates, and were recovered from SI (66.3%) and GITI (33.6%), but not respiratory tract, urine, or blood. Most anaerobes (79.2%) were isolated from solid-tumor patients, the most common infection in cancer patients was RTI (55.8%), mainly in leukemic patients, followed by SI (18%), only in solid-tumor patients, GITI (9.7%), BSI (9.4%), and UTI (7.1%). The most frequent isolates of *Fusobacterium necrophorum* (32.7%) and *Eubacterium lentum* (23.8%) were mostly recovered from solid-tumor patients. These were followed by *Clostridium perfringens* (11.9%), *Clostridium difficile* (10.9%), *Eubacterium limosum* (5.9%), and *Veillonella parvula* (5%).

**Conclusion:** Control measures are needed to minimize risks of nosocomial infection outbreaks by anaerobes. Continuous monitoring of the presence of anaerobes in various infection sites in hospitalized cancer patients is needed in order to be able to provide the best supportive care for cancer patients.

**Keywords:** Anaerobes; Leukemia; Mortality; Neutropenia.

### 389. Detection of Ampc Beta-Lactamases Using Sodium Salicylate

Mona T. Kashif, Aymen S. Yassin and Alaa El-Dien M.S. Hosny

*J. of Microbiological Methods*, 91: 354-357 (2012) IF: 2.086

AmpC  $\beta$ -lactamases are enzymes that hydrolyze all  $\beta$ -lactam antibiotics except cefipime and imipenem. Currently, there is no standard phenotypic method for detection of such enzymes. This study aims to report the use of sodium salicylate for AmpC  $\beta$ -lactamases detection and to compare its sensitivity and specificity to other commonly known inhibitors. A total of 135 clinical isolates were used to test the effectiveness of sodium salicylate in detection of plasmid- as well as chromosomally encoded AmpC  $\beta$ -lactamases. All isolates were tested by multiplex PCR testing as well as inhibitor-based methods using cloxacillin, phenylboronic acid and sodium salicylate for the detection of AmpC enzymes. Four isolates were confirmed as producers of plasmid-encoded AmpC  $\beta$ -lactamase and a single isolate was confirmed to have both plasmid and chromosomal genes. Cloxacillin and phenylboronic acid failed to detect most of the plasmid-encoded enzymes. Sodium salicylate was able to detect the *Escherichia coli* isolates with plasmid-encoded enzymes in addition to few other isolates that were chromosomally mediated. The sensitivity and specificity of sodium salicylate was 50% and 93%, respectively, higher than those of other known inhibitors. We thus conclude that sodium salicylate can be reliably used as an inhibitor in the detection of plasmid-encoded AmpC enzymes in *E. coli*.

**Keywords:** Ampc;  $\beta$ -Lactamases; Sodium salicylate.

### 390. Detection of Genus Salmonella and Serogroups A, B, C1, D and (Vi) Capsular Producing Strains Using Multiplex Polymerase Chain Reaction (Pcr) Method From Stool

O. M. Helmy, Y. M. Ragab and M. M. M. Hussein

*African Journal of Microbiology Research*, 6: 7383-7388 (2012) IF: 0.539

In many countries, *Salmonella* is the leading cause of food-borne outbreaks and infections. A multiplex PCR (mPCR) for the detection of genus *Salmonella* and serogroups A, B, C1, D and capsular (Vi) producing strains from swabs of stool samples was developed. In the mPCR, primers for invasion (*invA*), O (*prt*, *tyv*, *rfbj*, *wzx*C1) and Vi antigen genes (Vi) and internal amplification control primers were used. The results showed that all tested *Salmonella* serotypes were accurately identified by the assay, without nonspecific amplification except *Salm. derby* and *Salm. saint Paul*. Representative serogroups were used to artificially inoculate stool samples. The different serogroups were detected by mPCR after overnight pre-enrichment of stool swab in buffered peptone water with a detection limit of *Salmonella* cell suspension of 4 cfu/ g stool. The developed mPCR assay provides specific detection of genus *Salmonella* and serogroups A, B, C1, D and Vi positive strains directly from stool swabs. The developed method for *Salmonella* serogroup identification is rapid, easy and less subjective methods. This could be of great use by any facility that lacks the expensive typing sera and expertise needed for conventional serotyping.

**Keywords:** *Salmonella*; Multiplex pcr; Stool; Molecular serotyping; Somatic antigen.

### 391. Efficacy and Toxicity of Neutralizers Against Disinfectants and Antiseptics Used in Vaccine Production Facility

Norhan S. Sheraba, Aymen S. Yassin, Aly Fahmy and Magdy A. Amin

*African Journal of Microbiology Research*, 6: 6565-6571 (2012) IF: 0.528

Effective neutralization of chemical biocide is the first step in the accurate evaluation of antiseptics and disinfectants to avoid overestimation of the biocide activity. The aim of this study is to screen novel neutralizers (or neutralizer combinations) against different antiseptics and disinfectants that are highly used in the principle vaccine production facility in Egypt. Neutralizer efficacy (NE) ratios were determined by comparing the recovery of the challenging index microorganisms from the neutralizing solution in the presence, or the absence, of the biocide. Neutralizer toxicity (NT) ratios were determined by comparing the recovery of viable microorganisms in the neutralizer exposed population and the viability population. An effective and non-toxic neutralizer was initially identified by NE and NT ratios of  $\geq 0.75$  (75% recovery). The most potent neutralizers were 1% physiological peptone water, 0.1 % Tween 80 in 1% physiological peptone, 0.6% sodium thiosulphate and Dey-Engley. Due to the absence of a universal neutralizer, the evaluation of NE and toxicity is an essential step in testing any new biocide. The evaluation of neutralizer activity should be carried out separately for each index microorganism and neutralizer pair to identify the most potent compound in each case.

**Keywords:** Antiseptics; Disinfectants; Neutralizers.

### 392. Evaluation of Polymerase Chain Reaction and Culture for the Diagnosis of Corneal Ulcer

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*Life Science Journal*, 9: 746-755 (2012) IF: 0.075

**Purpose:** to compare polymerase chain reaction (PCR) to microbial culture for the detection and identification of bacterial and fungal microorganisms in microbial keratitis.

**Methods:** Corneal scrapings from 150 patients clinically diagnosed as microbial keratitis, who attended the Research Institute of Ophthalmology cornea clinic were cultured, analysed by PCR and the results were compared.

**Results:** of the 150 patient samples, 104 (69.3%) were culture-positive (76 for bacteria, 19 for fungi and 9 were mixed culture); and 46 (30.7%) were culture-negative. Of these 150 patient samples, 130 (86.7%) were positive by PCR (74 bacterial, 18 fungal and 38 mixed infection); and 20 (13%) were PCR-negative. Of the 76 culture-positive for bacteria, 73 (96%) were positive by PCR; 17 (89.5%) out of 19 samples culture-positive for fungi were positive by PCR and 8 (89%) out of 9 samples culture-positive for mixed infection were PCR-positive. Of the 46 culture-negative samples, 32 (69.5%) yielded pathogen deoxyribonucleic acid (DNA) products and 14 were PCR-negative.

The sensitivity of PCR in detecting bacterial, fungal, mixed culture and no growth keratitis was 94%, 86%, 88%, 79%

respectively while the specificity was 90%, 82%, 95% and 83% respectively.

**Conclusion:** PCR detects microbial DNA in the majority of bacterial and fungal corneal ulcers, and identifies microorganisms in a high proportion of culture-negative cases.

PCR may be used as an adjunct to culture to identify microorganisms in microbial keratitis. Although being expensive, PCR remains a promising tool for faster and highly sensitive diagnosis of microbial keratitis.

**Keywords:** Diagnosis; Microbial keratitis; Pcr; Culture.

### 393. The Interplay of Il-2 and Ifn- $\gamma$ in Response to Hcv Peptides in Healthy High Risk Egyptian Health Care Workers: A Pilot Study

Mona M. Rafik, Alaa El-Dien M.S. Hosny, Khaled O. Abdallah, Amal A. Abbas and Rania A.

*Journal of Applied Sciences Research*, 8: 5198-5205 (2012)

Characterization of virus-specific immune responses in seronegative persons, the highly risk groups such as health care workers (HCWs), may provide important clues as to the nature of protective immunity in HCV. We studied the Interleukin-2 (IL-2) and interferon gamma (IFN- $\gamma$ ) to different HCV peptides among 60 HCWs with and without evidence of HCV infection. Participants were classified according to the proliferation index in a CSFE proliferation assay.

Results showed positive HCWs produced a higher IL-2 in response to all peptides except NS4 and a higher IFN- $\gamma$  response to NS3 and 4 compared to negative HCWs. on the other hand, there was no difference in the IL-2 response with a higher IFN- $\gamma$  response to NS4 and 5 in chronic HCV- HCWs.

This differential pattern of IFN- $\gamma$  and IL-2 production demonstrates that the magnitude and type of cytokines produced in HCV infection are critical in determining the outcome of infection.

**Keywords:** Hepatitis C; Health care workers; Hcv peptides; Cytokines; Cfse; Proliferation assay.

### 394. A Study on Occurrence of Plasmid Mediated Ampc $\beta$ -Lactamases Among Gram Negative Clinical Isolates and Evaluation of Different Methods used for Their Detection

Alaa El-Dien M.S. Hosny and Mona T. Kashif

*Journal of Applied Sciences Research*, 8: 2280-2285 (2012)

AmpC enzyme is a  $\beta$ -lactamase that can hydrolyze cephamycins as well as other extended spectrum cephalosporins and not inhibited by clavulanic acid. in gram negative bacteria, this enzyme is chromosomally mediated in most isolates and less commonly plasmid mediated in few isolates. There is no standard phenotypic method for detection of such enzyme. in this study, isolates were tested for the presence of AmpC  $\beta$ -lactamase. in addition, the sensitivity and specificity, of different phenotypic methods used for its detection, have been evaluated. A number of 139 out of 240 gram negative clinical isolates were screen positive for AmpC  $\beta$ -lactamases by standard disc diffusion method. These positive isolates were identified using Api 20E identification system and the presence of AmpC  $\beta$ -lactamases were detected using multiplex PCR, AmpC disc test as well as cloxacillin and phenylboronic acid inhibitor based methods. Five

plasmid mediated AmpC enzymes including three CIT and two DHA related types were identified in *Serratia marcescens*, *klebsiellae* spp. and *Escherichia coli* isolates. to our knowledge, this is the first time to be reported, at least locally, for the presence of plasmid mediated AmpC enzyme in *Serratia marcescens*. the best sensitivity and specificity (100 and 67%, respectively) for detection of such enzyme were recorded for AmpC disc test; it was efficient in detecting all plasmid and most chromosomally mediated AmpC enzymes. in General, AmpC disc test proved to be superior phenotypic method compared to other inhibitor based methods. We recommend routine testing for the presence of AmpC  $\beta$ -lactamases in any gram negative isolates.

**Keywords:** Ampc  $\beta$ -Lactamases; Ampc disc test; Cloxacillin; Inhibitor based method; Phenylboronic acid.

### 395. The Application of Uniplex, Duplex, and Multiplex Pcr for the Absence of Specified Microorganism Testing of Pharmaceutical Excipients and Drug Products

Suzan M. Ragheb, Aymen S. Yassin and Magdy A. Amin

*Pda Journal of Pharmaceutical Science and Technology*, 66: 307-317 (2012)

Notable progress has been made in methods that encourage the use of polymerase chain reaction (PCR) as a rapid and accurate tool in microbiological testing of pharmaceuticals. in this study, the detection of the four main specified microorganisms according to the pharmacopeial recommendations, *Salmonella* spp, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*, was optimized in different pharmaceutical dosage forms and raw materials. Uniplex PCR was performed for the detection of each microorganism individually targeting the conserved region in each bacterial genome. Further optimizations were done to perform duplex and multiplex PCR assays considering relative concentrations of competitor primers used in the reaction. the uniplex PCR amplicons were successfully sequenced, confirming the conservation of used primers. Other validation parameters such as specificity, sensitivity, and robustness were examined closely. the method provides a high-throughput screening method to test different pharmaceutical preparations for specified microorganisms for the detection of microbiological contamination.

**Keywords:** Pcr; Usp; Indicator pathogens; Nonsterile pharmaceuticals; Technology transfer.

### 396. Scaling Up for the Industrial Production of Rifamycin B Fed-Batch Production Mode in Shake Flasks and Bench-Scale Fermentor

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*Fermentation Technology*, 1: 1-6 (2012)

The production of rifamycin B using the gene amplified variant of *Amycolatopsis mediterranei* (NCH) was initially optimized in shake flasks through medium modifications and fed-batch addition of uracil. the yield was increased by 21.7% (from 11.7 to 14.3 g/l) when F2m1 medium was used. the production was further verified and optimized in fedbatch- mode in a laboratory fermentor using F2m3 medium and the optimized conditions (agitation 500 rpm, aeration; 1.5 for 3 days then control DO at

30% thereafter, pH; 6.5 for 3 days then 7 thereafter and control temperature at 28°C). Fed-batching of glucose syrup (5% v/v at day 3) and glucose (1% at days 6 and 8) increased the yield from 17.8 to 20.9 g/l (17.3%) at day 10. A yield of upto 20 g/l was recorded when 0.1% uracil was fed-batched at day 2. Integration of the most optimum conditions for fed-batching glucose syrup, glucose and uracil further increased the yield from 17.8 to 24.8 g/l (39%) in 10 days. the overall optimization of rifamycin B production increased the yield almost 2 folds. Statistical analysis revealed that there is a significant increase in rifamycin B production by using One-Way ANOVA at  $p < 0.05$  in all the tested fed-batch addition regimes.

**Keywords:** Carbon sources; Fermentor; Nitrogen sources.

### 397. Antimicrobial Profile of Selected Snake Venoms and their Associated Enzymatic Activities

R. I. Shebl, A. F. Mohamed, A. E. Ali and M. A. Amin

*British Microbiology Research Journal*, 2: 251-263 (2012)

**Aims:** to investigate the antiviral and antibacterial profile of several crude snake venoms and to assess some of their enzymatic activities.

**Methodology:** the antiviral activities of *Naja haje*, *Bitis arietans*, *Naja nigricollis* and *Echis carinatus* snake venoms were investigated against Herpes simplex virus type1, Rift valley fever virus and Vesicular stomatitis virus using the end point of cytopathic effect method. Antibacterial activities of *Bitis arietans*, *Cerastes cerastes*, *Echis carinatus*, *Vipera lebetina*, *Naja naja*, *Pseudechis australis*, *Naja nigricollis* and *Naja haje* venoms were examined against *Staphylococcus aureus*, *Escherichia coli*, *Salmonella typhimurium* and *Pseudomonas aeruginosa* using disc diffusion method. Microdilution method was used to determine the venom's minimum inhibitory concentration. L-amino acid oxidase and phospholipase A2 activities of crude venoms were evaluated using enzymatic assays.

**Results:** *Naja nigricollis*, *Bitis arietans* and *Echis carinatus* snake venoms exhibited significant antiviral activities against all test viruses, except for *N. haje* treated cells. The mean depletion of viral infectivity titer of venom pretreated cells was higher than its depletion post viral infection for all three venoms showing antiviral activities. *Naja nigricollis* exhibited the highest antiviral activity against test viruses and recorded a mean depletion of viral infectivity titer in venom pretreated cells of 3.8 log (10) / ml, 3.2 log (10) / ml and 2.5 log (10) / ml for HSV-1, RVFV and VSV, respectively. *Pseudechis australis*, followed by *Naja naja* and *Naja nigricollis* venoms, showed the highest inhibitory activity against test bacteria with inhibition zones ranging from 11-17 mm, 8-14 mm and 8-13 mm, respectively.

Minimum inhibitory concentrations of test venoms against different bacterial strains ranged from 156 µg / ml to 1.25 mg / ml. Maximum L- amino oxidase activity was detected in *Naja naja*, *Cerastes cerastes* and *Pseudechis australis*. the highest Phospholipase A2 activity was identified in *Bitis arietans*, *Pseudechis australis*, *Naja naja* and *Naja nigricollis*.

**Conclusion:** It can be concluded that snake venoms or their bioactive derivatives can be promising therapeutic agents against some microbial infections. Further investigations will be carried out for purification and more characterization of the biologically active components in snake venoms.

**Keywords:** Snake venom; Antibacterial activity; Antiviral activity; L- Amino oxidase activity.

### 398. Cerastes Cerastes and Vipera Lebetina Snake Venoms Apoptotic – Stimulating Activity to Human Breast Cancer Cells and Related Gene Modulation

Shebl RI, Mohamed AF, Ali AE and Amin MA

*Journal of Cancer Science & Therapy*, 4: 317-323 (2012)

Apoptosis occurs normally during development and aging as a homeostatic mechanism to maintain cell populations. Dysregulation of apoptosis can disrupt the equilibrium between cell growth and cell death leading to the development of cancer. Thus, the investigation of new biological apoptotic activators could play an important role in cancer therapy. In the present study, *Cerastes cerastes* and *Vipera lebetina* snake venoms were evaluated for their ability to activate apoptosis in cancer cells where test venoms exhibited a concentration and time dependent cytotoxic effect on breast cancer (MCF-7) cells. Typical apoptotic morphological features were demonstrated in venom treated cells detected via transmission electron microscope. In addition, flow cytometric analysis showed an increase in the percentage of apoptotic cells post 24 h treatment relative to venom concentrations. At the molecular level, test venoms induced apoptosis were mediated by up regulation of pro-apoptotic genes (p53 & Bax) and down regulation of anti-apoptotic gene (Bcl-2) in MCF-7 cells, indicating that these venoms could serve as apoptotic stimulators, presenting a novel and potential therapeutic strategy for cancer treatment.

**Keywords:** *Cerastes cerastes*; *Vipera lebetina*; Breast cancer cells; P53 gene; Bax gene; Bcl-2 gene.

### 399. Clinical Screening for Bacteriocinogenic Enterococcus Faecalis Isolated from Intensive Care Unit Inpatient in Egypt

Ahmed O. El-Gendy, Tamer M. Essam, Magdy A. Amin, Shaban H. Ahmed and Ingolf F. Nes

*J. of Microbial and Biochemical Technology*, 4: 161-167 (2012)

A bacterium originally isolated from stool sample from ICU inpatient was biochemically and molecularly characterized and identified as *Enterococcus faecalis* OS6. This strain showed the ability to exert antimicrobial activities against some members of Gram-positive bacteria as *Lactobacilli* and *Enterococci*. However, no activities were detected against all tested Gram-negative and fungal indicator strains. Diminishing of antimicrobial activities upon heat and proteinase K treatments confirmed the proteinaceous nature of the recorded activity. Therefore, strain OS6 was extensively screened for the presence of 10 common bacteriocin structural genes where genes of Enterolysin A and Cytolysin were detected and confirmed by further gene sequencing. Further characterization of strain OS6 showed several virulence determinants including gelatinase, haemolysin, bile salt hydrolase and multiple antibiotic resistance traits towards 17 out of 31 different antibiotics. Most of these 17 antibiotics belonged to Cephalosporins, Aminoglycosides, Lincomycins, Polypeptides, Quinolones, Rifamycins and Sulfonamides classes. To the best of our knowledge, this is the first attempt to report production of bacteriocins (mainly Enterolysin A) in between pathogenic *E. faecalis* isolated from human clinical specimen in Egypt.

**Keywords:** Bacteriocin; Enterolysin A; *Enterococcus faecalis*.

#### 400. Isolation and Characterization of Relevant Algal and Bacterial Strains from Egyptian Environment for Potential Use in Photosynthetically Aerated Wastewater Treatment

Marwa El Rakaiby, Tamer Essam and Abdelgawad Hashem

*Journal of Bioremediation and Biodegradation*, 38: 1-5 (2012)

A number of environmental samples were collected from different locations in Egypt. Briefly, 9 bacterial strains and 4 algal strains were isolated and characterized. All isolated bacterial strains showed a remarkable ability to tolerate and/or biodegrade phenol (aromatic pollutant) and pyridine (hetero-aromatic pollutant). Phenol showed higher toxicity than pyridine to both bacterial and algal isolates. The bacterial isolates were identified as members of *Pseudomonas*, *Chryseomonas*, *Sphingomonas* and *Burkholderia* species. The highest biodegradation rate and capacity were reported to bacterial isolate M4, identified as *Pseudomonas* MT1. This strain was able to degrade up to 1700 and 3000 mg l<sup>-1</sup> of phenol and pyridine respectively. *Pseudomonas* MT1 showed the highest phenol biodegradation rate of 29 mg h<sup>-1</sup> and lag phase approximately of 8 h and was optimally grown on 1000 -1250 mg phenol l<sup>-1</sup>. All algal isolates were morphologically identified as members of the *Chlorella* genus. None of the isolated algal strains showed biodegradation ability of any of the tested organic pollutants. However, isolates A1, A2 and A4 showed remarkable tolerance to both phenol and/or pyridine. The highest tolerance capacity was reported to algal isolate A4, identified as *Chlorella vulgaris* MM1 with a toxicity cut off of 500 and 1000 mg l<sup>-1</sup> of phenol and pyridine respectively. Both *Pseudomonas* MT1 and *Chlorella vulgaris* MM1 had no inhibitory effect on each other. Therefore, they represented potential candidates for the construction of algal bacterial microcosm used for the photosynthetically aerated biological degradation of effluents loaded with various organic pollutants.

**Keywords:** Phenol; Pyridine; Wastewater; Photosynthesis.

#### 401. Screening for the Antimicrobial Activities of Alcoholic and Aqueous Extracts of Some Common Spices in Egypt

Maha M. Ismail, Tamer M. Essam, Aly F. Mohamed and Fathia E. Mourad

*International Journal of Microbiological Research*, 3: 200-207 (2012)

The extracts of 17 spices commonly used in Egypt as food condiments were screened for their antimicrobial activities against 7 standard microbial strains (*S. aureus*, *B. subtilis*, *E. coli*, *P. aeruginosa*, *S. typhi*, *C. albicans* and *A. niger*). Among the tested alcoholic extracts only 3 (clove, thyme and cinnamon) showed broad spectrum antimicrobial activities. Garlic juice too showed broad spectrum antimicrobial activities.

Only 4 alcoholic extracts (black pepper, safflower, coriander and myrrh) had no antimicrobial activities. The remaining extracts (53%) showed only anti-Gram positive bacteria activities. None of all tested aqueous extracts showed antifungal activity with lower antibacterial activities compared to their alcoholic ones. The antibacterial effect of alcoholic extracts was not concentration dependant, however their antifungal effect was concentration dependant. Interestingly, both alcoholic and aqueous extracts of cinnamon and alcoholic extract of clove showed the highest

antiviral activity where the TCID was reduced by about 1 log cycle. This was followed 50 by the aqueous extract of clove, garlic juice then aqueous extract of thyme, while both alcoholic and aqueous extracts of liquorice had no antiviral activity.

**Keywords:** Foodborne diseases; Spices; Antimicrobial activity; Antiviral activity.

#### 402. Involvement of Virulence Genes and Antibiotic Resistance in Clinical and Food Borne Diarrheagenic Escherichia Coli Isolates from Egypt

Marwa E.A. Aly, Tamer M. Essam and Magdy A. Amin

*World Journal of Medical Sciences*, 7: 276-284 (2012)

A total of 140 *E. coli* isolates showed at least one pathogenic determinant among the isolated 147 *E. coli* which were previously collected from clinical and food samples. The other 7 isolates were free from tested virulence genes. Among these 140 isolates, 123 had only the *UidA* gene, therefore, were classified as non-categorized pathogenic *E. coli*. The other 17 isolates had at least one characteristic gene of diarrheagenic *E. coli* and were identified and classified as enteropathogenic *E. coli* (8), enterotoxigenic *E. coli* (5) and enterohemorrhagic *E. coli* (4). Interestingly, a correlation was found among these isolates that increasing the number of virulence genes was accompanied with an increase in the antibiotic resistance until a cutoff of 2 virulence genes, above this limit the relation was inversely proportion. Evidentially, sensitive K12 *E. coli* was able to acquire ampicillin and/or kanamycin resistance traits from resistant pathogenic *E. coli* isolate among those collected in the present study. NSEM monitoring of different growth stages of the mated K12 *E. coli* and the donor resistant pathogenic *E. coli* showed that horizontal gene transfer by conjugation occur during the growth, suggesting that this was one of possible mechanisms through which the antibiotic resistance characters were transferred or acquired.

**Keywords:** Acquisition; Conjugation; *E. coli*; Multiplex PCR; Resistance.

#### 403. Antibiotic Resistance Profile of E. Coli Strains Isolated from Clinical Specimens and Food Samples in Egypt

Marwa E.A. Aly, Tamer M. Essam and Magdy A. Amin

*International Journal of Microbiological Research*, 3: 176-182 (2012)

A total of 147 *E. coli* strains were isolated from food samples and clinical specimens. The prevalence of *E. coli* in clinical specimens was much higher than in food samples. The antibiotic resistance profile of these strains was determined against 7 classes of antimicrobial agents (26 different members). Almost 90% of *E. coli* strains were resistant to at least one of the tested antibiotics. The highest antibiotic resistance was recorded against conventional Beta-lactams. However, this resistance was significantly lower when Beta-lactams combinations and cephalosporins were tested. The highest sensitivity of the isolates was to imipenem and polymyxin-B where all isolated *E. coli* strains were sensitive to imipenem. The resistance to tetracyclines, macrolides and sulfonamides/trimethoprim were almost in the same order of magnitude of 30-37%. The resistance to quinolones and aminoglycosides were 19 and 10 % respectively. Among isolated *E. coli* 52 strains (35%) exhibited multidrug resistance

(MDR) pattern to equal or more than 3 antibiotics classes with different mode of action. Interestingly, MDR E. coli isolated from food samples was higher than those isolated from clinical specimens.

**Keywords:** E. Coli; Antibiotics; Multi-drug resistance; F.

#### 404. Effect of Levofloxacin and Vitamin C on Bacterial Adherence and Preformed Biofilm on Urethral Catheter Surfaces

Eman El-Gebaly, Tamer Essam, Shabaan Hashem and Rehab A. El-Baky

*J. of Microbial and Biochemical Technology*, 4: 131-136 (2012)

The effect of levofloxacin (LEV) and vitamin-C (VIT-C) individually or in combinations on initial bacterial adherence and pre-formed (mature) biofilms on the surface of urethral catheters was studied. The isolated and studied uropathogens in the present study showed considerable diversity, where the major pathogens were identified as E.coli, Klebsiella sp., Citrobacter sp., Enterobacter sp., Proteus sp. and Pseudomonas sp. Using the static adherence assay, addition of LEV and VIT-C each alone at sub MIC concentrations (0.25 MIC and 0.5 MIC) and (80 and 100 mg ml<sup>-1</sup>) respectively, reduced the initial adherence ability of bacteria to the catheter by 35-94%. Besides, the inhibitory effect on the mature biofilm was estimated to be 40-90% in the presence of (MIC and 2MIC) LEV or (80 and 100 mg/ml) VIT-C. The highest inhibitory effects on both the initial adherence and mature biofilm were recorded when 0.5 MIC and 2 MIC of levofloxacin were added respectively. Combination of LEV and VIT-C significantly increased the inhibitory effect of both initial biofilm formation and the mature biofilm to 80-100%. In addition, scanning electron microscope (SEM) was used to verify the effect of the tested drugs on biofilm production. The obtained results confirmed the significant role of this combination in inhibition of urethral catheter biofilm formation.

**Keywords:** Ascorbic acid (Vitamin-C); Biofilm; Fluoroquinolones.

#### 405. Expression and Purification of Hepatitis B Surface Antigen S from Escherichia Coli; A New Simple Method

Mohamed S Elghanam, Ahmed S Attia, Hussein A Shoeb and Abd Elgawad M Hashem

*Bmc Research Notes*, 5: (2012)

**Background:** Hepatitis B is a liver disease primarily caused by hepatitis B virus (HBV) infection. It is distributed worldwide and associated with high mortality and morbidity rates. HBV infections can be avoided by the administration of the currently available vaccine and can be easily diagnosed through commercially available kits. Both the vaccine and the diagnostic kits depend on using the hepatitis B surface antigen (HBsAg) as an antigen. Developing countries such as, Egypt, suffer from the widespread of HBV infections and the limited resources to provide adequate supplies of either the vaccine or the diagnostic kits. Therefore the need for an easy, rapid, low cost method to produce HBsAg is urgently needed within this setting.

**Findings:** to achieve this goal, the gene encoding the HBsAg(S) protein was cloned and expressed as a fusion protein with a GST

tag in Escherichia coli. The recombinant protein was successfully expressed and purified in both good quality and quantity.

**Conclusions:** the simplified and the relatively low cost of the used protocol make this an attractive alternative to protocols currently used for the purification of HBsAg(S). The exploiting of this achievement for new diagnostics can be directed for application in the developing countries where they are extremely needed.

**Keywords:** Hbsag; New method; Purification.

#### 406. Plasmid Encoding Antimicrobial Resistance Among Environmental Salmonella Species and Molecular Characterization Using Random Amplified Polymorphic DNA Analysis

Mohamed A. El-sayed, Wael M. Tawakol, Yasser M. Ragab and Magdy A. Amin

*World Journal of Medical Sciences*, 7: 163-171 (2012)

The increase in antibiotic resistance among Gram-negative bacteria is a notable example of how bacteria can procure, maintain and express new genetic information that can confer resistance to one or several antibiotics. The emergence of multidrug resistant (MDR) Salmonella has become a serious problem. Our study was done to investigate the role of plasmid as a factor mediating such resistance pattern. This study was done on 40 Salmonella isolates from different food products. Antibiogram was done by Kirby Bauer disc diffusion method and the minimum inhibitory concentration (MIC) was determined using the microtiter broth dilution method. MDR isolates (23/40) were confirmed and identified to species level using API 20E. Plasmid extraction was done for MDR isolates by alkaline lysis. It was revealed that 60.86% (14/23) of MDR isolates were found to harbour plasmids. To demonstrate the role of plasmid in resistance, Salmonella isolates were subjected to plasmid curing using sodium dodecyl sulfate (SDS). The present study has investigated the degree of similarity between five MDR isolates on molecular basis using random amplified polymorphic DNA (RAPD) technique, in which a total of 5 primers were used showing good discriminatory power for all five isolates. The dendrogram showed a common lineage among all five isolates. Finally 16S ribosomal DNA sequencing has been performed for one Salmonella isolate.

**Keywords:** Salmonella plasmid rapid-Pcr 16S ribosomal DNA sequencing.

#### 407. Phenotypic Detection of Potential Antimicrobial Resistance among Environmental Salmonella Species

Magdy A. Amin, Wael M. Tawakol, Yasser M. Ragab and Mohamed A.El-sayed

*Int. J. of Microbiological Research*, 3: 38-45 (2012)

Emergence of multidrug resistance (MDR) in Salmonella strains is a serious development. Our study was done to investigate such resistance mechanisms which may play a role in partial or total resistance to these antimicrobial agents. This study was done on 40 Salmonella isolates from different food products. All isolates were plated primarily on MacConkey's agar then on bismuth sulphite agar, XLD and brilliant green MacConkey's agar and subjected to different biochemical reactions. MDR isolates were confirmed and identified to species level using API 20E.

Antibiogram was done by Kirby Bauer disc diffusion method and the minimum inhibitory concentration (MIC) was determined using the microtiter broth dilution method. The MDR isolates were further investigated to determine the potential resistance mechanisms to  $\beta$ -lactam antibiotics, chloramphenicol and ciprofloxacin using EDTA disc synergy test, AmpC disc test and efflux pump test. This study revealed that imipenem 97.5% (39/40) was the most effective antibiotic, while cefepime 47.5% (19/40) was the least effective. Out of 23 isolates (MDR), one isolate 4.35% (1/23) was AmpC producer, three isolates 13% (3/23) were Metallo- $\beta$ -lactamase (MBL) producers and nineteen isolates 82.61% (19/23) were efflux pump positive. This study suggests that efflux pump is an important mechanism for antimicrobial resistance among *Salmonella* spp.

**Keywords:** *Salmonella*; Multidrug resistance; Efflux pump; Edta disc synergy test.

#### Dept. of Pharmaceutical Chemistry

#### 408. Synthesis of New 7-Oxycoumarin Derivatives as Potent and Selective Monoamine Oxidase A Inhibitors

Abdelhafez OM, Amin KM, Ali HI, Abdalla MM, Batran RZ.

*J. Med Chem*, 55: 10424-10436 (2012) IF: 5.248

New series of 4-methyl and 3,4-dimethyl-7-oxycoumarin derivatives (oxadiazoles, thiadiazoles, triazoles, and thiazolidinones) were designed, synthesized, and evaluated for their monoamine oxidase (MAO) A and B inhibiting effect.

All the synthesized compounds showed in vitro high affinity and selectivity toward MAO-A isoenzyme, compared to clorgyline and moclobemide, with  $K_i$  values on the picomolar range. Moreover, most of the tested compounds displayed MAO inhibitory effect when tested in vivo. The docking experiments carried out on MAO-A and MAO-B structures proved new information about the enzyme-inhibitor interaction and the potential therapeutic application of 7-oxycoumarin scaffold.

**Keywords:** 7-Oxy-4-Methyl/3; 4-Dimethylcoumarins; HMAO inhibitors; Molecular modelling.

#### 409. Design and Synthesis of Novel Stiripentol Analogues as Potential Anticonvulsants

Mohamed N. Aboul-Enein, Aida A. El-Azzouny, Mohamed I. Attia, Yousreya A. Maklad, Kamilia M. Amin, Mohamed Abdel-Rehim and Mohammed F. El-Behairy

*Eur J Med Chem*, 47: 360-369 (2012) IF: 3.346

A series of stiripentol (STP) analogues namely, 2-[(1E)-1-(1,3-benzodioxol-5-yl)-4,4-dimethylpent-1-en-3-ylidene]-N-(aryl/H) hydrazinecarboxamides 7aeh, ( $\pm$ )-(5RS)-N-(aryl/H)-(1,3-benzodioxol-5-yl)-3-tertbutyl-4,5-dihydro-1H-pyrazole-1-carboxamides ( $\pm$ )-8aeh, and ( $\pm$ )-[(5RS)-(1,3-benzodioxol-5-yl)-3-tertbutyl-4,5-dihydro-1H-pyrazol-1-yl](aryl)methanones (!)-13aef was synthesized by adopting appropriate synthetic routes and was pharmacologically evaluated in the preliminary anticonvulsant screens. The selected bioactive new chemical entities were subjected to ED<sub>50</sub> determination and neurotoxicity evaluation. The most active congeners are 7h in MES screen and ( $\pm$ )-13b in scPTZ screen which displayed ED<sub>50</sub> values of 87 and

110 mg/kg, respectively, as compared to that of STP (ED<sub>50</sub> ¼ 277.7 and 115 mg/kg in MES and scPTZ, respectively).

**Keywords:** Stiripentol; Epilepsy; Semicarbazones; Pyrazolines; Anticonvulsants.

#### 410. Synthesis, Molecular Docking Study and Antitumor Activity of Novel 2-Phenylindole Derivatives

Sally S. El-Nakkady, Mona M. Hanna, Hanaa M. Roaiah and Iman A.Y. Ghannam

*Eur. J. Med. Chem.*, 47: 387-398 (2012) IF: 3.346

The starting material, 4-(1-indol-2-yl)phenol 1 was obtained via Fischer synthesis. Vilsmeier-Haack's formylation of 1 gave the carboxaldehyde derivative 2 which was subjected to different reactions affording the 3-substituted compounds 3-10. Compound 1 reacted with halo esters to give 11 and 12a,b. The reaction of 12a with various amino derivatives gave compounds 13-16. The hydrazone derivative 15a reacted with 1,3-diketones, ethyl acetoacetate and aromatic carboxylic acid derivatives to give 17a,b, 18 and 19a-e, respectively. Antitumor activity of target compounds were tested against breast cancer cell lines (MCF-7) and (MDA-MB-231). The most potent compound was 3e with IC<sub>50</sub> ¼ 1.60 nM against (MCF-7). Docking was performed on colchicine binding site of tubulin to study the binding mode of the designed compounds.

**Keywords:** 2-Phenylindoles; Indole carboxaldehyde; Antitumor activity; Breast cancer cell lines MCF-7 and MDA-MB-231; Docking study.

#### 411. New Pyrimido [5,4-E] Pyrrolo [1,2-C] Pyrimidines: Synthesis, 2D-Qsar, Anti-Inflammatory, Analgesic and Ulcerogenicity Studies

Hanna MM.

*Eur. J. Med. Chem.*, 55: 12-22 (2012) IF: 3.346

New pyrimido[5,4-e]pyrrolo[1,2-c]pyrimidines were synthesized. A series of ylidene carbohydrazides 14a-i, and hydrazonate 15, were obtained from the prepared 3-carbohydrazone derivative 13. Pyrazole derivatives 12, 16a,b, 18, 19, 20, were also prepared through different reactions. The anti-inflammatory and analgesic activities of all new compounds were evaluated and most of them exerted comparable activity to indomethacin and celecoxib. Ulcer indexes for the most active compounds were calculated and most of them showed less ulcerogenic effect than the reference drugs. The most potent anti-inflammatory compound 12 showed an IC<sub>50</sub> of 6.00 mmol/kg and low ulcer index. COX-1/COX-2 activity ratio of compounds 12 and 16b showed almost equal inhibitory effect on both isoenzymes. 2D-QSAR studies revealed good predictive and statistically significant QSAR models.

**Keywords:** Pyrimido[5;4-E]Pyrrolo[1;2-C] Pyrimidine; Anti-Inflammatory; Analgesic; Ulcer index; 2D-Qsar; Cox-1/Cox-2.

#### 412. Novel 1,3,4-Heterodiazole Analogues: Synthesis and in-Vitro Antitumor Activity

Azza T. Taher, Hanan H. Georgey and Hussein I. El-Subbagh

*Eur. J. Med. Chem.*, 47: 445-451 (2012) IF: 3.346

The synthesis of some new heterodiazole and their annulated imidazo[2,1-b]1,3,4-oxa/thiadiazolone 6a-d, 7a-d; 1,3,4-oxa or



thiadiazole[3,2-a]pyrimidine diamine 8a-d and 1,3,4-oxa or thiadiazole-3-piperidino-1-propamide 11a,b derivatives have been described. The obtained compounds were evaluated for their in-vitro antitumor activity. A single dose (10  $\mu$ M) of the test compounds were used in the full National Cancer Institute (NCI) 60 cell lines panel assay. Compounds 6c and 6d displayed appreciable anticancer activity against leukemia, non-small cell lung, CNS and showed moderate activity against colon, melanoma, and breast cancer cells lines. Compound 6c possessed remarkable broad-spectrum antitumor activity which almost 4 fold more active than the known drug 5-FU with GI50, TGI, and LC50 values of 6.0, 17.4, and 55.1  $\mu$ M, respectively.

**Keywords:** Heterodiazole; 1,3,4-Oxadiazole;Thiadiazole [3;2-A]Pyrimidine; Antitumor activity.

#### 413. Stereoselective Synthesis and Qsar Study of Cytotoxic 2-(4-Oxo-Thiazolidin-2-Ylidene)-2-Cyano-N-Arylacetamides

George RF.

*Eur. J. Med. Chem.*, 47: 377-86 (2012) IF: 3.346

(2Z,5Z) 2-[(5-Arylidene-4-oxo-3-phenyl)-thiazolidin-2-ylidene]-2-cyano-N-arylacetamides 4a-l were stereoselectively prepared via condensation of aromatic aldehydes with 4-thiazolidinones 3a-c. The latter were obtained via electrophilic attack of phenylisothiocyanate on 2-cyano-N-arylacetamides 1a-c followed by reaction with chloroacetyl chloride under basic condition. Single crystal X-ray study of 3a allows good confirmation for the assigned structure. Additionally, 5-arylhydrazono analogs 5a-e were prepared via condensation of the appropriate diazonium salts with 4-thiazolidinones 3a,b. Many of the synthesized compounds exhibited promising antitumor properties against colon HCT116, breast MCF7 and liver HEPG2 cell lines. 3D-Pharmacophore modeling and QSAR analysis were combined to explain the observed antitumor properties.

**Keywords:** 4-Thiazolidinones; 2-Cyano-N-Arylacetamides; Antitumor activity; Qsar.

#### 414. Synthesis, Vasorelaxant Activity, and Molecular Modeling Study of Some New Phthalazine Derivatives

Fadi M. Awadallah, Wafaa I. El-Eraky and Dalia O. Saleh

*Eur. J. Med. Chem.*, 52: 14-21 (2012) IF: 3.346

New phthalazine-based vasodilators were synthesized through the chloroacylation of the starting compound 1-hydrazinophthalazine 4 to give the two key intermediates 5 and 7. These intermediates were used to alkylate various cyclic amines to furnish the final compounds 6aeh and 8aeh. Compounds were tested for their vasorelaxant activities against nor-adrenaline-induced spasm on thoracic rat aorta rings and compared to the reference drug, prazosin. Seven compounds showed higher activity than prazosin, especially compound 8d having an IC<sub>50</sub>  $\frac{1}{4}$  0.10 mM. Molecular modeling studies, including fitting of the synthesized compounds to a 3D-pharmacophore and their docking into optimized homology model as  $\alpha$ 1-AR antagonists showed high docking score and fit values. Most vasodilation activities of tested compounds are consistent with their molecular modeling results.

**Keywords:** Phthalazine; Piperazine; Alpha-1 adrenergic receptors; Vasorelaxant; Molecular modeling.

#### 415. New Quinazolinone-pyrimidine Hybrids: Synthesis, Anti-Inflammatory and Ulcerogenicity Studies

Safinaz E. Abbas, Fadi M. Awadallah, Nashwa. Ibrahim, Eman G. Said and Gihan M. Kamel

*Eur. J. Med. Chem.*, 53: 141-149 (2012) IF: 3.346

Two groups of hybrid compounds: the quinazolinone-dihydropyrimidines and quinazolinone-pyrimidines, were synthesized. The starting derivative 3 was reacted with chloroacetyl chloride to give intermediate 5 which was condensed with the 2-mercaptopyrimidines 4aec affording compounds 6aec. These latter compounds underwent hydrolysis and N-alkylation reactions to give the dihydropyrimidine derivatives 7aec and 8aef, respectively. The chloro derivatives 9aec subsequently reacted with various anilines furnishing compounds 10aei. The anti-inflammatory activity of the synthesized compounds were evaluated using the carrageenan-induced rat paw oedema model and ulcer indices for the most active compounds were calculated. Five compounds were found more active and less ulcerogenic than diclofenac particularly compound 10g (IC<sub>50</sub>=116.73 mmol/kg; ulcer index= 11.38). Compound 10g was also 2-fold more selective inhibitor of COX-2 than COX-1.

**Keywords:** Quinazolinone; Pyrimidine; Dihydropyrimidine; Anti-inflammatory; Cox-1/Cox-2; Ulcerogenicity.

#### 416. On-Line Solid-Phase Enrichment Coupled to Packed Reactor Flow Injection Analysis in A Green Analytical Procedure to Determine Low Levels of Folic Acid Using Fluorescence Detection

Samy Emara, Tsutomu Masujima, Walaa Zarad, Maha Kamal and Ramzia EL-Bagary

*Chemistry Central Journal*, 55: 1-10 (2012) IF: 3.281

**Background:** Analysis of folic acid (FA) is not an easy task because of its presence in lower concentrations, its lower stability under acidic conditions, and its sensitiveness against light and high temperature. The present study is concerned with the development and validation of an automated environmentally friendly pre-column derivatization combined by solid-phase enrichment (SPEn) to determine low levels of FA.

**Results:** Cerium (IV) trihydroxyhydroperoxide (CTH) as a packed oxidant reactor has been used for oxidative cleavage of FA into highly fluorescent product, 2-amino-4-hydroxypteridine-6-carboxylic acid. FA was injected into a carrier stream of 0.04 M phosphate buffer, pH 3.4 at a flow-rate of 0.25 mL/min. The sample zone containing the analyte was passed through the CTH reactor thermostated at 40°C, and the fluorescent product was trapped and enriched on a head of small ODS column (10 mm x 4.6 mm i.d., 5  $\mu$ m particle size). The enriched product was then back-flush eluted by column-switching from the small ODS column to the detector with a greener mobile phase consisting of ethanol and phosphate buffer (0.04M, pH 3.4) in the ratio of 5:95 (v/v). The eluent was monitored fluorimetrically at emission and excitation wavelengths of 463 and 367 nm, respectively. The calibration graph was linear over concentrations of FA in the range of 1.25-50 ng/mL, with a detection limit of 0.49 ng/mL.

**Conclusion:** A new simple and sensitive green analytical procedure including on-line pre-column derivatization combined by SPEn has been developed for the routine quality control and

dosage form assay of FA at very low concentration level. the method was a powerful analytical technique that had excellent sensitivity, sufficient accuracy and required relatively simple and inexpensive instrumentation.

**Keywords:** Folic acid; on-Line solid phase enrichment; Flow injection analysis; Cerium (Iv) trihydroxyhydroperoxide; Fluorescence detection.

#### 417. Dapson in Heterocyclic Chemistry, Part VIII: Synthesis, Molecular Docking and Anticancer Activity of Some Novel Sulfonylbiscompounds Carrying Biologically Active 1,3-Dihydropyridine, Chromene and Chromenopyridine Moieties

Mansour S Al-Said, Mostafa M Ghorab and Yassin M Nissan

*Chem. Cent. J.*, 64: 1-14 (2012) IF: 3.281

Several new sulfonebiscompounds having a biologically active 1,2-dihydropyridine-2-one 3–19, acrylamide 20, chromene 21, 22 and chromenopyridine 23, 24 moieties were synthesized and evaluated as potential anticancer agents.

The structures of the products were confirmed via elemental analyses and spectral data. the screening tests showed that many of the biscompounds obtained exhibited good anticancer activity against human breast cell line (MCF7) comparable to doxorubicin which was used as reference drug. Compounds 11, 17 and 24 showed IC<sub>50</sub> values 35.40  $\mu$ M, 29.86  $\mu$ M and 30.99  $\mu$ M, respectively.

In order to elucidate the mechanism of action of the synthesized compounds as anticancer agents, docking on the active site of farnesyltransferase and arginine methyltransferase was also performed and good results were obtained.

**Keywords:** Sulfone; Pyridines; Chromenes; Pyridinochromenes; Anticancer activity.

#### 418. Synthesis and Biological Evaluation of Imidazolymethylacridones as Cytochrome P-450 Enzymes Inhibitors

Ashraf H. Abadi, Sahar M. Abou-Seri, Qingzhong Hu, Matthias Negri and Rolf W. Hartmann

*Medchemcomm*, 3: 663-666 (2012) IF: 2.8

Two positional isomers with the general formula 1H-imidazol-1-ylmethylacridin-9(10H)-one were synthesized (5, 6) and evaluated for their inhibitory activity versus CYP11B1, CYP11B2, CYP17 and CYP19.

Compound 5 was more effective than letrozole in inhibiting CYP19 (aromatase). Interestingly, compound 5 also inhibited CYP11B1 with an IC<sub>50</sub> of 21.2 nM. on the other hand compound 6 was almost completely inactive against all CYPs; this indicates that the positioning and spatial orientation of the imidazolymethyl moiety is of paramount importance to activity. Sequence alignment of the four steroidogenic CYP enzymes and docking studies with 5, 6 and letrozole supported this finding and suggested Ser478 to be an essential residue for both inhibition and selectivity.

These novel compounds may have benefits for the treatment of Cushing's syndrome, hypertension, congestive heart failure and myocardial fibrosis and breast cancer.

**Keywords:** Imidazolymethylacridones; Docking; Cytochrome P-450 Enzymes inhibitors.

#### 419. Synthesis and Bioactivity Evaluation of New 6-Aryl-5-Cyano Thiouracils as Potential Antimicrobial and Anticancer Agents

Azza Taher Taher and Sahar Mahmoud Abou-Seri

*Molecules*, 17: 9868-9886 (2012) IF: 2.386

Several novel 6-ary-5-cyano thiouracil derivatives were synthesized and explored for their activities as antibacterial, antifungal and anticancer agents. the antimicrobial evaluation revealed that compounds 7b and 7c possessed superior antibacterial activity against the Gram positive bacteria *S. aureus* and *B. subtilis* compared to the reference drug amoxicillin. Moreover, compound 4i was found to be a broad spectrum antimicrobial agent and exhibited the highest antifungal activity against *C. albicans* even higher than the reference drug amphotericin B (MIC= 2.34, 3.00  $\mu$ g/ml respectively).

On the other hand, selected compounds were tested for in vitro cytotoxicity at a single 10<sup>-5</sup> M concentration in accordance to the NCI (USA) protocol.

The preliminary screening results showed that most of the compounds had limited cytotoxic activity against renal cancer UO-31 and/or A498 cell lines. Nevertheless, compounds 6d and 6i displayed potent growth inhibitory effect toward non-small cell lung cancer HOP-92 and leukemia MOLT-4 cell lines, respectively.

**Keywords:** 6-Aryl-5-Cyano thiouracils; Antibacterial; Antifungal; Anticancer.

#### 420. Synthesis and Anti-Inflammatory Activity of Some Benzofuran and Benzopyran-4-One Derivatives

Fatma Abd El-Fattah Ragab, Nahed Mahmoud Eid, Ghaneya Sayed Hassan and Yassin Mohammed Nissan

*Chem Pharm Bull*, 60: 110-120 (2012) IF: 1.592

New series of furosalylic acids 3a–c, furosalylicanilides 6a–n, furobenzoxazines 8a–f, 1-benzofuran-3-arylprop-2-en-1-ones 12a,b, 6-(aryl-3-oxoprop-1-enyl)-4H-chromen-4-ones 16a–c and 6-[6-aryl-2-thioxo-2,5-dihydropyrimidin-4-yl]-4H-chromen-4-ones 17a–c were synthesized. Anti-inflammatory activityevaluation was performed using carrageenan-induced paw edema model in rats and prostaglandin E2 (PGE2) synthesis inhibition activity. Some of the tested compounds revealed comparable activity with less ulcerogenic effect than Diclofenac at a dose 100 mg/kg. All the synthesized compounds were docked on the active site of cyclooxygenase-2 (COX-2) enzyme and most of them showed good interactions with the amino acids of the active site comparable to the interactions exhibited by Diclofenac.

**Keywords:** Anti-Inflammatory activity; Prostaglandin E2; Benzofuran; Benzopyran-4-One.

#### 421. Novel 4-(4-Substituted-Thiazol-2-Ylamino)-N-(Pyridin-2-Yl)-Benzenesulfonamides as Cytotoxic and Radiosensitizing Agents

Mostafa M. Ghorab, Fatma A. Ragab, Helmy I. Heiba, Hebaallah M. Agha and Yassin M. Nissan

*Arch Pharm Res.*, 35: 59-68 (2012) IF: 1.592

A series of novel 4-(4-substituted-thiazol-2-ylamino)-N-(pyridin-2-yl) benzene-sulfonamides were synthesized and screened for their cytotoxic activity against human breast cancer cell line (MCF-7). Compounds 6, 7, 9, 10, 11, and 14 displayed significant activity against MCF-7 when compared to doxorubicin, which was used as a reference drug. the synergistic effect of Gamma radiation for the most active derivatives 7, 9, and 11 was also studied and their IC<sub>50</sub> values markedly decreased to 11.9  $\mu$ M, 11.7  $\mu$ M, and 11.6  $\mu$ M, respectively.

**Keywords:** Sulfonamides; Thiazoles; Cytotoxic; Radiosensitizing activities.

#### 422. Novel Brominated Quinoline and Pyrimidoquinoline Derivatives as Potential Cytotoxic Agents with Synergistic Effects of $\gamma$ -Radiation

Mostafa M. Ghorab, Fatma A. Ragab, Helmi I. Heiba, Yassin M Nissan and Walid M. Ghorab

*Arch Pharm Res.*, 35: 1335-1346 (2012) IF: 1.592

New quinoline derivatives 6, 7 and 19, pyrimidoquinoline derivatives 8-16 and triazolopyrimidoquinoline derivatives 17 and 18 bearing a bromo-substituent were synthesized starting from 3-(4-Bromophenylamino)-5,5-dimethylcyclohex-2-enone 3. All the newly synthesized compounds were evaluated for their in vitro anticancer activity against human breast cancer cell line (MCF7). Compounds 9, 11, 17 and 18 showed IC<sub>50</sub> values (36.4, 39.7, 39.02 and 36.4  $\mu$ M, respectively) comparable to that of the reference drug doxorubicin (IC<sub>50</sub> = 32.02  $\mu$ M). on the other hand, compound 6, 14 and 19 exhibited better activity than doxorubicin with IC<sub>50</sub> values of 8.5, 23.5 and 23.7  $\mu$ M. Additionally, the most potent compounds 6, 14 and 19 were evaluated for their ability to enhance the cell killing effect of  $\gamma$ -radiation.

**Keywords:** Quinoline; Pyrimidoquinoline; Triazolopyrimidoquinoline; Brominated;  $\gamma$ -Radiation.

#### 423. Synthesis of Novel Pyrazole and Dihydropyrazoles Derivatives as Potential Anti-Inflammatory and Analgesic Agents

Nagwa M. Abd-El Gawad, Hanan H. Georger, Nashwa A. Ibrahim, Noha H. Amin and Rania M. Abdelsalam

*Arch Pharm Res.*, 35: 807-821 (2012) IF: 1.592

Novel dihydropyrazole 5-8, 10 and pyrazole derivatives 12, 14, 15, 17 were synthesized. the structures of the newly synthesized compounds were elucidated by spectral and elemental analyses. the anti-inflammatory activity of all new compounds was evaluated using the carrageenan-induced rat paw edema test using indomethacin and celecoxib as reference drugs. the most active derivatives as anti-inflammatory agents were accordingly tested for their analgesic activity using the p-benzoquinone-induced writhing method in mice and results revealed that these compounds had also good analgesic activity.

The ulcerogenic liability of the selected compounds was also evaluated. Results showed that the selected derivatives had anti-inflammatory activity comparable to or slightly lower than the reference drugs, reaching about 82% inhibition with a considerable gastric safety profile.

**Keywords:** Pyrazole; Dihydropyrazole; Anti-Inflammatory; Analgesic.

#### 424. Facile Synthesis and Quantitative Structure-Activity Relationship Study of Antitumor Active 2-(4-Oxo-Thiazolidin-2-Ylidene)-3-Oxo-Propionitriles

Mona Maurice Hanna and Riham François George

*Chem Pharm Bull.*, 60: 1195-1206 (2012) IF: 1.592

2-(5-Arylidene-4-oxo-3-phenyl-thiazolidin-2-ylidene)-3-oxo propionitriles 4a-j were prepared via condensation of aromatic aldehydes with 4-thiazolidinones 3a, b. the latter was obtained via electrophilic attack of phenylisothiocyanate on 3-oxo-propionitriles 1a, b followed by reaction with chloroacetyl chloride under basic condition.

Additionally, 2-(5-heteroalicyclic methylene) analogues 5a-h were prepared via Mannich reaction of the appropriate secondary amines and formaldehyde with 4-thiazolidinones 3a, b. Many of the synthesized compounds exhibited promising antitumor properties against colon HCT116 and breast T47D cell lines. 3D-Pharmacophore modeling and quantitative structure-activity relationship (QSAR) analysis were combined to explain the observed antitumor properties.

**Keywords:** Thiazolidinone; Quantitative structure-activity Relationship; Antitumor activity; 3-Oxo-Propionitrile; Hct116; T47d.

#### 425. Design, Synthesis and Anti-Inflammatory Activity of Structurally Simple Anthranilic Acid Congeners Devoid of Ulcerogenic Side Effects

Mohamed Eissa A.A., Soliman G.A. and Khataibeh M.H.

*Chem Pharm Bull.*, 60: 1290-1300 (2012) IF: 1.592

Simple, three classes of new anthranilic acid derivatives were aimed at, synthesized and tested for their toxicity, anti-inflammatory, analgesic, antipyretic activity. Also, their potential protective role against ulcerative colitis in rats was performed. Furthermore, their effect on liver and kidney functions was detected through measurement of the serum level of ALT, AST, urea, creatinine and other parameters. Compounds 4, 5, 6b, 6c, 7c and 7e showed significant anti-inflammatory activity. From those 6b and 7e best improved the inflammatory indices even producing better reduction in the intensity of lesion score, ulcer area and wet weight/ length ratio and showed good analgesic activity. Fortunately, none of the tested compounds showed any hepatotoxicity or nephrotoxicity. None of the tested compounds showed any antipyretic activity. Conclusively, presence of a phenyl ring in the substituent added is a must, since any alteration in its nature led to decrease in activity. Also, the presence of an extra halogen in addition to the one already embedded in the main structure was detrimental to activity.

**Keywords:** Anthranilic acid derivatives; Anti-inflammatory activity; Ulcerative colitis; Hepatotoxicity evaluation; Nephrotoxicity evaluation.

#### 426. Synthesis of Novel Pyrazole and Pyrimidine Derivatives Bearing Sulfonamide Moiety as Antitumor and Radiosensitizing Agents

Mostafa M. Ghorab, Fatma A. Ragab, Helmy I. Heiba, Hanan A. Youssef and Marwa G. El-Gazzar

*Med Chem Res*, 21: 1376-1383 (2012) IF: 1.271

Several novel pyrazole 10–16 and pyrimidine 17–19 derivatives bearing Sulfonamide moieties were synthesized in order to study their antitumor activity. The synthesized compounds were characterized by elemental analysis, IR, <sup>1</sup>H-NMR, and mass spectral data, then screened as antitumor agents against human tumor liver and breast cell lines (HEPG2 and MCF7). All the tested compounds were more potent than the reference drug doxorubicin on human liver (HEPG2) cell line, while on human breast cancer (MCF7) cell line, they were less potent than the reference drug. Additionally, some of the synthesized compounds were evaluated for their ability to enhance the cell killing effect of  $\gamma$ -radiation.

**Keywords:** Pyrazole pyrimidine sulfonamide antitumor activity radiation.

#### 427. Two Liquid Chromatographic Methods for the Simultaneous Determination of Ibuprofen and Methocarbamol or Chlorzoxazone in the Presence of their Degradation Products

Ehab F. Elkady and Marwa A. Fouad

*J. Liq Chromatogr R T*, 35: 882-895 (2012) IF: 0.953

Two RP-LC methods have been developed for the simultaneous determination of ibuprofen (IBU) and two skeletal muscle relaxants, namely methocarbamol (MET) or chlorzoxazone (CHZ), in the presence of their degradation products. In the first method, the simultaneous determination of IBU and MET in the presence of guaifenesin (GUF), a degradation product of MET, was developed.

Chromatographic separation was achieved on an Inertsil CN-3 column (250mm $\times$ 4.6 mm, 5  $\mu$ m). Gradient elution based on 0.5% aqueous phosphoric acid (pH 2.8) - acetonitrile at a flow rate of 1 mL min<sup>-1</sup> was applied with UV detection at 229 nm for IBU and 274 nm for MET and GUF.

Linearity, accuracy, and precision were found to be acceptable over the concentration ranges of 5–160  $\mu$ g mL<sup>-1</sup> for IBU and 2.5–160  $\mu$ g mL<sup>-1</sup> for MET and GUF. In the second method, the simultaneous determination of IBU and CHZ in the presence of CHZ degradation product, 2-amino-4-chlorophenol (CDE), was developed. In this method, chromatographic separation was achieved on Reprosil-Pur C8 (250mm $\times$ 4.6 mm, 5  $\mu$ m).

A gradient mobile phase system consisting of acetonitrile and 0.2% aqueous triethylamine (pH 5.1) at a flow rate of 1 mL min<sup>-1</sup> was applied with UV detection at 229 nm for the three compounds. Linearity, accuracy, and precision were found to be acceptable over the concentration ranges of 2.5–250  $\mu$ g mL<sup>-1</sup> IBU and CHZ, and 2.5–150  $\mu$ g mL<sup>-1</sup> CDE. The optimized methods were validated and proved to be specific, robust, and accurate for the quality control of the cited drugs in synthetic mixtures and pharmaceutical preparations.

**Keywords:** Chlorzoxazone; Ibuprofen; Methocarbamol; Pharmaceutical preparation; Reversed-phase liquid chromatography; Stability indicating assay.

#### 428. Spectrofluorometric Determination of Certain Antihyperlipidemic Agents in Bulk and Pharmaceutical Preparations

Ramzia I. El-Bagary, Ehab F. Elkady and Ahmed M. Kadry

*Spectroscopy: an International Journal*, 27: 83-92 (2012)

IF: 0.805

A simple, rapid, and sensitive spectrofluorometric method was developed for the determination of three antihyperlipidemic drugs, namely, rosuvastatin calcium (RSV), ezetimibe (EZE), and pitavastatin calcium (PIT). The method is based on measuring the native fluorescence of the cited drugs at their optimum excitation and emission wavelengths. The fluorescence intensity was measured at  $\lambda_{em}$  362 nm, 309 nm, and 373 nm upon excitation at  $\lambda_{ex}$  315 nm, 260 nm, and 245 nm for RSV, EZE, and PIT, respectively. The calibration graphs were linear over the concentration ranges 0.50–10.0, 0.25–4.0, and 0.10–3.00  $\mu$ g mL<sup>-1</sup> for RSV, EZE, and PIT, respectively. Besides, a spectrofluorometric method for the simultaneous determination of RSV and EZE was developed. The fluorescence was measured at  $\lambda_{em}$  309 nm for EZE and 432 nm for RSV upon excitation at  $\lambda_{ex}$  260 nm for both. The proposed methods were applied to the determination of the cited drugs either in bulk and pharmaceutical preparations.

**Keywords:** Spectrofluorometry; Rosuvastatin calcium; Ezetimibe; Pitavastatin calcium; Native fluorescence; Pharmaceutical preparation.

#### 429. Dapson in Heterocyclic Chemistry Part Vi: Synthesis and Molecular Docking of Some Novel Sulfonebiscompounds of Expected Anticancer Activity

Ghorab M.M., Al-Said M.S. and Nissan Y.M.

*Arzneimittel-Forsch*, 62: 0-507 (2012) IF: 0.722

To discover new bioactive lead compounds for medicinal purposes, herein, sulfone biscompounds bearing dihydrothiazoles (3–9, 14, 15), acrylamide (11), thiazolidinones (12, 13, 20), thiophenes (16, 17) and benzothiophene (19) were prepared and tested for their anticancer activity. The structures of the products were confirmed from elemental analysis as well as spectral data. All the synthesized compounds showed remarkable anticancer activity against human breast cancer cell line especially, compound (3) with IC<sub>50</sub> value 23.02  $\mu$ M which was better than that of Doxorubicin by three folds. In order to elucidate the mechanism of action of their cytotoxic activity molecular docking on the active sites of farnesyl transferase and arginine methyl transferase was performed for all synthesized compounds and good results were obtained.

**Keywords:** Thiazole; Acrylamide; Thiophene; Benzothiophene; Anticancer activity.

#### 430. Synthesis, *in-Vitro* Anticancer Screening and Radiosensitizing Evaluation of Some New N-(Quinoxalin-2-Yl) Benzenesulfonamide Derivatives

M. M. Ghorab, F. A. Ragab, H. I. Heiba, M. G. El-Gazzar and M. G. El-Gazzar

*Arzneimittel-Forsch*, 62: 46-52 (2012) IF: 0.722

The objective of this work is to synthesize and investigate the anticancer activity of a new series of sulfaquinoxaline derivatives

by incorporating biologically active moieties (thiourethane, thiazole, imidazole, imidazopyrimidine, imidazopyrimidopyrimidine, thienopyrimidine, benzopyrimidinone, benzothiazole, thiazole and pyridine moieties). All the newly synthesized compounds were evaluated for their in-vitro anticancer activity against human liver cell line (HEPG2). All the tested compounds showed comparable activity to that of the reference drug 5-fluorouracil (IC<sub>50</sub> = 40 μM), and the most potent compounds were found to be compounds 4 and 17 (IC<sub>50</sub> = 4.29 and 11.27 μM, respectively). On the other hand, the most potent compounds 4 and 17 were evaluated as radiosensitizing agents.

**Keywords:** Sulfonamide; Quinoxaline; Anticancer; Radiosensitizing.

#### 431. Coupling of on-Line Pre-Column Oxidative Cleavage and Solid-Phase Enrichment with Liquid Chromatography using an Eco-Friendly Analytical Procedure to Determine Low Levels of Methotrexate

Samy Emar, Walaa Zarad, Maha Kamal and Ramzia EL-Bagary

*Journal of Analytical Sciences, Methods and Instrumentation*, 2: 194-202 (2012)

A simple, sensitive and precise green high-performance liquid chromatographic method including on-line pre-column oxidation combined by column switching with a short Hypersil ODS analytical column (100 mm × 4.0 mm i.d.) for enrichment and separation was developed and validated to determine low levels of methotrexate (MTX). The method was based on oxidative cleavage of MTX into highly fluorescence products, 2,4-diaminopteridine-6-carboxaldehyde and the corresponding 2,4-diaminopteridine-6-carboxylic acid, during the flow of phosphate buffer (0.04 M, pH 3.4) containing the analyte through the packed reactor of cerium (IV) trihydroxyhydroperoxide (CTH) at a flow-rate of 0.2 mL/min and 40°C. The fluorescent products were enriched on the head of ODS analytical column for the final separation. The separation was performed at room temperature using an environmentally friendly mobile phase consisting of ethanol and phosphate buffer (0.04 M, pH 3.4) in the ratio of 10:90 (v/v). The eluent was monitored at emission and excitation wavelengths of 463 and 367 nm, respectively. The method was successfully applied, without any interference from the excipients, for the determination of drug in tablets and vials with a detection limit of 0.06 ng/mL from 500 μL of sample MTX.

**Keywords:** Cerium (IV) trihydroxyhydroperoxide; HPLC; Methotrexate; ODS analytical column; on-Line Pre-Column oxidative cleavage.

#### 432. Synthesis of 4-(1H-Benzo[d] Imidazol-2-yl) Aniline Derivatives of Expected Anti-HCV Activity

M.K. Khattab, F.A.F. Ragab, S.A. Galal and H.I. El Diwani

*Jrprc.*, 2: 937-946 (2012)

Starting from 4-(1H-benzo [d] imidazol-2-yl) aniline (1), derivatives of expected anti-HCV activity were prepared. Reaction of compound 1 with maleic anhydride yielded the α,β-unsaturated carboxylic acid 2 which was cyclized using hydrazine hydrate, phenylhydrazine or 4-nitrophenylhydrazine to give the pyrazole derivatives 3, 4 & 5 respectively. Condensation of compound 1 with the pyrazolocarbaldehydes 6, 7, 8 & 9 afforded the corresponding Schiff's bases 11, 12, 13 & 14 respectively. The

structures of the new compounds were confirmed by their spectral data and microanalyses.

**Keywords:** Benzoimidazoles; Antihcv; Unsaturated ketone.

#### 433. Three Analytical Methods for Determination of Epinastine Hydrochloride in Bulk and in Ophthalmic Solutions

Ramzia I. El-Bagary, Amal Boshra, Maha M. El-Hakeem, Amira M. Abdelra'ouf

*Journal of Chemical and Pharmaceutical Research*, 4: 1361-1369 (2012)

Three simple and sensitive methods, namely, difference spectrophotometric, colorimetric and HPLC methods are described for the determination of epinastine hydrochloride (EPH) in pure form and ophthalmic solution. First, the drug is determined quantitatively by pH-induced difference spectrophotometry. The method is based on the measurement of the difference absorbance at 252nm of epinastine hydrochloride (EPH) in 0.1N NaOH against equivalent amount in 0.1N HCl as a blank. Beer's law was obeyed for the studied drug over the range of 16 to 96 μg.mL<sup>-1</sup>. In the second method, the drug is converted to its corresponding free base which is treated with chloranilic acid (CAA) solution in acetonitrile to give a colored product with an absorption maximum at 517 nm. Various experimental parameters and the stoichiometry of the reaction were investigated and optimized. Linearity is obeyed over the range of 20-220 μg.mL<sup>-1</sup>. The third is an HPLC method, which is the determination of EPH using acetonitrile: 0.1 M ammonium acetate buffer (40:60 v/v) as a mobile phase at a flow rate 1 mL/min and UV detection at 262nm. Methyl paraben was used as internal standard. The linearity range was from 20 to 100 μg.mL<sup>-1</sup>. The proposed methods were validated according to the guidelines of the ICH and were also statistically compared with the reference method showing no significant difference concerning accuracy and precision.

**Keywords:** Epinastine hydrochloride; Difference spectrophotometry; Chloranilic acid; HPLC; Ophthalmic solution.

#### 434. On-Line Coupling of Derivatization with Pre-Concentration to Determine Trace Levels of Methotrexate

Samy Emar, Tsutomu Masujima, Walaa Zarad, Maha Kamal and Ramzia EL-Bagary

*Journal of Pharmaceutical Analysis*, 3: 28-35 (2012)

A new simple, sensitive and precise green analytical procedure using an automated packed-reactor derivatization technique coupled with on-line solid-phase enrichment (SPEn) has been developed and evaluated to determine trace levels of methotrexate (MTX). The method was based on injection of MTX into a flowing stream of phosphate buffer (0.04 M, pH 3.4), carried through the packed oxidant reactor of Cerium (IV) trihydroxyhydroperoxide for oxidative cleavage of the drug into highly fluorescent product, 2,4-diaminopteridine 6-carboxylic acid, followed by SPEn on a head of short ODS column (10 mm × 4.6 mm i.d., 5 μm particle size). The flow rate was 0.25 mL/min and packed reactor temperature was 40°C. The trapped product was back-flush eluted from the ODS column to the detector by column-switching with an environmentally friendly mobile phase

consisting of ethanol and phosphate buffer (0.04 M, pH 3.4) in the ratio of 5:95 (v/v). The eluent was monitored at emission and excitation wavelengths of 460 and 360 nm, respectively. The calibration curve was linear over the concentration range of 1.25–50 ng/mL with a detection limit of 0.08 ng/mL.

**Keywords:** Methotrexate; Flow injection analysis; Cerium (IV) trihydroxy- hydroperoxide; On-line solid-phase enrichment; Fluorescence detection.

### 435. Two Chromatographic Methods for the Determination of Some Antimigraine Drugs

Ramzia I. El-Bagary, Nashwa G. Mohammed and Heba A. Nasr

*Analytical Chemistry Insights*, 7: 13-21 (2012)

Two stability indicating chromatographic methods were proposed for the determination of almotriptan, eletriptan, and rizatriptan, in presence of their acid degradation products. the first method is a quantitative densitometric thin layer chromatography. the developing systems were; acetonitrile: methanol: dichloromethane: ammonia (10:6:3:1 v/v), ethyl acetate: methanol: ammonia (15:4:1 v/v), and methanol: acetonitrile: ammonia (9:4:1 v/v) for almotriptan, eletriptan and rizatriptan respectively. the TLC plates were scanned at 235 nm. Linear relationships were obtained over concentration ranges (5–50 µg/spot) for almotriptan and rizatriptan, and (5–60 µg/spot) for eletriptan. the second method based on the separation and determination of the studied drugs, using RP-HPLC technique. the separation was achieved on C18 Hypersil column, elution was carried out using phosphate buffer pH 3: methanol: acetonitrile (2: 1:1 v/v) at flow rate 2 mL/min and UV detection at 235 nm. Linear relationships were obtained over concentration ranges (10–200 µg/mL) for almotriptan and eletriptan, and (10–180 µg/mL) for rizatriptan. the chromatographic methods were successfully applied for the determination of each of the studied drugs in pure form, tablet form, and in laboratory prepared mixtures with their acid degradation products.

**Keywords:** Chromatography; Antimigraine; Almotriptan; Eletriptan; Rizatriptan; High performance liquid chromatography; Thin layer chromatography.

### 436. Liquid Chromatographic Determination of Linagliptin in Bulk, in Plasma and in Its Pharmaceutical Preparation

Ramzia I. El-Bagary, Ehab F. Elkady and Bassam M. Ayoub

*International Journal of Biomedical Science*, 8: 209-214 (2012)

In this work, two reversed-phase liquid chromatographic (RP-LC) methods have been developed for the determination of linagliptin (LNG) based on isocratic elution using a mobile phase consisting of potassium dihydrogen phosphate buffer pH (4.6) - acetonitrile (20:80, v/v) at a flow rate of 1 mL min<sup>-1</sup>. Two detection techniques have been applied either UV detection at 299 nm in the first method or fluorometric detection at 239 nm for excitation and 355 nm for emission in the second method. Chromatographic separation in the two methods was achieved on a Symmetry® cyanide column (150 mm × 4.6 mm, 5 µm). Linearity, accuracy and precision were found to be acceptable over the concentration ranges of 2.5-80 µg mL<sup>-1</sup> for LNG in bulk and 2.5-15 µg mL<sup>-1</sup> for LNG in plasma with the first method and 5-160 µg mL<sup>-1</sup> for LNG in bulk with the second method. the optimized methods were

validated and proved to be specific, robust and accurate for the quality control of the cited drug in its pharmaceutical preparation.

**Keywords:** Linagliptin; Reversed-Phase liquid chromatography; Fluorometric detection; Pharmaceutical preparation; Plasma.

### 437. Development and Validation of A Reversed? Phase Column Liquid Chromatographic Method for Simultaneous Determination of Two Novel Gliptins in their Binary Mixtures with Metformin

Mohammad Abdul-Azim Mohammad, Ehab Farouk Elkady and Marwa Ahmed Fouad

*European Journal of Chemistry*, 3: 152-155 (2012)

A new, simple, accurate, and precise liquid chromatographic method has been developed and validated for the determination of two novel dipeptidylpeptidase?4 (DPP?4) inhibitors; namely vildagliptin (VLG) and saxagliptin HCl (SXG) simultaneously in their binary mixtures with metformin HCl (MET). Chromatographic separation was achieved on an Inertsil® CN?3 column (250 mm x 4.6 mm, 5 µm). Isocratic elution using a mobile phase of potassium dihydrogen phosphate buffer pH (4.6) ? acetonitrile (15:85, v:v) at a flow rate of 1 mL/min with UV detection at 208 nm was performed. the liquid chromatographic method was used for the simultaneous determination of either VLG, SXG and MET in the range of 5?200, 0.5?20 and 50?2000 ?g/mL, respectively. the methods developed were satisfactorily applied to the analysis of the pharmaceutical formulations and proved to be specific and accurate for the quality control of the cited drugs in pharmaceutical dosage forms.

**Keywords:** Metformin saxagliptin vildagliptin isocratic elution Pharmaceutical Preparation Reversed? Phase Liquid Chromatography.

### 438. Simultaneous Determination of Miconazole and Hydrocortisone or Mometasone using Reversed Phase Liquid Chromatography

Ramzia Ismail El-Bagary, Ehab Farouk Elkady, Marwa Hosny Tammam and Ayman Abo Elmaaty

*European Journal of Chemistry*, 3: 421-425 (2012)

Two simple, rapid and precise reversed phase liquid chromatographic methods have been developed and validated for the simultaneous determination of miconazole nitrate in two binary mixtures, with hydrocortisone acetate (Mixture 1) and mometasone furoate (Mixture 2). for the two mixtures, chromatographic separation was carried out on a C18 column. For mixture 1, a mobile phase consisting of 2.22 mM sodium dihydrogen phosphate (Triethylamine 0.2%): acetonitrile (45:55, v:v) at a flow rate of 0.9 mL/min was used at ambient temperature. Quantitative determination of miconazole and hydrocortisone was achieved with UV detection at 215 and 245 nm, respectively. Linearity, accuracy and precision were found to be acceptable over the concentration range of 30-80 µg/mL for miconazole and 4-80 µg/mL for hydrocortisone. for mixture 2, a mobile phase consisting of acetonitrile:water (Triethylamine 0.2%) (70:30, v:v) at a flow rate of 0.9 mL/min was used at ambient temperature. Quantitative determinations of miconazole and mometasone were achieved with UV detection at 215 and 250 nm, respectively. Linearity, accuracy and precision were found to be acceptable over the concentration range of 10-200 µg/mL for

miconazole and 2-60 µg/mL for mometasone. the optimized methods were proved to be specific, robust and accurate for the quality control of the cited drugs in pharmaceutical preparations.

**Keywords:** Determination; Miconazole nitrate; Mometasone furoate; Hydrocortisone acetate; Pharmaceutical preparation; Reversed phase liquid chromatography.

#### 439. A Novel Method for Tizanidine Hydrochloride Determination in Aqueous Solution Based on Fluorescence Quenching of Functionalised Cds Quantum Dots as Luminescent Probes

Marwa Ahmed Fouad and Ehab Farouk Elkady

*European Journal of Chemistry*, 3: 40-43 (2012)

A novel, sensitive and convenient method for the determination of tizanidine hydrochloride (TZD) based on the fluorescence quenching of thioglycolic acid-capped CdS quantum dots (TGA-CdS QDs) is proposed. Luminescent CdS semiconductor quantum dots modified by thioglycolic acid were synthesized from cadmium nitrate and sodium sulfide in alkaline aqueous solution. the modified CdS QDs are water-soluble, stable and highly luminescent. When TZD was added into the CdS QDs colloidal solution, the surface of CdS QDs generates the electrostatic interaction in aqueous medium, which induces the quenching of fluorescence emission at 518 nm upon excitation at 340 nm. Under the optimal conditions, the Stern-Volmer calibration plot of  $F_0/F$  against concentration of TZD was linear in the range of 3.0-18.0 µg/mL with a correlation coefficient of 0.9953. the detection limit was 1.35 µg/mL. the relative standard deviation for five determinations of 9 µg/mL TZD was 2.29%. the proposed method was successfully applied to commercial tablets with satisfactory results. the results were found to be in good agreement with those obtained by the reference method. the possible fluorescence quenching mechanism for the reaction is also discussed.

**Keywords:** Quantum Dots Determination Nanotechnology Fluorescence Quenching Tizanidine Hydrochloride Pharmaceutical Preparation.

#### 440. Liquid Chromatographic Determination of Alogliptin in Bulk and in Its Pharmaceutical Preparation

Ramzia I. El-Bagary, Ehab F. Elkady and Bassam M. Ayoub

*International Journal of Biomedical Science*, 8: 215-218 (2012)

In this work, a reversed-phase liquid chromatographic (RP-LC) method has been developed for the determination of alogliptin (ALG) based on isocratic elution using a mobile phase consisting of potassium dihydrogen phosphate buffer pH (4.6) - acetonitrile (20:80, v/v) at a flow rate of 1 mL min<sup>-1</sup> with UV detection at 215 nm. Chromatographic separation was achieved on a Symmetry® cyanide column (150 mm × 4.6 mm, 5 µm). Linearity, accuracy and precision were found to be acceptable over the concentration range of 5-160 µg mL<sup>-1</sup> for ALG in bulk. the optimized method was validated and proved to be specific, robust and accurate for the quality control of ALG in pharmaceutical preparations.

**Keywords:** Alogliptin; Reversed-Phase liquid chromatography; Isocratic elution; Pharmaceutical preparation.

#### 441. Design & Synthesis of Some Quinazoline Derivatives of Anticipated Antimicrobial Activity.

EL-Moghazy, Samir M. Abdel-Gawad, Nagwa M. Eissa and Amal A.M.

*International Journal of Pharmacy and Pharmaceutical Sciences*, 4: 540-553 (2012)

The present work is concerned with the synthesis of some new compounds comprising different 2, 3-disubstituted 4(3H) – quinazolinones as series 5- 7, 10- 13, 15- 17, 19 and 20, 2, 3, 4-trisubstituted quinazolines as in series 8 and 9 and fused quinazolines as in 14 and 18. the building block of these different compounds is the 3-amino-2-substituted quinazolin-4(3H)-ones 5 a- d. to study the effect of steric hindrance and positional isomerism on the antimicrobial activity; substitution in the 2 position of the quinazoline ring was accomplished by tolyl derivatives or naphthyl radicals. Also, the 2-chloro-N-(4-oxo-2-substituted-quinazolin-3(4H)-yl) acetamido 15 a-d were synthesized and used as starting materials to prepare other new tricyclic derivatives 14 and 18. in addition, these intermediates 15 a-d were reacted with various hydrazides of drugs like isoniazide, norfloxacin and ofloxacin to yield the biodynamic compounds 17, 19, and 20. Furthermore, reaction of the chloroacetamido intermediates 15 a-d with potassium cyanate afforded compounds 16 a-d. the antimicrobial activity was tested for some new compounds against Gram positive and Gram negative microorganisms and the fungus *Candida albicans*. Additionally, minimum inhibitory concentration (MIC) was determined for nine compounds. of these 10h, 14b, 15a were expressed as broad spectrum and 5a, 10b, 11a, 12a, 20a as narrow spectrum against variable microorganisms.

**Keywords:** Synthesis of quinazoline and quinazolinone derivatives; Anti-microbial activity.

#### 442. Lipase Catalysed Kinetic Resolution of Stiripentol

Elisabeth Egholm Jacobsen, Thorleif Anthonsen, Mohammed Farrag El-Behairy, Eirik Sundby, Mohamed Nabil Aboul-Enein, Mohamed Ibrahim Attiam, Aida Abd El-Sattar El-Azzouny, Kamilia M. Amin and Mohamed Abdel-Rehim

*International Journal of Chemistry*, 4: 7-13 (2012)

Kinetic resolution of rac-Stiripentol, catalysed by lipase A from *Candida antarctica* by esterification with vinyl butanoate was performed with an E-value of 24. This allowed isolation of (3S)-Stiripentol with an ee of 86 % and the corresponding (3R)-butanoate with an ee of 87 %. Enzymatic hydrolysis of the ester product gave (3R)-Stiripentol with 94 % ee.

**Keywords:** Kinetic resolution; Stiripentol enantiomers; *Candida antarctica* lipase A; Chiral Hplc.



#### 443. Development and Validation of A UV Spectrophotometric Method for the Simultaneous Determination of Ciprofloxacin Hydrochloride and Metronidazole in Binary Mixture

Marianne Alphonse Mahrouse

*Journal of Chemical and Pharmaceutical Research*, 4: 4710-4715 (2012)

A new, simple, accurate and sensitive UV spectrophotometric method was adopted and validated for the quantitative determination of ciprofloxacin hydrochloride (CIP) and metronidazole (MET), simultaneously, either in pure form or in pharmaceutical dosage form.

Second derivative ratio spectrophotometry technique (2DD) was applied, by measuring the amplitude of the maximum at 253 nm, using a normalized spectrum of MET as divisor, for the determination of CIP. MET was quantified by measuring the amplitude of the minimum at 301 nm, using the normalized spectrum of CIP as divisor.

Linearity was obtained over the concentration range 2 – 16 µg mL<sup>-1</sup> and 4 – 16 µg mL<sup>-1</sup>, for CIP and MET, respectively. Mean percentage accuracy was found to be 100.39 ± 0.677 and 100.21 ± 0.982, for CIP and MET, respectively. the proposed procedure was successfully applied for laboratory prepared mixtures without prior separation.

The percentages recoveries of CIP and MET in tablet were more than 98%. the method was validated in respect to linearity, accuracy, precision and limit of detection and that of quantification, which prove suitability of the developed method for the routine estimation of both drugs in bulk powder and solid dosage form.

**Keywords:** Ciprofloxacin hydrochloride; Metronidazole; Second derivative ratio.

#### 444. Spectrophotometric Methods Based on Charge Transfer Complexation Reactions for the Determination of Saxagliptin in Bulk and Pharmaceutical Preparation

Ramzia I. El-Bagary, Ehab F. Elkady and Bassam M. Ayoub

*International Journal of Biomedical Science*, 8: 204-208 (2012)

Simple, accurate and precise spectrophotometric methods have been developed for the determination of saxagliptin in bulk and dosage forms. the proposed methods are based on the charge transfer complexes of saxagliptin with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and 7,7,8,8-tetracyanoquinodimethane (TCNQ). All the variables were studied to optimize the reactions' conditions. Beer's law was obeyed in the concentration ranges of 50-300 µg/ml and 10-110 µg/ml with DDQ and TCNQ, respectively. the developed methods were validated and proved to be precise and accurate for the quality control of the saxagliptin in its pharmaceutical dosage form.

**Keywords:** Saxagliptin; Spectrophotometry; Charge transfer reactions; Pharmaceutical preparation.

#### Dept. of Pharmaceutical Organic Chemistry

#### 445. Anticancer and Radiosensitizing Evaluation of Some New Pyranothiazole-Schiff Bases Bearing the Biologically Active Sulfonamide Moiety

Mostafa M. Ghorab, Mohamed Shaaban, Hanan M. Refaat, Helmy I. Heiba and Sara S. Ibrahim

*Eur J Med Chem*, 53: 403-407 (2012) IF: 3.346

The present work reports the synthesis of some new Schiff bases, 5-(substituted benzyldeneamino)-6-cyano-7H-7-(4-methoxyphenyl)-2-(4-sulphamoylphenylamino) pyrano[2,3-d]thiazole (5e15). the design of the structures of these compounds complies with the general pharmacophoric requirements for CA inhibiting anticancer drugs. the newly synthesized compounds were evaluated for their in vitro anticancer activity against human breast cancer cell line (MCF7). Most of the screened compounds showed interesting cytotoxic activities compared to doxorubicin as a reference drug. Compounds 4, 6-8 and 11 (IC<sub>50</sub>: 27.51, 10.25, 9.55, 9.39 and 9.70 mM, respectively) exhibited higher cytotoxic activities than the reference drug doxorubicin (IC<sub>50</sub>: 32.00 mM). Additionally, the previously mentioned compounds were evaluated again for their ability to enhance the cell killing effect of g-radiation.

**Keywords:** Pyranothiazole; Sulfonamides; Carbonic anhydrase Inhibitors; Cytotoxicity; Radiosensitizing activities.

#### 446. Synthesis, Antitumor Activity and SAR Study of Novel [1,2,4]Triazino[4,5-A] Benzimidazole Derivatives

Hala Bakr El-Nassan

*Eur. J. Med. Chem.*, 53: 22-27 (2012) IF: 3.346

A series of novel 1,2,3,4-tetrahydro[1,2,4]triazino[4,5-a] benzimidazoles carrying variety of aryl and heteroaryl groups at position 1 were synthesized. the newly synthesized compounds were tested in vitro on human breast adenocarcinoma cell line (MCF7). Some of the test compounds showed potent antitumor activity, especially compound 3c [1-(2-chlorophenyl) derivative] which displayed the highest activity among the test compounds.

**Keywords:** Benzimidazole; [1;2;4] triazino [4;5-A] benzimidazole; Antitumor activity; MCF7.

#### 447. Synthesis of Novel Pyrazolo [3,4-D]Pyrimidine Derivatives as Potential Anti-Breast Cancer Agents

Mohammed K. Abd El Hamid, Marko D. Mihovilovic and Hala B. El-Nassan

*Eur. J. Med. Chem.*, 57: 323-328 (2012) IF: 3.346

A series of new 1-aryl-4-benzyldenehydrazinyl-3-methylsulphanyl- pyrazolo[3,4-d]pyrimidines was synthesized. the cytotoxic activity of the newly synthesized compounds against human breast cancer cell line, MCF7 was investigated. Most of the test compounds showed potent antitumor activity comparable to that of doxorubicin. the 1-phenyl series (6aei) exhibited better antitumor activity than 1-(4-methoxyphenyl) series (6jep). 4-[2-(4-Fluorobenzyldene)hydrazinyl]-3-(methylsulphanyl)-1-phenyl-1H-pyrazolo[3,4-d]pyrimidine (6d) was the most active compound in this study with IC<sub>50</sub> equal to 7.5 nM.

**Keywords:** Pyrazolo [3;4-D] Pyrimidine.



#### 448. Synthesis of New Indole Derivatives Structurally Related to Donepezil and their Biological Evaluation as Acetylcholinesterase Inhibitors

Mohamed M. Ismail, Mona M. Kamel, Lamia W. Mohamed and Samar I. Faggal

*Molecules*, 17: 4811-4823 (2012) IF: 2.386

New series of indole derivatives analogous to donepezil, a well known anti-Alzheimer and acetylcholinesterase inhibitor drug, was synthesized. A full chemical characterization of the new compounds is provided. Biological evaluation of the new compounds as acetylcholinesterase inhibitors was performed. Most of the compounds were found to have potent acetylcholinesterase inhibitor activity compared to donepezil as standard. The compound 1-(2-(4-(2-fluorobenzyl) piperazin-1-yl)acetyl)indoline-2,3-dione (IIIId) was found to be the most potent.

**Keywords:** Indole; Isatin; oxindole; Acetylcholinesterase inhibitors; Alzheimer; Donepezil.

#### 449. Synthesis and Biological Evaluation of Thiophene Derivatives as Acetylcholinesterase Inhibitors

Mohamed M. Ismail, Mona M. Kamel, Lamia W. Mohamed, Samar I. Faggal and Mai A. Galal

*Molecules*, 17: 7217-7231 (2012) IF: 2.386

A series of new thiophene derivatives has been synthesized using the Gewald protocol. The acetylcholinesterase inhibition activity was assayed according to Ellman's method using donepezil as reference. Some of the compounds were found to be more potent inhibitors than the reference. 2-(2-(4-(4-Methoxyphenyl) piperazin-1-yl)acetamido)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide (IIIId) showed 60% inhibition, compared to only 40% inhibition by donepezil.

**Keywords:** Thiophene; Gewald; Ellman; Acetylcholinesterase; Alzheimer's.

#### 450. Design and Synthesis of Novel 1,4-Benzodiazepine Derivatives and their Biological Evaluation as Cholinesterase Inhibitors

Lamia W. Mohamed and Mohamed F. El-yamany

*Arch Pharm Res.*, 35: 1369-1377 (2012) IF: 1.592

A new series of 1,4-benzodiazepine-2,5-dione structurally related to cyclophenin has been synthesized. The new compounds were assayed *in vivo* and *in vitro* for their ability to inhibit acetylcholinesterase enzyme and were found to have potent reversible anticholinesterase activity when tested *in vitro* for isolated frog rectus abdominis and guinea pig ileum in addition to increasing brain cholinesterase level in rats when percentage inhibition were tested *in vivo*, moreover compounds 5a, 5b, 5c and 5g were the most active. LD50 was performed for these derivatives and they displayed high safety margin.

**Keywords:** Key Words: 1,4-Benzodiazepine; Acetylcholine; Alzheimer's Disease; Cyclophenin; Cyclophenol.

#### 451. Synthesis and Anticancer Activity of Some Novel Fused Pyridine Ring System

Afaf K. Elansary, Ashraf A. Moneer, Hanan H. Kadry and Ehab M. Gedawy

*Arch Pharm Res.*, 11: 1909-1917 (2012) IF: 1.592

New series of pyrido[3',2':4,5]thieno[3,2-d]pyrimidines (7a,b) and thieno[2,3-b:4,5-b']dipyridine (11a-c) were synthesized from 4-aryl-6-(4-chlorophenyl)-2-thioxo-1,2-dihydro pyridine-3-carbonitriles 4a,b via application of Thorpe-Zielger reaction. The novel target compounds were evaluated *in vitro* for their anticancer activity against human breast adenocarcinoma MCF-7 and colon carcinoma cell line (HCT 116). Most of the tested compounds exploited potent to moderate growth inhibitory activity, in particular compound 11d, which exhibited superior potency to the reference drug Doxorubicin (IC50 = 5.95, 6.09 and 8.48, 8.15  $\mu$ M, respectively). The structures of the compounds obtained were determined by spectroscopic data.

**Keywords:** Synthesis; Pyridothienopyrimidine; Thienodipyridine; Anticancer activity.

#### 452. Synthesis and Anti-Inflammatory Activity of Novel Pyridazine and Pyridazinone Derivatives as Non-Ulcerogenic Agents

Makarem M. Saeed, Nadia A. Khalil, Eman M. Ahmed and Kholoud I. Eissa

*Arch Pharm Res.*, 35: 2077-2092 (2012) IF: 1.592

Herein, we report the synthesis and pharmacological properties of several series of pyridazine and pyridazinone derivatives. All the synthesized compounds were tested, *in vivo*, for their anti-inflammatory and ulcerogenic properties against indomethacin, as a reference compound. Compounds 4a and 9d have shown a potent anti-inflammatory activity more than indomethacin with rapid onset of action and safe gastric profile. The latter compounds were then selected for further investigation. In the MTT assay *in vitro*, both compounds were identified as potent and selective COX-2 inhibitors.

**Keywords:** Pyridazine; Pyridazinone; Anti-Inflammatory Activity; Ulcerogenicity.

#### 453. Novel Pyrimidinone Derivatives: Synthesis, Antitumor and Antimicrobial Evaluation

Azza Taher Taher and Amira Atef Helwa

*Chemical and Pharmaceutical Bulletin*, 60: 521-530 (2012) IF: 1.592

Starting from 6-aryl-4-oxo-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (4a-d), a series of mono- and dialkyl derivatives 5a-j and 6a,b was synthesized. Hydrazinolysis of 4a,b,d & 5d afforded the hydrazino derivatives 7a-c which were cyclised to give the triazolopyrimidinones 8a-c and the pyrimidotriazinones 9a-c through the reaction with formic acid and chloroacetyl chloride respectively. Most of the newly synthesized compounds were evaluated for their *in-vitro* antitumor activity.

Compounds 6a and 6b displayed promising anticancer activity against leukaemia, non-small cell lung, melanoma, and renal cancer. On the other hand, all compounds prepared were screened

for their in-vitro antibacterial and antifungal activities. Compounds 5h and 5j showed significant activity against *Staphylococcus aureus*, while compounds 5e, 7c and 8c displayed moderate inhibitory activity against *Candida albicans*.

**Keywords:** Pyrimidinone; Synthesis; Antitumor activity; Antimicrobial activity.

#### 454. Synthesis, Antitumor and Antimicrobial Testing of Some New Thiopyrimidine Analogues

Azza Taher Taher and Amira Atef Helwa

*Chemical and Pharmaceutical Bulletin*, 60 (10): 1305-1313 (2012) IF: 1.592

The synthesis of some new 4-chloro-pyrimidine-5-carbonitriles (3b-d), 4-substituted-amino-pyrimidine-5-carbonitriles (4a-g), trioxo and dioxo-thiazolo [3,2-a] pyrimidine-6-carbonitriles (5a-c and 6a-h) have been described. The obtained compounds were evaluated for their in-vitro antitumor activity. A single dose (10  $\mu$ M) of the test compounds was used in the National Cancer Institute (NCI) 60 cell lines panel assay. Compounds 3c and 4f showed high inhibitory activity against leukemia, whereas, compounds 3b and 4d, g displayed moderate activity.

On the other hand, all compounds were screened for their in-vitro antibacterial and antifungal activities. Compounds 3d and 4b exhibited significant antibacterial activity against *Staphylococcus aureus*. Compound 4e showed two folds inhibitory activity against *Enterobacter aerogenes* compared with the reference drug Tobramycin.

**Keywords:** Thiopyrimidine derivatives; Synthesis; Antitumor; Antimicrobial activities.

#### 455. Synthesis of Certain 2-Substituted-1H-Benzimidazole Derivatives as Antimicrobial and Cytotoxic Agents

Azza Taher Taher, Nadia Abdalla Khalil, Eman Mohamed Ahmed and Yasser Mohamed Ragab

*Chem Pharm Bull*, 778-784: (2012) IF: 1.592

A series of 2-substituted-1H-benzimidazole derivatives were synthesized and evaluated for antimicrobial, antifungal and cytotoxic activities. The results showed that all tested compounds showed potent antimicrobial activity against some species of Gram-negative bacteria (*Pseudomonas aeruginosa*, *Escherichia coli*, *Salmonella typhi*) and fungi (*Candida albicans*) with minimum inhibitory concentrations (MICs) lower than 0.016  $\mu$ g/mL. In contrast, all tested compounds were inactive against *Staphylococcus aureus* (Gram-positive bacterium). The final targets were also tested for their antitumor activity in vitro on cervical carcinoma (HeLa) cell line.

Eight of the test compounds displayed more potent cytotoxic effect than doxorubicin at nanomolar concentrations. Compounds 2c and 3c exerted the strongest cytotoxic effect with IC<sub>50</sub> 15 and 13 nM, respectively.

**Keywords:** Benzimidazole; Synthesis; Antimicrobial; Cytotoxic.

#### 456. Phenytoin-Based Bivalent Ligands: Design, Synthesis and Anticonvulsant Activity

Samir Botros, Nadia A. Khalil, Bassem H. Naguib and Yara El-Dash

*Arch Pharm Res*, 35: 2105-2116 (2012) IF: 1.592

Synthesis, characterization and anticonvulsant properties of new bivalent ligands derived from phenytoin were described. Initial anticonvulsant screening was performed using maximal electroshock (MES) and pentylenetetrazole (PTZ) screens in mice. The neurotoxicity for compounds that showed significant anticonvulsant activity was determined applying the rotorod test. Most of the test compounds were found to be effective in at least one seizure model in a dose of 100mg/kg. Compound 5e exhibited marked anticonvulsant activity in both MES and PTZ screens. The computer-aided prediction of biological activity was carried out.

**Keywords:** Phenytoin; Bivalent ligands; Anticonvulsant activity.

#### 457. Synthesis and Biological Evaluation of Novel Pyrazoline Derivatives as Anti-Inflammatory and Antioxidant Agents

Nadia A. Khali, Eman M. Ahmed, Hala B. El-Nassan, Osama K. Ahmed and Ahmed M. Al-Abd

*Arch Pharm Res*, 35: 995-1002 (2012) IF: 1.592

A series of novel 5-aryl-3-cyclopropyl-4,5-dihydropyrazole derivatives 2a-p were synthesized via cyclization of chalcones 1a-h with thiosemicarbazide or semicarbazide HCl and evaluated as anti-inflammatory/antioxidant agents. The structures were confirmed by elemental analyses and spectral data. The free radical scavenging activity toward superoxide was determined. Their effect on hepatocytes viability and nitric oxide (NO) production in LPS-stimulated macrophages was also determined. The results showed that compounds 2e and 2n demonstrated the highest free-radical scavenging and anti-inflammatory activities, thus can be useful in the prevention of oxidative stress and inflammation-related disorders.

**Keywords:** Pyrazoline; Anti-Inflammatory; Antioxidant; Free-radical scavenging.

#### 458. Design, Synthesis, and Evaluation of Anti-Inflammatory and Ulcerogenicity of Novel Pyridazinone Derivatives

K. A. M. Abouzid, N. A. Khalil, E. M. Ahmed, A. Esmat and A. M. Al-Abd

*Med Chem Res*, 21: 3581-3590 (2012) IF: 1.271

A series of pyridazinone-containing compounds were designed and synthesized as congeners for diclofenac, the most potent and widely used NSAID. The target compounds were evaluated for their anti-inflammatory activity on rat paw edema inflammation model against diclofenac as a reference compound. Seven of the tested compounds demonstrated more than 50% inhibition of carrageenan-induced rat paw edema at a dose 10 mg/kg. The compounds, 6-(2-bromophenylamino) pyridazin-3(2H)-one 2a and 6-(2,6-dimethylphenylamino)pyridazin-3(2H)-one 2e, displayed 74 and 73.5% inflammation inhibitory activity, respectively, which is comparable to diclofenac (78.3%) at the

same dose level after 4 h. the most active compounds as anti-inflammatory agents, 2a,2e, and 6a, displayed fewer number of ulcers and milder ulcer score than indomethacin in ulcerogenicity screening.

**Keywords:** Pyridazinone; Anti-Inflammatory.

#### 459. Design, Synthesis and *in Vitro* PDE4 Inhibition Activity of Certain Quinazolinone Derivatives for Treatment of Asthma

Afaf K. Elansary, Hanan H. Kadry, Eman M. Ahmed and Amr Sayed Motawi Sonousi

*Med Chem Res*, 21: 3327-3335 (2012) IF: 1.271

In this study, a novel series of quinazolinone derivatives analogue to niraquazone structure were synthesized. the compounds tested for their inhibitory activity against phosphodiesterase 4B revealed that compound 6d shows promising inhibitory activity comparable to that of Rolipram, whereas compounds 6a and 6c exhibited moderate inhibitory activity major classes of compounds are currently used in the treatment of asthma, including bronchodilators (particularly  $\alpha^1$ -adrenoceptor agonists), immunosuppressive agents (corticosteroids), antiallergic agents for prophylactic use and xanthines (e.g. theophylline) (Vassallo and Lipsky,1998), which appear to possess bronchodilator and anti-inflammatory as well as immunomodulator properties. Newer drugs include leukotriene antagonists such as montelukast (Reques and Rodriguez, 1999). to date, much research has been directed towards the discovery of new antiasthmatic agents with high selectivity and efficacy and a reduced side-effect profile.

**Keywords:** Phosphodiesterase 4 (Pde4) Inhibitors; Quinazolinone; Asthma; Synthesis.

#### 460. Synthesis and Anti-Inflammatory Activity of 1-Acetyl/Propanoyl-5-Aryl-3-(4-Morpholinophenyl)-4,5-Dihydro-1H-Pyrazole Derivatives

Omneya M. Khalil

*Med Chem Res*, 21: 3240-3245 (2012) IF: 1.271

A series of novel pyrazoline derivatives containing 4-morpholinophenyl moiety were synthesized to investigate their potential anti-inflammatory activity. The chemical structures of the compounds were elucidated by spectral data and elemental analyses. the test compounds in the series exhibited different levels of anti-inflammatory activities when compared with reference drug indomethacin.

**Keywords:** Synthesis; Pyrazolines; Anti-Inflammatory Activity.

#### 461. Synthesis and Evaluation of Anti-Proliferative Activity of 1,4-Disubstituted Phthalazines

Khaled A. M. Abouzid, Nadia A. Khalil and Eman M. Ahmed

*Med Chem Res*, 21: 3288-3293 (2012) IF: 1.271

A series of new phthalazine derivatives 3a-i and 4a-c were synthesized via the reaction of 1-chlorophthalazine derivative 2 with either N-substituted-piperazines, primary or their secondary amines. the structure of the synthesized, new compounds were characterized by spectral data. the anti-proliferative activity on human breast cancer cell line MCF-7 of the synthesized

compounds was determined. the results showed that six of the test compounds (3a, 3g, 3i, and 4a-c) displayed potent cytotoxic activity ranging from 1.4 to 2.3  $\mu\text{mol}$ .

**Keywords:** Breast cancer; Anti-Proliferative activity; Phthalazine; Phthalazinone.

#### 462. Design, Synthesis and Biological Activity of Certain Quinazolinone Derivatives as Potent Phosphodiesterase 4 Inhibitors

Afaf K. Elansary, Hanan H. Kadry, Eman M. Ahmed and Amr Sayed Motawi Sonousi

*Med Chem Res*, 21: 3557-3567 (2012) IF: 1.271

In this study, a series of 3-butylquinazolinone linked with different substituent to N1 of quinazolinone nucleus have been synthesized. Some of the new final compounds tested in vitro for their inhibitory activity against phosphodiesterase 4B which is the enzyme responsible for the hydrolysis of cyclic adenosine mono phosphate, the second messenger involved in the regulation of important cell functions. Compound 7f (100%) showed inhibition better than rolipram (90%), while the other tested compounds showed moderate activity. Docking study has been done to rationalize the obtained biological results. in this study, a series of 3-butylquinazolinone linked with different substituent to N1 of quinazolinone nucleus have been synthesized. Some of the new final compounds tested in vitro for their inhibitory activity against phosphodiesterase 4B which is the enzyme responsible for the hydrolysis of cyclic adenosine mono phosphate, the second messenger involved in the regulation of important cell functions. Compound 7f (100%) showed inhibition better than rolipram (90%), while the other tested compounds showed moderate activity. Docking study has been done to rationalize the obtained biological results.

**Keywords:** Synthesis; Phosphodiesterase4b (Pde4b) Inhibitor; Quinazolinones.

#### 463. Synthesis of Potential Anticancer Derivatives of Pyrido[1,2-A]Benzimidazoles

Hanan M. Refaat

*Med. Chem. Res.*, 21: 1253-1260 (2012) IF: 1.271

In this study, the starting compounds, 2-cyanomethylbenzimidazoles (1 or 2) were reacted with ethyl acetoacetate, ethyl benzoylacetate, or 2-acetylbutyrolactone to give the novel series of 4-cyano-3-substituted-1-oxo-1H, 5H-pyrido[1,2-a]benzimidazole (3-6, 15, 16). the latter was chlorinated to give compounds 7-10, 17, 18 then aminated with 4-(2-fluorophenyl) piperazine to afford compounds 11-14, 19, 20. the structures of the new compounds were confirmed by elemental analysis as well as 1H-NMR, IR, and mass data. All the synthesized products were subjected to in vitro anticancer screening that revealed that all the tested compounds exhibited antitumor activity against human breast adenocarcinoma (MCF7) cell line, with IC<sub>50</sub>'s 3.43-14.70  $\mu\text{g/ml}$ .

**Keywords:** 4-Cyano-1-Oxo-Pyrido [1;2-A] Benzimidazoles.

#### 464. Synthesis of Potent Anticancer Thieno [2,3-d] Pyrimidine Derivatives

M.M. Kandeel, Ashraf A. Mounir, Hanan M. Refaat and Asmaa E. Kassab

*J. Chem. Res.*, 266-275 (2012) IF: 0.633

As part of our program to identify novel cytotoxic agents, various series of hexahydrocycloocta[4,5]thieno[2,3-d] pyrimidines and pyrimidin-4-ones substituted by aryl at the C-2 position together with phenylethylamino, substituted amino, hydrazinyl or arylidenehydrazinyl substituents at the C-4 position were synthesised. These compounds were prepared as bioisosteres of gefitinib, an antitumour drug used for the treatment of gastrointestinal stromal tumours.

All compounds exhibited antitumour activity against (HCT 116) cell line in vitro. Eight compounds (IC<sub>50</sub>: 3.89, 4.65, 6.63, 6.94, 7.89, 9.53, 12.00 and 12.30 µg mL<sup>-1</sup>, respectively) exhibited 4.3 to 1.3 fold more potent antitumour activity than imatinib (IC<sub>50</sub>: 16.93 µg mL<sup>-1</sup>). Also, a docking study of the newly synthesised compounds with the active site of CDK2 was described.

**Keywords:** Hexahydrocycloocta [4;5] Thieno [2;3-d] Pyrimidines; Pyrimidin-4-Ones; Antitumour activity; Docking study.

#### 465. Synthesis of Thieno[2,3-d]Pyrimidines, Thieno[2,3-d]Triazinones and Thieno[2,3-e] Diazepinones of Anticipated Anti-Cancer Activity

M.M. Kandeel, Ashraf A. Mounir, Hanan M. Refaat and Asmaa E. Kassab

*J. Chem. Res.*, 105-110 (2012) IF: 0.633

A novel series of 4-aminohexahydrocycloocta[4,5]thieno[2,3-d]pyrimidines, hexahydrocycloocta[4,5]thieno[2,3-d]-1,2,3-triazin-4-one and its N-3 substituted derivatives in addition to 3-aryl hexahydrocycloocta[4,5] thieno[2,3-e]-1,4-diazepin-5-ones were synthesised. Also, 2-(N-ethylcarbamothioylamino) hexahydrocycloocta[b] thiophene-3-carbonitrile and 19-imino tetradecahydrocycloocta[4□,5□] thieno[2□,3□:4,5]pyrimido[1,6-a] cycloocta[4,5]thieno[3,2-e]pyrimidine-9-thione were prepared. Almost all the synthesised compounds exhibited anti-tumour activity against human colon carcinoma (HCT 116) cell line in vitro. Five compounds (IC<sub>50</sub>: 15.92, 22.59, 25.85, 27.40 and 29.70 µM, respectively) exhibited 2.16 to 1.15 fold more potent antitumour activity than imatinib (IC<sub>50</sub>: 34.40 µM).

**Keywords:** Hexahydrocycloocta [4;5] Thieno [2;3-D] Pyrimidines; Hexahydrocycloocta [4;5] Thieno [2;3-D]-1;2;3-Triazin-4-Ones; Hexahydrocycloocta [4;5] Thieno [2;3-E]-1;4-Diazepin-5-Ones; Antitumour activity.

#### 466. Synthesis of Tricyclic Systems Containing A Fused Thieno[3,4-D]Pyrimidine Nucleus

Farag A. El-Telbany, Maha Abd El Hakeem, Omneya M. Khalil and Demiana S. Mikhail

*Journal of Chemical Research*, 480-483 (2012) IF: 0.633

The synthesis and characterisation of novel tricyclic systems containing a fused thieno[3,4-d]pyrimidine nucleus starting from

a useful synthon, ethyl-4-cyano-3-ethoxymethyleneamino-5-phenylamino-2-thiophenecarboxylate, are reported.

**Keywords:** Imidate; Aminothiophene-2-Carboxylates; Thieno [3;4-D] Pyrimidine; Dimroth Rearrangement; Tricyclic heterocycles.

#### 467. Synthesis and Biological Assessment of Some New Acrylonitrile Derivatives as Potential Antitumor and Antimicrobial Agents

Azza Taher Taher

*Life Science Journal*, 9 (1): 991-1005 (2012) IF: 0.073

A series of novel acrylonitrile derivatives 4-10 have been synthesized and characterized by spectral data. The in-vitro antitumor activity of all compounds was assessed in the MCF-7 human breast cancer cell line. The results showed that compound 8a exhibited promising anticancer activity with IC<sub>50</sub> = 9.92 µg/mL while, compounds 4b, 4c, 7b, 8c and 10b possessed moderate cytotoxic effect with IC<sub>50</sub> ranging 15.64-20.76 µg/mL. The final targets were also tested for their antimicrobial activity. The results revealed that compounds 4a, 5b, 8a and 8c showed remarkable broad spectrum antimicrobial activity, while compounds 5c, 8a and 8c displayed high antifungal activity against *Candida albicans* compared to amphotericin B reference drug with IC<sub>50</sub> = 9.30, 6.25 and 2.30 µg/mL, respectively.

**Keywords:** Acrylonitrile; Synthesis; Antitumor; Antimicrobial activities.

#### 468. Design, Synthesis and Antitumor Evaluation of Novel Pyrazolo [3,4-D]Pyrimidine Derivatives

Manal M. Kandeel, Lamia W. Mohamed, Mohammed K. Abd El Hamid and Ahmed T. Negmeldin

*Sci Pharm*, 80: 531-545 (2012)

A new series of pyrazolo[3,4-d]pyrimidines has been synthesized. The new compounds were tested for their antitumor activity on 60 different cell lines, and some of the compounds were found to have potent antitumor activity. In particular, 2-hydroxybenzaldehyde [1-(4-chlorophenyl)-3-methyl-1H-pyrazolo-[3,4-d]pyrimidin-4-yl]hydrazone (VIIa) was found to be the most effective among the other derivatives, showing IC<sub>50</sub> values of 0.326 to 4.31 µM on 57 different cell lines.

**Keywords:** Pyrazolopyrimidines; Antitumor activity; Cytotoxic activity; Synthesis.

#### 469. Synthesis of Effective Anticancer Thieno [2,3-D] Pyrimidine-4-Ones and Thieno [3,2-E]Triazolo[4,3-C] Pyrimidines

M. M. Kandeel, Ashraf A. Mounir, Hanan M. Refaat and Asmaa E. Kassab

*International Journal of Pharmacy and Pharmaceutical Sciences*, 4: 438-448 (2012)

In continuation to our research program concerned with structural modification of thieno[2,3-d]pyrimidines with the purpose of enhancing their anticancer activity, various series of hexahydrocycloocta [4,5] thieno [2,3-d] pyrimidin-4-ones, hexahydrocycloocta [4,5] thieno [3,2-e]-1,2,4-triazolo[4,3-

c]pyrimidine-3(2H)-thiones and 4-substituted hydrazinylhexahydrocycloocta [4,5] thieno [2,3-d]pyrimidines were synthesized. Most of the synthesized compounds exhibited antitumor activity against human colon carcinoma (HCT 116) cell line in vitro. Compounds 4a, 4b, 3, 12b and 5c (IC<sub>50</sub>: 11.90, 12.43, 15.91, 25.80 and 32.11 μM, respectively) exhibited 2.89 to 1.07 fold more potent antitumor activity than imatinib (IC<sub>50</sub>: 34.40 μM). Also, a docking study of the newly synthesized compounds with the active site of CDK2 was described to explore their affinity and binding mode to CDK2.

**Keywords:** Hexahydrocycloocta [4;5] Thieno [2;3-D] Pyrimidin-4-Ones; Hexahydrocycloocta [4;5] Thieno [3;2-E] Triazolo [4;3-C]Pyrimidine-3(2H)-Thiones; 4- Substituted Hydrazinylhexahydrocycloocta [4;5] Thieno [2;3-D] Pyrimidines; Antitumor Activity.

#### 470. Utilizing of 4-(Benzothiazol-2-Yl) Phenylamine as A Precursor of Bioactive Agents

Mohamed A. Shaaban, Ossama M. Al Badry, Aliaa M. Kamal and Mohamad A. Abd El-Gawad

*Organic Chemistry an Indian Journal*, 8: 349-356 (2012)

Several heterocyclic compounds show either anticancer or antimicrobial activity, the initial goal of this study was directed towards combining some of those heterocyclic moieties- that have either activity- together to test whether the newly formed compounds will demonstrate both activity or one activity will predominate over the other or both activity will diminish. This was accomplished via Scheme 1 and Scheme 2 where diazotization of 4-(benzothiazol-2-yl)phenylamine 1 followed by reacting this functionalized hydrazone with a variety of binucleophiles to give the key intermediates that reacted with amino reagents viz. hydrazine, urea or thiourea to yield some of the goal compounds (Scheme 1). Reacting compound 1 with carbonyl or isothiocyanate reagents followed by cyclization of the given key intermediates afforded a set of novel target compounds (Scheme 2). These final compounds were tested for in vitro antimicrobial and anticancer activity. Two compounds showed both antimicrobial and anticancer activity while the other compounds were highly active either as antimicrobial only or as anticancer only.

**Keywords:** 4-(Benzothiazol-2- Yl) Phenylamine; Pharmacophores; Anticancer; Antimicrobial; Improving chemotherapy regimen design.

#### 471. Synthesis of Some Novel Chromene Derivatives

M.M. Kandeel, Aliaa.M. Kamal, Eman K.A. Abdelall and Heba A.H. Elshemy

*Organic Chemistry an Indian Journal*, 8: 342-348 (2012)

2-Amino-4-aryl-7-alkoxy-4H-chromene-3-carbonitriles 2a&b were intended to be used for the preparation of novel substituted tricyclic chromopyrimidine derivatives for their expected antitumor activity. Reaction of aminocyanochromenes with different carboxylic acids and their derivatives deemed to be the passage to those goal compounds yet unexpectedly 4-arylchromene-2-ones 4a&b and 6a&b and N,N- diacetyl aminocyanochromene 5a&b were resulted from the reaction of the aminocyanochromene 2a&b with the acids, acid chlorides and acetic anhydride sequentially this was proved using supporting evidence provided by single X-ray crystallography.

**Keywords:** Heterocycles; Synthesis; 7-Alkoxy-2-Amino-3-Cyanochromenes; Chromo[2;3-D]Pyrimidines; X-Ray crystallography.

#### 472. Design and Synthesis of Substituted Chromenes as Potential Anticancer Agents

Aliaa M. Kamal, Manal M. Kandeel, Eman K. Abd El-all and Heba A. H. Elshemy

*International Journal of Pharmaceutical Research and Development*, 4 (3): 310-322 (2012)

Inhibition of tubulin polymerization is among the important targets that are useful in cancer therapy. Since 4-aryl-4H-chromenes are found to be tubulin destabilizers, an idea of a great interest is to combine this 4-aryl-4H-chromene nucleus with other nuclei targeting tubulin to disclose the activity of the resulting compounds. the goal compounds were synthesized and evaluated for in vitro anticancer activity. Several compounds showed excellent-very good cytotoxic activity compared to the used reference drug. Docking of a group of these biologically active compounds was carried out at colchicine binding site of tubulin and very interesting results were obtained.

**Keywords:** Tubulin Destabilizers, 4-Aryl-4H-Chromenes, Pharmacophores, Cytotoxic activity, Combinatorial chemistry.

#### 473. Synthesis of Novel Chromenes as Cytotoxic Agents

Manal M. Kandeel, Aliaa. M. Kamal, Eman K. A. Abdelall and Heba A. H. Elshemy

*Der Pharma Chemica*, 4: 1653-1661 (2012)

Novel substituted chromenes, chromenopyrimidine derivatives and chromenotriazolo-pyrimidines were synthesized. Several compounds were evaluated for their antitumor activity, most of them revealed promising cytotoxic activity against breast cancer cell line MCF-7 in comparison to colchicine as positive control.

**Keywords:** Heterocycles; Substituted chromenes; Chromenopyrimidine; Chromenotriazolo-Pyrimidines; Cytotoxic activity.

#### Dept. of Pharmaceutical Technology and Industrial Pharmacy

#### 474. Development and Characterization of Colloidal Soft Nano-Carriers for Transdermal Delivery and Bioavailability Enhancement of an Angiotensin II Receptor Blocker

Rania M. Hathout and Ahmed H. Elshafeey

*European Journal of Pharmaceutics and Biopharmaceutics*, 82: 230-240 (2012) IF: 4.269

The purpose of this study was to develop and characterize a successful colloidal soft nano-carrier viz. microemulsion system, for the transdermal delivery of an angiotensin II receptor blocker: olmesartan medoxomil. Different microemulsion formulations were prepared. the microemulsions were characterized visually, with the polarizing microscope, and by photon correlation spectroscopy. in addition, the pH and conductivity ( $\sigma$ ) of the formulations were measured. the type and structure of

microemulsions formed were determined using conductivity measurements analysis, Freezing Differential Scanning Calorimetry (FDSC) and Diffusion-Ordered Spectroscopy (DOSY).

Alterations in the molecular conformations of porcine skin were determined using Attenuated Total Reflectance Fourier Transform Infrared (ATR-FTIR) biophysical assessment. Olmesartan medoxomil delivery from the investigated formulations was assessed across porcine skin ex-vivo using Franz diffusion cells; the drug was analyzed by liquid chromatography mass spectroscopy (LC/MS/MS).

A comparative pharmacokinetic study was done on healthy human subjects between the selected microemulsion and the commercial oral tablets. The physico-chemical and spectroscopic methods revealed the presence of water-in-oil and bicontinuous structures. Biophysical assessment demonstrated various stratum corneum (SC) changes. Olmesartan medoxomil was delivered successfully across the skin with flux achieving  $3.65\mu\text{gcm}^{-2}\text{h}^{-1}$ . Higher bioavailability compared to commercial oral tablets with a more sustainment behavior was achieved.

**Keywords:** Microemulsion; Olmesartan; Tape stripping; Skin permeation; Infrared spectroscopy; Human volunteers.

#### 475. Preparation and Biopharmaceutical Evaluation Tacrolimus Loaded Biodegradable Nanoparticles for Liver Targeting

Tammam S., Mathur S. and Afifi N.

*J. Biomed Nanotechnol*, 8: 439-449 (2012) IF: 4.216

Tacrolimus is a potent immunosuppressant used in liver transplantation. It has a narrow therapeutic index and variable pharmacokinetics. This makes dose adjustment and therapeutic drug monitoring a complicated task besides increasing adverse effects, mainly nephrotoxicity. Poly(lactide) tacrolimus nanoparticles (PLA-TAC-NP) were formulated with the aim of targeting tacrolimus to the liver and spleen since antigen presentation occurs in the graft and lymphatics. This allows better graft survival with decreased side effects, especially nephrotoxicity.

Tacrolimus was incorporated into PLA nanoparticles via the emulsion-solvent evaporation method. Dynamic light scattering (DLS) showed that particles had a mean diameter of  $255\pm 4.58\text{ nm}$  with unimodal distribution.

Results were confirmed by scanning electron microscopy (SEM), atomic force microscopy (AFM) and transmission electron microscopy (TEM). Zeta Potential was  $-60.08\pm 5.83\text{ mV}$ , whereas entrapment efficiency was  $64.71\pm 4.27\%$ . TAC release pattern from PLA-NP was determined by the dialysis bag method showing 77% drug release within 4 days.

Human monocytes were isolated by density gradient centrifugation and used to detect uptake of previously opsonised PLA-TAC-NP. PLA-TAC-NP phagocytosis was confirmed by TEM. The extent of phagocytosis was determined by HPLC analysis to be  $80.48\pm 11.61\%$ . This shows that the prepared PLA-TAC-NP, formulated as lyophilized powder, are promising for TAC targeting to the liver and spleen via the reticuloendothelial system (RES).

**Keywords:** Immunosuppression; Liver targeting; Res; Pla; Nanoparticles.

#### 476. Ultrasound-Induced New Cellular Mechanism Involved in Drug Resistance

Mariame A. Hassan, Yukihiro Furusawa, Masami Minemura, Natalya Rapoport, Toshiro Sugiyama and Takashi Kondo

*Plos One*, 7: 1-12 (2012) IF: 4.092

The acoustic effects in a biological milieu offer several scenarios for the reversal of multidrug resistance. In this study, we have observed higher sensitivity of doxorubicin-resistant uterine sarcoma MES-SA/DX5 cells to ultrasound exposure compared to its parent counterpart MES-SA cells; however, the results showed that the acoustic irradiation was genotoxic and could promote neotic division in exposed cells that was more pronounced in the resistant variant. The neotic progeny, imaged microscopically 24 hr post sonication, could contribute in modulating the final cell survival when an apoptotic dose of doxorubicin was combined with ultrasound applied either simultaneously or sequentially in dual-treatment protocols.

Depending on the time and order of application of ultrasound and doxorubicin in combination treatments, there was either desensitization of the parent cells or sensitization of the resistant cells to doxorubicin action.

**Keywords:** Doxorubicin-Resistant uterine sarcoma; Ultrasound.

#### 477. Alkannin, Hsp70 Inducer, Protects Against UVB-Induced Apoptosis in Human Keratinocytes

Yoko Yoshihisa, Mariame Ali Hassan, Yukihiro Furusawa, Yoshiaki Tabuchi, Takashi Kondo and Tadamichi Shimizu

*Plos One*, 7: 1-9 (2012) IF: 4.092

Alkannin is an active constituent from the root extract of *Alkanna tinctoria* of the Boraginaceae family and it may have utility as a heat shock protein 70 (HSP70) inducer in living organisms. Here, the effects of alkannin-induced HSP70 on ultraviolet (UV) B ( $40\text{ mJ/cm}^2$ )-induced apoptosis were investigated in human keratinocyte HaCaT cells. Pretreatment of cells with alkannin (1 mM) caused significant inhibition of UVB-induced apoptosis and caspase-3 cleavage. On the other hand, the addition of KNK437 (HSP70 inhibitor) reversed the action of alkannin increasing UVB-induced apoptosis in a dose-dependent manner. In addition, differences in gene expression associated with the suppression of UVB-induced apoptosis in the presence of alkannin were investigated using Gene Chip assay. Our results indicate that alkannin suppresses UVB-induced apoptosis through the induction of HSP70 in human keratinocytes, and therefore, we suggest the usefulness of using alkannin as an antiaging agent.

**Keywords:** Alkannin; Apoptosis; Ultraviolet.

#### 478. Novel Diphenyl Dimethyl Bicarboxylate Provesicular Powders with Enhanced Hepatocurative Activity: Preparation, Optimization, in Vitro/ in Vivo Evaluation

Mona Hassan Aburahma and Ghada Ahmed Abdelbary

*Int. J. of Pharmaceutics*, 422: 139-150 (2012) IF: 3.35

Diphenyl dimethyl bicarboxylate (DDB) is a hepatocurative agent used for treatment of various liver diseases. However, DDB therapeutic effectiveness is restricted by its low oral bioavailability that arises from its poor solubility and dissolution.

Aiming at surmounting the aforementioned restrictions, DDB proves vesicular dry powders exemplified by proniosomes and proliposomes were prepared using film-deposition technique employing sorbitol as a carrier. Upon dilution with water, the proves vesicular powders rapidly transformed into vesicular ispersions, either liposomes or niosomes, which were characterized regarding their percent encapsulation efficiency (EE%), vesicle size and distribution, morphology and in vitro drug release. the revealed optimal proves vesicular powder was exposed to solid state characterization, stability testing and in vivo performance evaluation. Results showed that proves vesicular powders with acceptable flowability can be prepared using a weight ratio of lipids mixture to sorbitol of 1:20. Proniosomal powder composed of Tween 80:cholesterol: stearylamine in molar ratio 7:3:0.5 loaded on sorbitol was selected as the optimal formulation as it showed the highest EE% and dissolution enhancement for DDB. the elevated levels of liver enzymes in hepatically injured Albino Wister rats were significantly reduced ( $P < 0.05$ ) after oral administration of the optimal proniosomal powder in comparison to free DDB. This improvement was confirmed histopathologically by minimizing the associated hepatic injury. Accordingly, proniosomes can be assertively considered as a promising stable precursor for immediate preparation of niosomal carrier for DDB with enhanced dissolution and hepatocurative activity.

**Keywords:** Diphenyl dimethyl bicarboxylate; Pro-Vesicular powder; Physicochemical characterization; Proliposomes; Proniosomes; Hepatocurative activity.

#### 479. Enhanced Gene Transfection using Calcium Phosphate Co-Precipitates and Low-Intensity Pulsed Ultrasound

Mariame A. Hassan, Iman S. Ahmed, Paul Campbell and Takashi Kondo

*European Journal of Pharmaceutical Sciences*, 47: 768-773 (2012) IF: 3.212

The capability to controllably disrupt the cell membrane by ultrasound (US), thus facilitating entry of exogenous species, has now reached a state of some maturity. However, a compelling question asks whether there is a residual role for US in enhancing transfection: that is, once the genetic material has been delivered to the cytosol, can US assist in its transport into the nucleus? the present experiment was designed with a view to addressing this question. as such, our experimental setup discriminates between: (i) the precursor cell membrane permeabilization step, and (ii) any subsequent intracellular trafficking into the nucleus. in this study, calcium phosphate co-precipitates (CaP) were used to internalize plasmid DNA encoding for luciferase (pDNA-Luc) (>90%) in HeLa cells.

After 2 h incubation with the CaP-pDNA-Luc, cells were washed and insonated for varying durations. the results showed that US can indeed enhance the intracellular trafficking of previously internalized genes when longer insonation periods are implemented, culminating with an increased probability for successful nuclear localization, as inferred from an enhanced luciferase expression. Moreover, the results suggest that the intracellular role of US might be mediated through a pathway that appears not to be limited to destabilizing the endosomal vesicles. The study thus provides new information regarding the intracellular effects of US, and in effect represents a new

modality combining US and CaP carriers for improved efficiency in gene delivery.

**Keywords:** Calcium phosphate co-Precipitates; Gene delivery; Intracellular trafficking; Ultrasound.

#### 480. Development of Novel Flexible Sugar Ester Vesicles as Carrier Systems for the Antioxidant Enzyme Catalase for Wound Healing Applications

Heidi M. Abdel-Mageed, Hanan M. El-Laithy, Laila G. Mahran, Afaf S. Fahmy, Karsten Mäder and Saleh A. Mohamed

*Process Biochem*, 47: 1155-1162 (2012) IF: 2.648

The antioxidant enzyme catalase (CAT) was encapsulated in biocompatible flexible non-ionic sugar esters (SEs) nano-vesicles for potential topical administration. The effects of the SE hydrophilic lipophilic balance (HLB) value and the carbon chain length of the fatty acid ester of different SEs on the encapsulation efficiency (EE) were studied. Morphology of the vesicles was not altered upon CAT encapsulation using freeze fracture electron microscopy. The extrusion measurements indicated that there was an increase in the vesicle's flexibility index upon the inclusion of phospholipids. the mean diameter of the CAT-EV (ester vesicle; HSC and HSC-PL) was 222–275 nm using laser diffraction measurements. the catalytic efficiency ( $V_{max}/K_m$ ) of CAT was improved after encapsulation by a factor of 1.7. Both free CAT and CATEV showed maximum catalytic activity at pH 7.0, and CAT-EV was more stable than free CAT at acidic pH, which is advantageous for successful topical delivery.

Encapsulation of CAT in SE vesicles protected it against trypsin treatment. Encapsulated CAT retained more than 60% residual activity after 12 successive decomposition cycles of  $H_2O_2$ . CAT-EV activity was significantly preserved compared to that of free CAT at 4 °C for 180 days. the in vivo study showed a significant effect of the prepared CAT nano-vesicles on wound healing.

**Keywords:** Catalase; Sugar esters; Nano-vesicles; Encapsulation; Wound healing.

#### 481. Biodegradable Donepezil Lipospheres for Depot Injection: Optimization and in-Vivo Evaluation

Soad A. Yehia, Ahmed H. Elshafeey and Ibrahim Elsayed

*J. of Pharmacy and Pharmacology*, 64: 1425-1437 (2012) IF: 2.175

**Objectives:** the purpose of this study was to develop an injectable depot liposphere delivery system with high loading capacity for controlled delivery of donepezil to decrease dosing frequency and increase patient compliance.

**Methods:** A 3(2) full factorial design was employed to study the effect of lipid type and drug-to-lipid ratio on the yield, encapsulation efficiency, mean diameter and the time required for 50% drug release ( $t(50\%)$ ). the pharmacokinetic behaviour of the lipospheres in rabbits was studied using tandem mass spectrometry.

**Key Findings:** the yields of preparations were in the range of 66.22-90.90%, with high encapsulation efficiencies (89.68-97.55%) and mean particle size of 20.68-35.94  $\mu\text{m}$ . Both lipid type and drug-to-lipid ratio significantly affected  $t(50\%)$  ( $P < 0.0001$ ), where the lipids can be arranged: glyceryl tripalmitate > compritol > cetyl alcohol, and the drug-to-lipid ratios can be arranged: 1:40 > 1:20 > 1:10. the flow time of lipospheres through 19-gauge syringe needle was less than 6s indicating good

syringeability. the mean residence time of the subcutaneous and intramuscular lipospheres was significantly higher than the solution (almost 20 fold increase), with values of 11.04, 11.34 and 0.53 days, respectively (P<0.01).

**Conclusion:** Subcutaneous and intramuscular delivery of donepezil glyceryl tripalmitate lipospheres achieves depot release, allowing less frequent dosing.

**Keywords:** Alzheimer'S disease; Depot injection; Donepezil; Glyceryl tripalmitate; Lipospheres.

#### 482. Statistical Approach for Assessing the Influence of Calcium Silicate and HPMC on the Formulation of Novel Alfuzosin Hydrochloride Mucoadhesive-Floating Beads as Gastroretentive Drug Delivery Systems

Rania Hassan Fahmy

*Aaps Pharmscitech*, 13: 990-1004 (2012) IF: 1.432

Multiparticulate floating drug delivery systems have proven potential as controlled-release gastroretentive drug delivery systems that avoid the "all or none" gastric emptying nature of single-unit floating dosage forms. an objective of the presence investigation was to develop calcium silicate (CaSi)/ calcium alginate (Ca-Alg)/hydroxypropyl methylcellulose (HPMC) mucoadhesive-floating beads that provide time- and site-specific drug release of alfuzosin hydrochloride (Alf). Beads were prepared by simultaneous internal and external gelation method utilizing 32 factorial design as an experimental design; with two main factors evaluated for their influence on the prepared beads; the concentration of CaSi as floating aid (X1) and the percentage of HPMC as viscosity enhancer and mucoadhesive polymer (X2), each of them was tested in three levels. Developed formulations were evaluated for yield, entrapment efficiency, particle size, surface topography, and buoyancy. Differential scanning calorimetry, Fourier transform infrared spectroscopy (FT-IR), in-vitro drug release, as well as in-vitro mucoadhesion using rat stomach mucosal membrane were also conducted. Percentage yield and entrapment efficiency ranged from 57.03% to 78.51% and from 49.78% to 83.26%, respectively. Statistical analysis using ANOVA proved that increasing the concentration of either CaSi or HPMC significantly increased the beads yield. Both CaSi and HPMC concentrations were found to significantly affect Alf release from the beads. Additionally, higher CaSi concentration significantly increased the beads diameter while HPMC concentration showed significant positive effect on the beads mucoadhesive properties. CaSi/Ca-Alg/HPMC beads represent simple floating-mucoadhesive gastroretentive system that could be useful in chronopharmacotherapy of benign prostatic hyperplasia.

**Keywords:** Alfuzosin hydrochloride; Calcium silicate; Gastroretentive; Mucoadhesive-Floating beads.

#### 483. Microemulsions as Vehicles for Topical Administration of Voriconazole: Formulation and in Vitro Evaluation

Gladious Naguib El-Hadidy, Howida Kamal Ibrahim, Magdi Ibrahim Mohamed and Mohamed Farid El-Milligi

*Drug. Dev. Ind. Pharm.*, 38: 64-72 (2012) IF: 1.396

This work was undertaken to investigate microemulsion (ME) as a topical delivery system for the poorly watersoluble

voriconazole. Different ME components were selected for the preparation of plain ME systems with suitable rheological properties for topical use. Two permeation enhancers were incorporated, namely sodium deoxycholate or oleic acid. Drug-loaded MEs were evaluated for their physical appearance, pH, rheological properties and in vitro permeation studies using guinea pig skin. MEs based on polyoxyethylene(10)oleyl ether (Brij 97) as the surfactant showed pseudoplastic flow with thixotropic behavior and were loaded with voriconazole. Jojoba oil-based MEs successfully prolonged voriconazole release up to 4 h. No significant changes in physical or rheological properties were recorded on storage for 12 months at ambient conditions. the presence of permeation enhancers favored transdermal rather than dermal delivery. Sodium deoxycholate was more effective than oleic acid for enhancing the voriconazole permeation. Voriconazole-loaded MEs, with and without enhancers, showed significantly better antifungal activity against *Candida albicans* than voriconazole supersaturated solution. in conclusion, the studied ME formulae could be promising vehicles for topical delivery of voriconazole.

**Keywords:** Microemulsion; Antifungal; Permeation enhancers; in Vitro skin permeation study; Antifungal activity.

#### 484. Floating Furosemide Gel Beads: in Vitro and in Vivo Evaluation

Elmeshad A. N. and El-Ashmoony M. M.

*Journal of Drug Delivery and Scientific Technology*, 22: 317-325 (2012) IF: 0.679

Buoyant beads enclosing furosemide were prepared by cross-linking chitosan with dioctyl sodium sulphosuccinate (DOSS) and characterized according to: entrapment efficiency, in vitro release, in vitro and in vivo buoyancy. the effect of various factors (DOSS and chitosan concentrations, drug: polymer ratio and loading technique) on bead properties were assessed. Interaction between chitosan and DOSS was evaluated by DSC and FTIR. SEM demonstrated that the dried beads were spherical in shape with an inward cavity enclosing furosemide in the range of 1.8-62.25. Most beads floated over SGF for 12 h. Beads retarded the release of furosemide compared to pure drug powder and Lasix tablets. the t50 % ranged from 1.79-4.1 h and release followed zero or diffusion kinetics. Beads remained buoyant in the stomach of dogs for 6 h. Beads were stable at 40 °C and 75 % RH for 3 months. Results showed that chitosan beads proved to be effective carrier for furosemide, maximizing its therapeutic effect at the site of absorption in a controlled release pattern.

**Keywords:** Floating gastroretentive drug delivery; Gel beads; Furosemide; Chitosan; Xray imaging.

#### 485. Formulation and Optimization of Tenoxicam Orodispersible Tablets by Solid Deposition Technique

H.M. Aboud, A.A. Ali and A. Abd Elbary

*J. Drug Del. Sci. Tech*, 22: 555-561 (2012) IF: 0.679

Tenoxicam is a poorly water-soluble NSAID drug and dissolution plays an important role in its absorption, so the present investigation was to develop and characterize orodispersible tablets of tenoxicam using solid deposition technique on superdisintegrants in order to improve its dissolution and aqueous



solubility to facilitate faster onset of action. the superdisintegrants used were croscopovidone, cross-carmellose sodium, sodium starch glycolate and pregelatinised maize starch in ratios of 1:1, 1:2 and 1:4 (w/w) drug:carrier. Drug excipients compatibility study was carried out using DSC, IR spectroscopy and SEM photography. General characterization of the prepared tablets was performed, in addition to wetting time, in vitro disintegration time and in vitro dissolution studies. the formula containing cross-carmellose sodium as a carrier in a ratio of 1:2 showed highest dissolution rate and shortest disintegration time. It was subjected to stability stress testing and drug concentration was detected by stability indicating HPLC assay method and in conclusion, the results of this work suggest that stable rapid release tenoxicam orodispersible tablets can be developed by solid deposition method.

**Keywords:** Orodispersible tablets; Tenoxicam; Solid deposition; Superdisintegrants; Stability indicating assay.

#### 486. Formulation of Risperidone as Self-Nanoemulsifying Drug Delivery System in Form of Effervescent Tablets

Kareem AbuBakr Soliman, Howida Kamal Ibrahim and Mahmoud Mohamed Ghorab

*Journal of Dispersion Science and Technology*, 33: 1127-1133 (2012) IF: 0.56

Risperidone is an atypical antipsychotic drug used to treat schizophrenia. This study aims to formulate risperidone as effervescent tablets to improve patient compliance. Different nanoemulsion combinations were loaded with risperidone to improve its poor water solubility then adsorbed on Aeroperl. the formula showing highest drug dissolution was formulated as effervescent tablets. Factorial design was applied for different tablet formulation variables and the prepared formulae were tested for different criteria in comparison with their corresponding formulae containing drug without nanoemulsion formulation. Statistical analysis was used to determine the most desirable tablet formula considering its Carr index, effervescence time, and drug release.

**Keywords:** Aeroperl; Effervescent tablets; Nanoemulsion; risperidone.

#### 487. Formulation and *in-Vitro* Evaluation of Isotretinoin Tablets

M. M. Ghorab and Mayada Elhadi Babiker

*Journal of Chemical and Pharmaceutical Research*, 4 (5): 2817-2831 (2012)

Isotretinoin (13-cis-Retinoic acid) is a poor water soluble drug, commonly used in the treatment of severe cases of acne. the aim of this project is to formulate isotretinoin in form of tablet and enhance its solubility and dissolution rate; by the use of formulations containing either surfactant (SLS and Tween 20) or HP- $\beta$ -CD. the critical micelle concentration for each surfactant was determined. Surfactant enriched tablets were prepared by physical mixture and co-precipitation method. Binary system of the drug with HP-  $\beta$  -CD was prepared using different ratios and techniques. the freeze drying technique gave the best drug-HP-  $\beta$  -CD complexation. the in-vitro dissolution study for the prepared mixtures and the prepared tablets was performed. Binary system

of molecular ratio 1: 5 of the drug to HP-  $\beta$  -CD gave the highest solubility and dissolution rate for isotretinoin in comparison with other formulae. Therefore, it could be concluded from the study that, incorporation of surfactant and HP-  $\beta$  -CD in the formulation of isotretinoin tablets significantly improved Isotretinoin solubility.

**Keywords:** Isotretinoin, Surfactant enriched tablets, Hp-  $\beta$ - Cd, Co-Evaporation, Freeze drying.

#### 488. Industrialization of Chewable Sugar Coated Tablets of Phytomenadione-B Cyclodextrin Complexes

Ghorab D. M and Ibrahim I.S

*Journal of Pharmaceutical Research and Opinion*, 2: (10) 129–137 (2012)

Vitamin k1 (phytomenadione) is a procoagulant factor, used in cases of hemorrhage or risk of hemorrhage. Being a component of hepatic carboxylase system, phytomenadione is involved in carboxylation of clotting factors II (prothrombin), VII, IX and X, and of clotting inhibitors protein C and protein S in the postribosomal phase. Yet, orally ingested phytomenadione is absorbed primarily in the middle portions of the small intestine. Moreover, optimum absorption is possible only in the presence of bile and pancreatic juice. Thus, Systemic availability after oral dosing is only approximately 50%, with large interindividual differences due to its limited aqueous solubility. Since aqueous solubility of a drug could be regarded as a key factor responsible for low oral bioavailability of poor water soluble drugs, thereby limiting their therapeutic potential.

Consequently, the rationale of this study was to improve the biological performance of Phytomenadione by forming inclusion complexes with  $\beta$  cyclodextrin to enhance its solubility, dissolution rate, and stability. Furthermore, to enhance the solubilization power of the complexation, it was investigated in the presence and absence of PEG 4000 and 6000 as water soluble polymers and the formed binary and ternary systems were then incorporated into chewable sugar coated tablets (CSCT). Stability studies were performed on the prepared CSCT to confirm the enhancement of chemical stability. the best chosen formula was manufactured and distributed by Nile Company under the proprietary name of Vitadione.

**Keywords:** Vitamin K (Phytomenadione); Binary and ternary cyclodextrin systems; Chewable tablets; Technology transfer.

#### 489. Bioadhesive Brain Targeted Nasal Delivery of an Ant Ischemic Drug

N. M. Morsi, D.M. Ghorab and H.A.Badie

*International Journal of Pharmaceutical and Biological Archives*, 3: 1067-1076 (2012)

Transnasal delivery is a non-invasive method of by-passing the BBB to deliver the drug substances and peptides to the CNS. Vinpocetine SLNs was prepared by the high shear homogenization and ultrasonication method. Ten different bioadhesive nasal gels were prepared with Vinpocetine SLNs. Particle size analysis before and after SLNs dispersion in the prepared gel and after storage 30 days in the refrigerator, Rheological Measurements, Evaluation of ex-vivo bioadhesive strength, Histopathological studies and Ex vivo permeation

studies were performed to evaluate the prepared Vinpocetine SLNs bioadhesive nasal gels. Vinpocetine SLNs tissue distribution and in vivo pharmacokinetic study. the drug targeting index (DTI%) was 380.46% and the nose to brain direct transport percentage (DTP%) was 73.71% suggesting a high targeting efficiency of the prepared Vinpocetine SLNs bioadhesive nasal gel formula G10.

**Keywords:** Vinpocetine; Tissue distribution; Bioadhesion; Nasal gel; Mucoadhesive.

#### 490. Floating Tablets A Controlled Release Stomach Targeted Drug Delivery System of Diltiazem Hydrochloride

Elnawawy T. M., Swailem A.M., Ghorab D. M. and Nour S. A.

*Journal of Pharmaceutical Research and Opinion*, 173-183 (2012)

Diltiazem hydrochloride is a potent calcium channel blocker which is freely soluble in water and readily absorbed from stomach. the present investigation was concerned with the development and evaluation of a gastro retentive drug delivery system of Diltiazem hydrochloride in the form of floating matrix tablets, to control the release of the drug. A 23 factorial design was followed to formulate Diltiazem hydrochloride floating tablets. Experiments were built using three independent factors, namely, drug/polymer ratio potassium bicarbonate concentration and citric acid concentration each at two levels leading to 24 formulae. the data of chosen responses, namely floating duration, floating lag time, t50% and t80%, were analyzed according to the established factorial design. the results were analyzed statistically. the ANOVA was performed and the main effects and interactions were calculated. the three polymers used were hydroxypropylmethylcellulose, methylcellulose and sodium alginate. It was found generally that for all three polymers used the increase in the drug/polymer ratio, potassium carbonate concentration or citric acid concentration increased the t50% and t80% indicating that the formulated floating tablets succeeded in retardation of Diltiazem hydrochloride and thus controlling its release.

**Keywords:** Diltiazem hydrochloride; Floating tablets; Factorial design; Controlled release.

#### 491. Solubility Enhancement of Olmesartan by Utilization of Solid Dispersion and Complexation Techniques

Tayseer Mohamed Elnawawy, Abdel Monaem Swailem, Dalia Mahmoud Ghorab and Samia Abdel kader Nour.

*International Journal of Novel Drug Delivery Technology*, 2: 297-303 (2012)

**Objective:** the aim of the present study was to enhance the dissolution of poorly-water soluble Olmesartan medoxomil by solid dispersion preparation and formation of inclusion complexes.

**Methods:** Solubility determinations prepared by solvent evaporation method and by fusion (melting) method. the inclusion complexes of OLM with BCD were prepared in different D/C ratios (1:1, 1:2, 1:3, 1:4 and 1:5) by kneading method.

**Results:** in comparison to pure drug and the physical mixtures of the different carriers both the drug solubility and its dissolution

rate was significantly increased from the different preparations. Particularly, solid dispersions of Drug: Polyethylene glycol 6000 in ratios of 1:3 and 1:5 achieved a rapid and complete drug release within 15 min at pH 6.8. Physical characteristics of Olmesartan medoxomil and solid dispersions prepared were investigated in solid state in terms of morphology by scanning electron microscopy, and characterized by x-ray diffraction, differential scanning calorimetry and Fourier transform infrared spectroscopy. All revealed physical change in the prepared solid dispersion. Such changes were not accompanied by chemical change in any of the polymer or Olmesartan medoxomil.

**Conclusion:** in conclusion, solid dispersion prepared with Polyethylene glycol 6000 by fusion method appeared to alleviate the solubility problems of Olmesartan medoxomil and improved its dissolution profile.

**Keywords:** Olmesartan medoxomil; Solubilization; Solid Dispersions; Inclusion complexes.

#### 492. Preparation of Zaleplon Microparticles Using Emulsion Solvent Diffusion Technique

Ahmed Abd El-Bary, Omaira El-Gazayerly, Arwa El-Hagrasy and Ibtehal Salah Ad-din

*J. Pharm Drug Deliv Res*, 1: 1-7 (2012)

Zaleplon is a BCS class II drug suffering from poor solubility. in a trial to improve its dissolution, emulsion solvent diffusion method (ESD) was used to prepare zaleplon microparticles using sodium lauryl sulfate (SLS) as surfactant. Optimization of drug system was achieved. Particle size values of the prepared microparticles were ranged from 6.57  $\mu\text{m}$  to 20.30  $\mu\text{m}$  with narrow particle size distribution range. Differential scanning calorimetry (DSC) and x-ray diffraction (XRD) were used for the characterization of the prepared systems. DSC and XRD patterns showed that the zaleplon microparticles possessed decreased crystallinity. Dissolution studies demonstrated that the systemized zaleplon microparticles exhibited significantly enhanced dissolution rate when compared to pure zaleplon. A correlation could be observed between the microparticle morphology and the dissolution rate, where zaleplon microparticles that exhibited the fastest dissolution profiles had a distinctive rod shape compared to the other systems. in contrast, pure zaleplon powder appeared as irregularly-shaped particles. In conclusion, the dissolution rate of zaleplon can be enhanced to a great extent by ESD technique.

**Keywords:** Zaleplon; Poor water solubility; BCS class II drug; Emulsion solvent diffusion; Microparticles.

#### 493. Radioiodination of Cephalexin with $^{125}\text{I}$ and Its Biological Behavior in Mice

Ahmed Abd El-Bary, Abeer M. Amin, Afaf El-Wetery, Shoukry Saad and Marwa Shoukry

*Pharmacology and Pharmacy*, 3: 97-102 (2012)

A procedure for radioiodination of Cephalexin with iodine- $^{125}\text{I}$  was carried out via an electrophilic substitution reaction. Using 3.7 MBq of  $\text{Na}^{125}\text{I}$ , 200  $\mu\text{l}$  of cephalexin as substrate, 200  $\mu\text{l}$  of iodogen as oxidizing agent in acetone at 40°C for 20 min, a maximum radiochemical yield of  $^{125}\text{I}$ -Ceph (95%) was obtained. the labeled compound was separated and purified by means of high-pressure liquid chromatography (HPLC). the biological distribution in normal and inflamed (septic) mice indicates the

suitability of radioiodinated cephalixin for imaging of inflammation

**Keywords:** Cephalixin; Na<sup>125</sup>I; Electrophilic substitution reaction; Radioiodination; Inflammation.

#### 494. Formulation and Evaluation of Fluconazole Topical Gel

Doaa A. Helal, Dalia Abd El-Rhman, Sally A. Abdel-Halim and Mohamed A. El-Nabarawi

*International Journal of Pharmacy and Pharmaceutical Sciences*, 4: 176-183 (2012)

Fluconazole is an imidazole derivative used for the treatment of local and systemic fungal infection. the oral use of fluconazole is not recommended as it has many side effects. the present study was designed to formulate and evaluate different formulae of topical gel containing fluconazole for treatment of fungal infection of skin. the gel was formulated by using different polymers with different concentration as Carbopol 940, Hydroxypropyl methylcellulose E4M, Methyl cellulose, Pectin and Pluronic P407. Ten different formulae were prepared and characterized physically in term of color, syneresis, spreadability, pH, drug content and rheological properties. Drug-excipients compatibility studies were confirmed by carrying out DSC and FT-IR. in-vitro drug release in phosphate buffer pH 5.5 and permeation study through cellulose membrane, using a modified Franz diffusion cell, were performed. *Candida albicans* was used as a model fungus to evaluate the antifungal activity of the prepared formulae achieved using Nizoral® cream as control. the results of in vitro drug release and its permeation studies showed that the highest values was from F3(91.3% of drug released after 2 hr). Also F3 shows the highest antifungal activity. the rheological behavior of the prepared formulae showed shear-thinning flow indicating structural breakdown of the existing intermolecular interactions between polymeric chains. Moreover, the stability study revealed no significant difference between before and after storage for selected formula.

**Keywords:** Fluconazole; Topical gel.

#### 495. A Pharmaceutical Study on Different Approaches for Itopride Hydrochloride Sustainment: *in Vitro* and *in Vivo* Evaluation

Soad A. Yehia, Ahmed H. Elshafeey, Aliaa ElMeshad and Hamoud A. Al-Bialely

*Journal of Chemical and Pharmaceutical Research*, 4: 1398-1412 (2012)

Recent trends indicate that dosage form drug delivery systems are especially suitable for achieving sustained or delayed release oral formulations with low risk of dose dumping, flexibility of blending to attain different release patterns as well as reproducibility. One of the approaches toward this goal was to develop and formulate extended release matrix oral tablets of itopride hydrochloride (ITO) as a highly water soluble drug and to increase its gastric retention time. Matrix tablets of (ITO) were developed using different methods such as: (wetting granulation, direct compression, and coating compression), by using different types of polymers (hydroxypropyl methyl cellulose (HPMC) K15M, hydroxypropyl cellulose (HPC) low viscosity, Eudragit® RL100, and Carnauba wax). the prepared tablets were evaluated

according to various physicochemical characteristics such as: weight and thickness variation, drug content, hardness, friability, and in vitro drug release. Tablet weight variation ranged from 395 ± 0.34 to 409 ± 1.78 mg, thickness ranged from 3.16 ± 1.37 to 3.74 mm, drug content ranged from 94.5 ± 1.01% to 106.2 ± 0.08%, friability ranged from 0.04 ± 0.69 to 0.84 ± 0.45, and hardness ranged from 5.25 ± 0.25 to 8.80 ± 0.4 Kg/cm<sup>2</sup>. Results indicated that drug release depended upon method of preparation and polymer type. Furthermore, in vivo testing of the optimum sustained release tablet formulation (F23) using coating compression by HPMC as coat was performed in human subjects, and determined and compared to that of a commercial oral tablet (Ganaton®) as a reference formulation. the obtained the maximum plasma concentration (C<sub>max</sub>) and the area under the curve from zero to infinity (AUC (0- ∞)) values were higher following formulated tablet administration than after Ganaton® administration. the percentage relative bioavailability of ITO from the selected formula in human volunteers was found to be 243% compared to Ganaton®.

**Keywords:** Sustained release; Wet granulation; Direct compression; Coating compression; Gastric retention time; Itopride hydrochloride; Bioavailability.

#### 496. Formulation and Evaluation of Dispersed Paroxetine Liposomes in Gel

Mohamed A. El-Nabarawi, Ehab R. Bendas, Randa Tag A. El Rehem and Mohammed Y. S. Abary

*J. of Chemical and Pharmaceutical Research*, 4: 2209-2222 (2012)

Paroxetine (PARX) is the most potent serotonin reuptake blocker antidepressant clinically available. This study is aimed to encapsulation of paroxetine in liposomes and formulation and evaluation of dispersed paroxetine in different gel bases. Paroxetine liposomes were prepared by reverse phase evaporation technique using soya lecithin, cholesterol and drug in different weight ratios. the prepared liposomes were characterized for size, shape, entrapment efficiency. the studies demonstrated successful preparation of paroxetine liposomes. the effect of using different weight ratios of soybean lecithin phosphatidylcholine: cholesterol (SLP: CHOL) on entrapment efficiency and on drug release was studied. Liposomes showed entrapment efficiency percent (% EE) of 81.22% ± 3.08 for paroxetine. the optimized paroxetine liposomes formula was F5 (7:7) molar ratio of (SLP: CHOL), which after that was incorporated in different based gels at different concentrations as Pluronic F127 (PF127-G) (20%, 25% and 30%), Carbopol 934 (C934-G) (1%, 1.5% and 2%) and Hydroxypropyl methylcellulose E4M (HPMC-G) (2%, 4% and 6%) and evaluated through in-vitro release, viscosity, pH and drug content.

**Keywords:** Liposomes; Paroxetine; Gel; *in-Vitro* Drug Release Study.

#### 497. *In Vitro* and *in Vivo* Evaluation of Aceclofenac Lyophilized Orally Disintegrating Tablets

Mohamed Aly Abd El Aziz Aly El Degwy, Saydia Tayel, Mohamed A. El-Nabarawi and Randa Tag A. El Rehem **Mepaco**

*Int. J. of Pharmaceutical Science and Research*, 3: 443-459 (2012)

Aceclofenac, a non-steroidal anti-inflammatory drug, with poor solubility and bioavailability was taken as candidate for enhancement of in vitro dissolution and in vivo bioavailability.

Development of Aceclofenac orally disintegrating tablet (ODT) using lyophilization technique was adopted.

The ODTs were prepared by freeze-drying an aqueous dispersion of Aceclofenac, matrix former, filler (sugar alcohol), and an anti-collapse. The tablets were evaluated compendial (uniformity of weight, uniformity of content, friability, in vitro disintegration time and in vitro dissolution), together with wetting time, in vivo disintegration time, moisture analysis and scanning electron microscopy.

The compendial results showed that lyophilized ODTs disintegrated within few seconds and showed significantly faster dissolution rate of Aceclofenac in comparison with commercially available immediate release tablet Aceclofenac tablet (Bristaflam®). In vivo evaluation for the best chosen Aceclofenac ODT formulation (LA#10) was done for determination of the drug pharmacokinetics in comparison with the immediate release tablet Aceclofenac tablet (Bristaflam® 100 mg).

A randomized crossover design was adopted in the comparative bioavailability study done on four healthy volunteers. Statistical analysis revealed significant difference between the Bristaflam IR tablet and Aceclofenac ODT (LA#10) regarding the following pharmacokinetic parameters:  $C_{max}$ ,  $T_{max}$ ,  $t_{1/2}$ ,  $AUC(0-24)$ ,  $AUC(0-?)$  ( $p < 0.05$ ); while insignificant difference regarding Mean residence time (MRT) ( $p > 0.05$ ). The relative bioavailability of the Aceclofenac ODT (LA# 10) was 186.12% relative to the IR tablet (Bristaflam®) taken as reference standard.

**Keywords:** Aceclofenac; Freeze-Drying; Orally Disintegrating Tablets; in Vivo Absorption; Bioavailability; Dissolution Rate.

#### 498. A New Topical Fluconazole Microsponge Loaded Hydrogel: Preparation and Characterization

Nevine S Abdelmalak and Shahira F El-Menshawe

*International Journal of Pharmacy and Pharmaceutical Sciences*, 4: 460-468 (2012)

Invasive fungal infections can be devastating, especially in immunocompromised patients. Oral administration of fluconazole (FLZ) often produces gastric irritation, heart-burn, vomiting and sometimes patient can develop ulceration resulting in a less patient compliance with long term therapy. The aim of the present study was to formulate topical microsponge-based delivery system containing FLZ for controlled release of the drug and consequently avoiding its oral side effects. Ethyl cellulose (EC) and Eudragit RS 100 based microsponges were prepared using quasi-emulsion solvent diffusion method. The effect of formulation variables such as drug to polymer ratio, polymer type, polyvinyl alcohol (PVA) concentration and type of internal phase on the physical characteristics of the microsponges was examined using 24 factorial design. Results revealed that FLZ loading and microsponge particle size were increased with increasing the polymer fraction. Moreover, EC significantly increased the drug entrapment efficiency (EE%) and the mean particle size. There was a reverse proportionality between the PVA concentration and both the EE% and the mean particle size. Regarding the solvent type, ethanol significantly increased the EE% and the particle size when compared to methylene chloride. A selected FLZ microsponge (F3, containing FLZ and EC in 1:1 ratio and prepared using 0.75% PVA and methylene chloride) was incorporated in carbopol gel formulation and evaluated for its in vitro release characteristics. The developed microsponges were spherical and porous. There was no interaction between drug and polymer molecules. The drug release through cellulose dialysis

membrane showed fickian release pattern. Further antifungal activity and in vivo animal studies for the obtained formula are recommended.

**Keywords:** Fluconazole; Microsponge; Controlled release; Porous structure; Particle size; Entrapment efficiency.

#### 499. Formulation of Coated Polymer Reinforced Gellan Gum Beads of Tizanidine HCL Using Fractional Factorial Design

Nevine Shawky Abdel Malak

*International Journal of Pharmacy and Pharmaceutical Sciences*, 4: 369-379 (2012)

Microparticulate oral sustained release dosage form of Tizanidine HCl (TZ) a short half life water soluble drug was developed, to reduce dosing frequency, and to improve the patient compliance during the treatment of the muscle pain. A 2 4-1 fractional factorial design was employed to explore the effect of percentage of drug added in relation to polymer (X1), cross linking agent type(X2), cross linking agent concentration(X3) and curing time(X4) on the entrapment efficiency(%EE) (Y1) and the mean dissolution time (MDT) (Y2). Increasing the percentage of drug added, the concentration of cross linking agents had a negative effect on the EE and MDT while using both Zn and Ca ions significantly increased the % EE and the MDT when compared to Zn ions alone. Candidate batch with high %EE and high MDT was subjected to polymer reinforcement and coating.

Beads prepared at pH 11.5 and reinforced using ethyl cellulose and coated with EudragitR RS100 significantly increased the %EE up to 90% and extended the in vitro drug release for more than 8 h in a controlled manner following the Higuchi model

**Keywords:** Gellan gum; Beads; Fractional factorial design; Polymer reinforced and coated; Tizanidine HCL.

#### 500. Optimization of Class II Bcs Drug Using Solid Dispersion Technique

El-Nabarawi M. A., El-Miligi, M. F. and Khalil, I. A.

*Int. J. of Pharmacy and Pharmaceutical Sciences*, 4: 554-571 (2012)

The aim of this study was to develop Aceclofenac solid dispersion (ACSD) formulation using different types of carriers. Aceclofenac is class II BCS which mean high permeability, practically insolubility in acidic medium and slightly soluble in basic medium. This solid dispersion should have many properties. Firstly, it should have high solubility and dissolution not less than 85% in 5 minutes in simulated saliva fluid (SSF) (pH 6.8 medium). Secondly, it should have high solubility and dissolution not less than 85% in 30 minutes in simulated gastric fluid SGF (pH 1.2 medium). Finally, all these properties should achieve the acceptable level of drug content and process yield (85-115%). By achieving these properties, it gave the ability to formulate Aceclofenac fast disintegrating tablet beside immediate release tablet with high drug dissolution. This study was conducted on two phases (screening phase and optimization phase). In screening phase, different types of carriers were used to prepare binary solid dispersion at different levels. In optimization phase, Polymer carriers were selected as primary carrier due to meeting target attribute. Precipitation inhibitor and pH modifier were selected as optimizer carriers. One factor at a time (OFAT) experimental design was applied to develop space design and

determine the control space of ACSDs that have optimum solubility and dissolution. the prepared solid dispersions with drug were characterized for drug content, process yield, a solubility study and in-vitro drug dissolution study in SSF pH (6.8) and SGF pH (1.2). Also, a physicochemical characterization (differential scanning calorimetry, Fourier transform Infra-Red and Powder X-ray diffraction) of AC and its SD were done. There was no interaction between AC and additives physical mixtures were observed according to differential scanning calorimetry (DSC) thermograms and Infra-Red (IR) spectrums. the crystal structure of AC was reformed to partially or amorphous form by the additives in SD. in screening phase, Binary solid dispersion (BSD) containing polymer and surfactant gave higher solubility and faster dissolution rate when compared to corresponding pure drug. While, pH modifier BSD were enhanced solubility and initial dissolution rate followed by returning to the original drug profile. This may attributed to drug precipitation after a period of time. in optimization phase, Ternary solid dispersion (TSD) containing precipitation inhibitor enhanced solubility and dissolution rate. Also, TSD containing pH modifier enhanced solubility and only initial dissolution rate when compared to its BSD. QSD had highest solubility and dissolution rate due to increase wettability, amorphous formation, control microenvironment pH of solid dispersion and prevent precipitation of AC in QSD. Therefore, preparation of Aceclofenac QSD was optimized AC properties that suitable for different type of tablets in a different pH.

**Keywords:** Aceclofenac; Solid dispersion; Carrier; Solubility; Dissolution.

### 501. Development of A New Carvedilol Tablet with Rapid Onset of Action

Amna M.A. Makky, Iman S. Ahmed, Mohamed A. El-Nabarawi and Rehab A. Abd El-Monei

*American Journal of Drug Discovery and Development*, 2: 55-71 (2012)

The purpose of this study was to develop Freeze-dried Tablets (FDTs) for rapid absorption of carvedilol, an antihypertensive drug with poor solubility and poor bioavailability. Binary and ternary systems were first made of drug and different ratios of HPMC and Inutec and then were formulated into FDTs. Formulation of FDTs was based on 23 factorial design to study the influence of formulation variables namely, concentration of polymer matrix-former, concentration of collapse protectant and type of polymer used in formation of drug binary and ternary systems on tablet characteristics such as friability, in vitro disintegration time, in vivo disintegration time and initial dissolution. an optimized FDT formulation (RO) containing 2% gelatin, 1% glycine and binary system made of Drug: Inutec in the ratio 1:0.5 showed excellent mechanical strength, in vitro and in vivo disintegration times of less than 10 sec and more than 30% drug dissolved during the first 3 min compared to only 11% for the drug powder and 8% drug from an immediate release commercially available tablet (Carvepress). When the optimized FDT (RO) was administered to hypertensive rats it resulted in a significant decrease ( $p = 0.0015$ ) in systolic blood pressure within the first 15 min compared to the immediate release conventional tablet as a reference which indicate the rapid dissolution and absorption of carvedilol from the FDT.

**Keywords:** Carvedilol; Freeze dried; Tablets; Blood pressure.

### 502. Development and Characterization of Ketorolac Tromethamine (KT) Orobuccal Films

El-Nabarawi M.A, Makky A.M, El-Setouhy D. A, Abd Elmonem R. A and Jasti B.A

*International Journal of Pharmacy and Pharmaceutical Sciences*, 4: 186-193 (2012)

Ketorolac Tromethamine (KT) is a potent non steroidal anti-inflammatory analgesic drug is characterized by gastrointestinal (GI) side effects. KT orobuccal films (OBFs) were developed to either chew (oro) or to be localized delivery of medicinal agent to a specific site in the buccal cavity (buccal), thus reduce GI side effects and improve the drug bioavailability. Twenty seven KTOBFs were prepared by solvent casting technique using hydroxy propyl methyl cellulose (HPMC), sodium carboxy methyl cellulose (SCMC), Ethyl cellulose (EC), Eudragit RL100, Lutrol F127, and Carbopol 934 in combinations of these polymers (9:1 to 5:5) using HPMC as a basic polymer. Drug polymer interactions were investigated using Fourier transform infrared spectroscopy (FTIR), and differential scanning calorimetry (DSC). KTOBFs were evaluated for film appearance, thickness, weight, drug content, surface pH, tensile strength, percent elongation, moisture absorption capacity, mucoadhesion force, in vitro drug release and stability study. FTIR and DSC patterns showed no interaction between drug and polymers which were used. KTOBFs showed acceptable film thickness, weight, surface pH, moisture absorption capacity, elasticity, mucoadhesion and drug content. HPMC appeared to improve the properties of the films, affecting the bioadhesiveness and increasing elasticity. SCMC, Eudragit RL 100, and Lutrol F127 as co-polymers with HPMC improved the properties of KTOBFs rather than EC and Carbopol 934 in terms of elasticity, mucoadhesion, and in vitro drug release. Stability study for KTOBFs showed no change in properties during 10 months storage at room temperature. This study is a promising issue for developing KTOBFs. KTOBFs have rapid onset of action and improve patient compliance due to their small size and reduced thickness compared to lozenges and tablets.

**Keywords:** Ketorolac; Orobuccal film; Rapid dissolving; Mucoadhesion.

### 503. Optimization of Aceclofenac Once Daily Matrix Tablets: *in-Vitro* and *in-Vivo* Studies

Mohsen A, Khoweysa O M and Shoukri R A

*Journal of Pharmaceutical Research and Opinion*, 2: 12-22 (2012)

Aceclofenac is a non-steroidal anti-inflammatory drug (NSAID) indicated for symptomatic treatment of pain and inflammation. the short biological half-life (4 h) and dosing frequency make aceclofenac a suitable candidate for sustained release formulations. Sustained release matrix tablets of aceclofenac with Eudragit® RSPO and Eudragit® RLPO were prepared using three techniques; direct compression, wet granulation and solid dispersion. the most optimum matrix formula was manipulated by addition of an immediate release layer for prompt release of the drug.

All tablets were evaluated regarding their physical properties and in-vitro release over 24 hours. All the tablets were found within the permissible limits for various physical parameters. in-vitro release studies revealed that Eudragit RSPO retarded the release

more than Eudragit RLPO and solid dispersion was the most suitable preparation technique. Formulation F5 was selected for further optimization by addition of fast release layer.

The double layer tablet (F19) was successful in prolonging drug release up to 24 hours. Pharmacokinetic studies in albino rabbits were conducted for the optimized formula (Registration No. PI-260). the results of pharmacokinetic studies showed that F19 exhibited longer MRT when compared to the commercial brand of aceclofenac immediate release tablet (Bristaflam®), demonstrating the sustained release properties of F19.

**Keywords:** Eudragit rspo; Eudragit ripo; Direct compression; Solid dispersion; Wet granulation; Pharmacokinetics using rabbit model.

#### 504. Novel Sustained Release Orally Disintegrating Tablet Containing Aceclofenac Lipospheres: *in-Vitro* and *in-Vivo* Studies

Abdulaziz Mohsen Al-mahallawi, Omneya M Khowessah and Raguia Ali Shoukri

*Inventi Impact Pharm Tech*, (2012)

Aceclofenac is a non-steroidal anti-inflammatory drug used for treatment of pain and inflammation. the short biological half-life (4 h) and dosing frequency more than once daily make aceclofenac a suitable candidate for sustained release formulations. Sustained release lipospheres of aceclofenac were prepared using cetyl alcohol and Compritol 888 ATO. the prepared lipospheres were characterized for their percentage yield, encapsulation efficiency, particle size, surface morphology, micromeritic properties and *in-vitro* release over 24 hours.

The optimum formula was incorporated into a lyophilized system to produce sustained release orally disintegrating tablet (SR-ODT), which intended to disintegrate rapidly within the mouth into lipospheres that will deliver aceclofenac in sustained release manner after swallowing. the prepared SR-ODTs were evaluated regarding weight variation, friability, content uniformity, disintegration, *in-vitro* release and *in-vivo* pharmacokinetics in albino rabbits.

All the prepared lipospheres showed satisfactory results regarding the investigated properties. According to the *in-vitro* release data, formula FI (prepared using cetyl alcohol at lipid: drug ratio of 1:1 and 0.5% PVA) was selected as the optimum formula, and thus, used for preparation of the SR-ODT. the prepared SR-ODT demonstrated acceptable weight variation, friability and content uniformity.

Also, the SR-ODT showed rapid *in-vitro* disintegration time (10 s) and it was successful in sustaining drug release up to 24 hours. the results of pharmacokinetic studies showed that the SR-ODT exhibited longer MRT and lower C<sub>max</sub> when compared with the values of the commercial brand of aceclofenac immediate release tablet (Bristaflam®), confirming our target in the preparation a sustained release formula.

**Keywords:** Sr-Odt; cetyl alcohol; Compritol 888 Ato; Lipid microspheres; Melt dispersion technique.

#### 505. *in Vivo* Evaluation and Application of Central Composite Design in the Optimization of Amisulpride Self-Emulsifying Drug Delivery System

Ahmed A. Aboelwafa and Amal I.A. Makhlouf

*American Journal of Drug Discovery and Development*, 2: 1-16 (2012)

Amisulpride is practically insoluble in water and suffers from irregular and low bioavailability (48%). This could be due to low solubility and being a substrate for P-glycoprotein efflux. the aim of this study is to develop and statistically optimize self-emulsifying drug delivery system (SEDDS) formulation containing bio-enhancers and P-glycoprotein inhibitors components, for the improvement of dissolution and oral absorption of amisulpride; using central composite rotatable design (CCRD). Preliminary screening was carried out to determine amisulpride solubility in various oils and surfactants. Formulations were prepared using oil (Capryol-90®), two surfactants (Cremophor EL® and Labrasol®, "Smix") and co-surfactant (Transcutol HP®). CCRD was applied for optimization. Oil percentage, Smix: co-surfactant ratio and Cremophor EL: Labrasol ratio in Smix, were selected as independent variables, while mean droplet sizes, drug loading and light absorbance of diluted SEDDS as dependent variables. Second-order polynomial equations were fitted to data. Optimized formulation, containing 10% oil, 1.31 as Smix: co-surfactant ratio and 2 as ratio of Cremophor EL: Labrasol in Smix was prepared according to software determined levels using desirability function and overlay plot. It provided drug loading of 50 mg/ml and released amisulpride completely within 15 min irrespective of type or pH of dissolution medium. Optimized SEDDS showed significant ( $P < 0.01$ ) increase in *in vivo* bioavailability compared to drug suspension. CCRD could be considered as an efficient approach for the optimization of SEDDS. Also, the optimized SEDDS formulation demonstrated a great potential as a possible alternative to traditional oral formulations of amisulpride.

**Keywords:** Amisulpride; Self-Emulsifying; Central Composite; Rabbits; P-Glycoprotein

#### 506. Electrically Assisted Transdermal Delivery of Escin

Mahmoud H. Teaima, Randa Tag Abd Elrehim, Doaa A. Elsetouhy, Mohamed A. Elnabarawi and Bhaskara R. Jasti

*International Journal of Pharmacy and Pharmaceutical Sciences*, 4: 663-672 (2012)

Escin is a neutral glycosidic drug with antiinflammatory, antiedematous, vasoprotective and venotonic activity used in treatment of chronic venous insufficiency (CVI), hemorrhoids and postoperative oedema. the present study was carried out to enhance the transdermal delivery of escin which is a neutral high molecular weight compound. the effect of different variables on iontophoretic delivery of escin was assessed; also, the effect of the combined physical (iontophoresis) and chemical (penetration enhancers) modulation of skin barrier on the transdermal delivery of escin was investigated. Finally, the *in vivo* activity of selected escin gel formulae was assessed in comparison to a marketed product. Laser Doppler flowmetry (LDF) was used to measure the change in skin perfusion following the passive and iontophoretic application of the commercial and selected formulae respectively. the results of the present study revealed that, iontophoresis can be



a useful tool for enhancing escin transport across the skin although being neutral high molecular weight compound; also, iontophoresis and penetration enhancers synergistically increased escin transdermal delivery compared to any of them alone.

**Keywords:** Escin; Transdermal iontophoresis; Electroosmosis; chronic venous insufficiency (Cvi); Vasoprotective drug.

### 507. Design and *in-Vitro* Evaluation of Olanzapine-Loaded Self Nanoemulsifying Drug Delivery System

Mona Aboul-Einien, Galal El Mahrouq and Nermeen Elkasabgy

*International Journal of Institutional Pharmacy and Life Sciences*, 2: 12-32 (2012)

**Purpose:** the purpose of this work was to prepare olanzapine loaded self-nanoemulsifying drug delivery systems (SNEDDS) with enhanced self-emulsification properties and hence, a better chance for oral absorption.

**Methods:** Various oils, surfactants and co-surfactants were investigated. Preliminary investigations were carried out for the selection of the proper ingredients of the self-emulsifying system depending on the drug solubility and the emulsification power. Ternary phase diagrams were then constructed for the identification of the adequate proportions of ingredients of the self-emulsifying systems. Self-emulsification time, effect of dilution (with different volumes at different pH values), mean globule size as well as polydispersity index values (PDI) were used to compare between the prepared formulas. Formulas with PDI values < 0.3 were selected to be loaded with different amounts of the drug and they were physically evaluated.

**Results:** Two optimum systems loaded with 20 mg olanzapine were found to fulfill the criteria of SNEDDS. Both systems were composed of oil mixture (isopropylpalmitate: Capryol 90®(3:1 w/w)), surfactant mixture (Cremophor RH40®:Tween® 80 (1:1 w/w)) and a co-surfactant (Transcutol® HP) at different proportions. They had rapid self-emulsification time (< 15 sec) and were robust to dilution and pH change. Also, they had mean globule size < 20 nm and maintained their PDI < 0.3.

**Conclusion:** Adjusting the components of the ternary system and their proportions facilitates the preparation of olanzapine- loaded self-nanoemulsifying systems with satisfactory physical characteristics.

**Keywords:** Nano-Emulsions; Olanzapine; Self- emulsifying drug delivery systems; Ternary phase diagram.

### 508. Sterile Lyophilized Pantoprazole Sesquihydrate: Formulation and Manufacturing Economics

Mearal A. Hussien, Howida K. Ibrahim and Dalia M.Ghorab

*International Journal of Novel Drug Delivery Technology*, 2: 276-282 (2012)

**Objective:** the objective of this study was to formulate pantoprazole sodium sesquihydrate as a stable lyophilized powder for injection to be manufactured locally in Egypt. This could overcome the problems of high cost and unavailability of imported products. Work started with the development and validation of an easy and simple HPLC stability indicating assay for pantoprazole.

**Methods:** Four compatible cryo/lyoprotectants were selected based on pre-formulation studies, namely, ethenyldiamine sodium tetra acetate, mannitol, lactose and sucrose. Twelve formulae

were prepared and lyophilized at 2: 1, 1: 1 and 1: 2 drug to cryo/lyoprotectants molecular ratios. Sodium hydroxide was used as buffering agent and sodium chloride as tonicity adjuster. The obtained products were evaluated for their appearance, ease of reconstitution, clarity, as well as, pH and drug content of the reconstituted solutions.

**Results:** Lactose and mannitol based formulae fulfilled the requirements for parenteral use and were subjected to accelerated stability study. Mannitol based formulae showed marked degradation on storage at 40°C and 75% relative humidity for 6 months.

**Conclusion:** Economic studies of manufacturing the lactose based lyophilized pantoprazole formulae showed that the average market consumption allows its production on large scale with much more affordable price than the imported products.

**Keywords:** Pantoprazole; Parenteral powder; Stability indicating assay; Freeze drying; Economics; Price structure.

### 509. Formulation and Evaluation of Enteric Coated Capsules Containing Olanzapine- Loaded Solid Lipid Nanoparticles

Galal M. El-Mahrouk, Mona H. Aboul-Einien and Nermeen A. Elkasabgy

*Ijpi'S Journal of Pharmaceutics and Cosmetology*, 2: 1-15 (2012)

**Purpose:** This study aimed to develop olanzapine- loaded solid lipid nanoparticles (SLNs) filled in enteric- coated capsules in an attempt to improve its bioavailability by increasing its lymphatic uptake.

**Methods:** SLNs were prepared by a modified high shear method using two different lipids. Mannitol was added to the SLN dispersion as a cryoprotectant. Sodium chloride and polyvinyl pyrrolidone K25 were added to preserve the amorphous nature of the freeze- dried preparations. The prepared SLNs were characterized for their physicochemical properties. The amorphous nature of the freeze- dried products was confirmed by differential scanning calorimetry and X- ray diffraction studies. The freeze- dried SLN formulas were then filled in hard gelatin capsules which were enteric coated by Eudragit® L100. The in- vitro olanzapine release from the prepared capsules was studied at gastric pH for two hours and at intestinal pH for another 22 hours. The stability of capsules stored for six months was investigated. Moreover, olanzapine absorption from the enteric coated capsules filled with selected SLN formula was compared to that from commercially available tablets in rabbits.

**Results:** Both investigated freeze- dried SLN formulas showed drug content approaching 100%, particle size in the nano range, reconstitution time within 0.6 minutes as well as satisfactory moisture content and flow properties. The in vitro drug release from the investigated capsules exceeded 90% after eight hours and the total amount of drug absorbed from such capsules reached 1.3- fold that from oral commercial tablets.

**Keywords:** Solid lipid nanoparticles; Freeze-drying; Peyer'S patches; Enhanced bioavailability.

### 510. Preparation and Characterization of Ofloxacin Loaded Biodegradable Poly D, L-Lactide Nanoparticles: A Factorial Design Study

Mahmoud M. Ghorab, Randa Tag and Salwa Salah

*Inventi Rapid:Pharm Tech.*, (2012)

This study was aimed to develop a polymeric drug delivery system for controlling the ocular delivery of ofloxacin. to achieve this goal, Ofloxacin-loaded (poly D, L-Lactide (DLPLA) nanoparticles (NPs) were prepared by solvent diffusion technique. the 2\*32 full factorial experimental design was used to study the influence of three different independent variables (drug to polymer ratio, surfactant type and surfactant concentration) on two responses: particle size and encapsulation efficiency. Analysis of variance (ANOVA) was used to evaluate the significance of the difference between the tested factors using computer software Stat View version 4.57. the physicochemical characteristics of DL-PLA nanoparticles were evaluated using particle size analyzer, scanning electron microscopy, differential scanning calorimetry and X-ray diffractometry. All independent variables were found to significantly influence the particle size and the entrapment efficiency. the nanoparticles formulations showed particle size diameter in the range of (200+3.92 – 860+4.32 nm) and a drug loading percent in the range of (23.53+ 1.61 – 44.43+1.11). the in vitro drug release profiles showed half-life (t1/2) up to 7.4 hours indicating the suitability of DL-PLA nanoparticles in controlling Ofloxacin release. the Ofloxacin was released in a biphasic fashion including an initial burst release followed by a sustained release for the next 12 hours. the drug release from all formulae was governed by Fickian diffusion. Based on the statistical model ofloxacin-loaded polymeric nanoparticle suspensions of less than 1 $\mu$ m in size could be produced and that may be of clinical importance as ocular delivery system in treatment of bacterial infection.

**Keywords:** Ofloxacin; Nanoparticles; DL-Pla; Spontaneous emulsification solvent diffusion.

### 511. Development and *in-Vitro* Evaluation of Olanzapine- Loaded Solid Lipid Nanoparticles in Solid Matrix

Galal M. El-Mahrouk, Mona H. Aboul-Einien and Nermeen A. Elkasabgy

*Jipi'S Journal of Pharmaceutics and Cosmetology*, (2012)

**Introduction:** the aim of the study is to develop olanzapine- loaded solid lipid nanoparticles (SLNs) in a solidified form and to investigate the effect of different formulation factors on their quality.

**Methods:** SLNs were prepared by a modified high shear homogenization and sonication method using different types and concentrations of lipids and surfactants. Compritol® ATO 888 and glyceryl tripalmitate were used as lipids, while Tween 80, Pluronic F68 and polyvinyl alcohol were used as surfactants. Two selected formulas of the prepared SLN dispersions were solidified by freeze- drying in presence of different concentrations of trehalose, mannitol or sucrose as cryoprotectants. the drug-entrapment efficiency and the particle size of the prepared SLNs were investigated while in dispersion as well as after freeze-drying. Olanzapine release pattern was used to evaluate the prepared SLNs in dispersion and the reconstitution time was estimated for freeze- dried formulas. Moreover, Differential scanning calorimetry, X-Ray diffractometry and Transmission

electron microscopy were carried out to characterize the prepared SLNs.

**Results:** for all the prepared SLNs the drug loading efficiency exceeded 90% and the particle size was in the nanorange. the highest drug- loading efficiency, the smallest particle size and the best drug release pattern were obtained by formulas containing 2% Tween 80 and a drug: lipid ratio of 1: 10. Mannitol (15%) was found to be the most efficient cryoprotectant among the investigated ones.

**Conclusion:** the prepared freeze- dried SLNs proved to be potential carriers for olanzapine, which can be formulated in different dosage forms.

**Keywords:** Colloidal carriers; Cryoprotectants; Modified high shear homogenization; Schizophrenia.

### Dept. of Pharmacognosy

### 512. Induced Resistance by A Long-Chain Bacterial Volatile: Elicitation of Plant Systemic Defense by A C13 Volatile Produced by *Paenibacillus Polymyxa*

Boyoung Lee, Mohamed A. Farag, Hyo Bee Park, Joseph W. Kloepper, Soo Hyun Lee and Choong-Min Ryu

*Plos One*, 7: 1-11 (2012) IF: 4.092

**Background:** Some strains of plant growth-promoting rhizobacteria (PGPR) elicit induced systemic resistance (ISR) by emission of volatile organic compounds (VOCs) including short chain alcohols, acetoin, and 2,3-butanediol. the objective of this study was to evaluate whether species-specific VOCs from PGPR strain *Paenibacillus polymyxa* E681 can promote growth and induce resistance in *Arabidopsis*.

**Methodology/Principal Findings:** the efficacy of induction was strain-specific, with stronger protection against *Pseudomonas syringae* pv. *maculicola* ES4326 in plants exposed to VOCs from *P. polymyxa* E681 versus *Arabidopsis* plants exposed to VOCs from a reference strain *Bacillus subtilis* GB03, which was previously shown to elicit ISR and plant growth promotion. VOC emissions released from E681 primed transcriptional expression of the salicylic acid, jasmonic acid, and ethylene signaling marker genes PR1, ChiB, and VSP2, respectively. in addition, strain E681 produced more than thirty low molecular-weight VOCs, of which tridecane was only produced by E681 and not found in GB03 or IN937a volatile blends. These strain-specific VOCs induced PR1 and VSP2 genes.

**Conclusions/Significance:** These results provide new insight into the existence of a long chain VOC signaling molecule produced by *P. polymyxa* that can serve as a bacterial trigger of induced systemic resistance in *planta*.

**Keywords:** Pgpr; Volatiles; Immunity; Gcms; Defense; Soil bacteria.

### 513. Steroidal Metabolites Transformed by *Marchantia Polymorpha* Cultures Block Breast Cancer Estrogen Biosynthesis

Mohamed-Elamir F, Hegazy Amira M, Gamal-Eldeen -Ali M, El-Halawany Abou El-Hamd H. Mohamed and Paul W. Pare'

*Cell Biochem Biophys*, 63: 85-96 (2012) IF: 3.743

Suspension of cultured cells of *Marchantia polymorpha* have the potential to hydrogenate the olefinic bonds present in androst-1,4-dien-3,17-dione (boldione, 1) to afford dihydroandrost-3,17-dione



derivatives including: androst-4-ene-3,17-dione (androstenedione, 4-AD, 2), 5 $\alpha$ -androstane-3,17-dione (androstenedione, AD, 4), and the less abundant metabolite 5 $\alpha$ -androst-1-ene-3,17-dione (1-androstenedione, 1-AD, 3). After isolation and purification, these metabolites were characterized on the basis of spectroscopic analyses using 1D and 2D NMR as well as mass spectrometry. Cytotoxicity of the biotransformation products against breast adenocarcinoma cells (MCF-7) was assessed by a 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide assay and cell death (apoptosis or necrosis) was assayed by acridine orange/ethidium bromide staining.

Aromatase (cytochrome P450 19 enzyme, CYP19) inhibitory activity was measured by a tritiated water release assay and by direct measurement of biotransformed steroids using the tritium labeled substrate 3H-androst-4-ene-3,17-dione. CYP19 mRNA expression in MCF-7 cells was analyzed by real-time PCR. Steroidal products 3 and 4 revealed a highly significant inhibition of MCF-7 cell growth that was predominantly due to apoptosis not necrosis.

Steroidal products 3 and 4 are both potent inhibitors of aromatase activity and CYP19 mRNA expression, while 2 is a known substrate for aromatase. These data establish that metabolites 3 and 4 are potent chemical agents against breast cancer via aromatase inhibitory mechanism. Results were interpreted via virtual docking of the biotransformation products to the human placental aromatase active site.

**Keywords:** Cultured plant cells.

#### 514. Anti-Oestrogenic Diarylheptanoids from *Aframomum Melegueta* with in Silico Oestrogen Receptor Alpha Binding Conformation Similar to Enterodiol and Enterolactone

Ali M. El-Halawany and Masao Hattori

*Food Chem*, 134: 219-226 (2012) IF: 3.655

*Aframomum melegueta* is a spice widely used in African folk medicine. The chloroform soluble fraction of *A. melegueta* seeds yielded four new diarylheptanoids named gingerenone D (1), dihydrogingerenone A (2), dihydrogingerenone B (3), and dihydrogingerenone C (4), in addition to six known diarylheptanoids and hydroxyphenylalkanones.

The most potent oestrogen receptor binding ability in an oestrogen receptor alpha (ER $\alpha$ ) competitive-binding assay was for compounds 1, 2 and 5 with IC<sub>50</sub> values of 50, 79 and 39 nM, respectively, compared with 18 nM for the natural steroid 17 $\beta$ -oestradiol (E<sub>2</sub>). In addition, the diarylheptanoids 1, 2 and 5 showed anti-oestrogenic activity in a receptor cofactor assay system for ER $\alpha$ , while the hydroxyphenylalkanone, [6] dehydrogingerdione, (7) exhibited an agonistic action.

**Results:** were interpreted via virtual docking of the active compounds to an ER $\alpha$  crystal structure, in comparison with the known oestrogenic compounds: enterodiol (END), enterolactone (ENL), genistein and E<sub>2</sub>. The anti-oestrogenic compounds 1, 2 and 5 showed a binding similarity to that of END and ENL while compound 7 was similar in binding to genistein and E<sub>2</sub> interpreting its agonistic effect.

**Keywords:** *Aframomum melegueta*; Diarylheptanoids; ER $\alpha$ ; Enterodiol; Enterolactone; Gingerenone; SERM.

#### 515. In Vitro Anti-Influenza Virus Activity of A Cardiotonic Glycoside from *Adenium Obesum* (Forssk)

Hiroaki Kiyoharaa, Chikara Ichino, Yuka Kawamura, Takayuki Nagai, Noriko Sato, Haruki Yamada, Maha M. Salama and Essam Abdel-Sattar

*Phytomedicine*, 19: 111-114 (2012) IF: 3.268

Methanolic extracts of six Saudi plants were screened for their in vitro antiviral activity using influenza virus A/PR/8/34 (H1N1) and MDCK cells in an MTT assay. The results indicated that the extracts of *Adenium obesum* and *Tephrosia nubica* possessed antiviral activity (99.3 and 93.3% inhibition at the concentration of 10  $\mu$ g/ml, respectively).

Based on these results *A. obesum* was selected for further study by applying bioactivity-guided fractionation to isolate its antiviral principle. The antiviral principle was isolated from the chloroform fraction through solvent fractionation, combined open liquid chromatography and HPLC. The isolated active compound A was identified as oleandrogenin- $\beta$ -glucosyl (1 $\rightarrow$ 4)- $\beta$ -D-digitalose, on the basis of its spectral analysis (MS, 1D and 2D NMR). The isolated glycoside showed reduction of virus titre by 69.3% inhibition at concentration of 1  $\mu$ g/ml (IC<sub>50</sub> = 0.86  $\mu$ g/ml).

**Keywords:** *Adenium obesum*; *Tephrosia nubica*; Oleandrogenin- glucosyldigitaloside; Antiviral.

#### 516. 6-Gingerol Ameliorated Doxorubicin-Induced Cardiotoxicity: Role of Nuclear Factor Kappa B and Protein Glycation

Wesam M. El-Bakly, Manal L. Louka, Ali M. El-Halawany and Mona F. Schaalan

*Cancer Chemoth Pharm*, 70: 833-841 (2012) IF: 2.833

**Purpose** Doxorubicin is a widely used antitumour drug. Cardiotoxicity is considered a major limitation for its clinical use. The present study was designed to assess the possible antioxidant and antiapoptotic effects of 6-gingerol in attenuating doxorubicin-induced cardiac damage.

**Method** Male albino rats were treated with either intraperitoneal doxorubicin (18 mg/kg divided into six equal doses for 2 weeks) and/or oral 6-gingerol (10 mg/kg starting 5 days before and continued till the end of the experiment).

**Results** 6-gingerol significantly ameliorated the doxorubicin-induced elevation in the cardiac enzymes. The stimulation of oxidative stress by doxorubicin was evidenced by the significant decrease in the serum soluble receptor for advanced glycation endproduct allowing unopposed serum advanced glycation endproduct availability. Moreover, doxorubicin activated nuclear factor kappa B (NF- $\kappa$ B) which was indicated by an increase in its immunohistochemical staining in the nucleus. In addition, doxorubicin-induced cardiotoxicity was accompanied by elevation of cardiac caspase-3. Notably, pretreatment with 6-gingerol significantly ameliorated the changes in sRAGE, NF- $\kappa$ B and cardiac caspase-3. Cardiac enzymes showed significant positive correlation with NF- $\kappa$ B and caspase-3 but negative with serum sRAGE, suggesting their role in doxorubicin-induced cardiac injury. These findings were confirmed by cardiac tissue histopathology.

**Conclusion** 6-gingerol, a known single compound from ginger with anticancer activity, was shown to have a promising role in cardioprotection against doxorubicin-induced cardiotoxicity. This

study suggested a novel mechanism for 6-gingerol cardioprotection, which might be mediated through its antioxidative effect and modulation of NF- $\kappa$ B as well as apoptosis.

**Keywords:** Doxorubicin (Dox)-Cardiotoxicity.

### 517. Acaricidal Activity of Swietenia Mahogany and Swietenia Macrophylla Ethanolic Extracts Against Varroa Destructor in Honeybee Colonies

Soheir M. El Zalabani, Hesham I. El-Askary, Ola M. Mousa, Marwa Y. Issa, Ahmed A. Zaitoun and Essam Abdel-Sattar

*Exp Parasitol*, 130: 166-170 (2012) IF: 2.122

The acaricidal (miticidal) activity of 90% ethanolic extracts of leaves and stem bark of *Swietenia mahogany* and *Swietenia macrophylla* were tested against *Varroa destructor* mite. Four concentrations were used over two different time intervals under laboratory and field conditions. In general, it was noticed that the acaricidal effect based on mortality and LC50 of all tested extracts against the *Varroa* mite was concentration and time dependant. The acaricidal action against *Varroa* mites was relatively the least for the *S. macrophylla* stem bark extract at 500 ppm concentration after 48 h while it reached 100% and 95% in case of *S. mahogany* bark and *S. macrophylla* leaves, respectively. The % infestation with *Varroa* in colonies treated with the different extracts at various time intervals showed that the rate of infestation decreased to 0.0% after 12 days from the beginning of treatments with 500 ppm of *S. mahogany* leaves extract compared to 0.79% decrease after treatment with Mitac, a reference drug (60 mg/colony). The rate of infestation in case of treatments with *S. mahogany* bark, *S. macrophylla* leaves and *S. macrophylla* bark was decreased to 0.11%, 2.41% and 1.08%, respectively. The highest reduction was observed with *S. mahogany* leaves extract followed by *S. mahogany* bark. All the tested extracts showed less or no effect on honey bees at the different concentrations and at different bioassay times. This study suggested that the use of natural plant extracts or their products as ecofriendly biodegradable agents could be of high value for the control of *Varroa* mite.

**Keywords:** *Swietenia mahogany*; *Swietenia macrophylla*; *Varroa destructor*.

### 518. Pharmacognostical Study of Chorisia Insignis Hbk. Grown in Egypt

Taha El Alfy, Salma El Saw, Sahar Abd El Tawab and Doaa Moawad

*Bulletin of Faculty of Pharmacy, Cairo University*, 50: 17-39 (2012) IF: 2

*Chorisia insignis* HBK. is a perennial deciduous plant native to South America. This study presents the macro and micromorphological features of the plant and the determination of its pharmacopoeial constants (Moisture = 12.80%, Total ash = 11.72%, Water soluble ash = 9.24%, Acid insoluble ash = 0.16% and Crude fibre = 20.33%). Furthermore, the DNA of the plant was extracted from leaf samples and analyzed by polymerase chain reaction (PCR) using 12 decamer primers. The DNA fingerprint showed a total of 95 fragments. Protein electrophoresis was carried out using SDS-PAGE (sodium dodecyl sulphate polyacrylamide gel electrophoresis) technique to monitor the seed storage protein expressed by the active genes of

the whole genomic DNA of *C. insignis* HBK. The data obtained revealed the presence of 20 sharp protein bands having a wide range of molecular weights. The percentage of protein in the seeds was found to be 26.83% as determined using micro-Kjeldahl method. Analysis of the total amino acids content of the seeds revealed the identification of 15 amino acids, mainly glutamic acid (26.71%), aspartic acid (11.98%) and glycine (11.00%).

**Keywords:** Botany; *Chorisia insignis*; DNA fingerprint; Pharmacopoeial constants; Protein electrophoresis.

### 519. Antioxidant and Cardioprotective Activity of Stachys Schimperii Vatke Extract Against Doxorubicin-Induced Cardiotoxicity

Essam Abdel-Sattar, Sabah Hussein El-Gayeda, Ibrahim Shehata, Osama M. Ashour, Ayman A. Nagy and Ahmed M. Mohamadin

*Bulletin of Faculty of Pharmacy, Cairo University*, 50: 41-47 (2012) IF: 2

Cardiotoxicity is one of the major side effects of anthracycline antibiotics. Most studies implicated increased oxidative stress as the major determinant of doxorubicin (DOX) cardiotoxicity. The aim of the current investigation was to study the possible cardioprotective effect of *Stachys schimperii* Vatke (family Lamiaceae) on DOX-induced cardiotoxicity in rats based on biochemical and histopathological parameters. The phenolic profile of the methanol extract was determined qualitatively by HPLC. Isoscutellarein 7-O-[2,6-di-O-(6-acetyl)- $\beta$ -D-allopyranosyl]- $\beta$ -D-glucopyranoside (compound 1) was isolated and identified from EB fraction as a major constituent for the first time from this *Stachys* species. The methanolic extract and the combined EtOAc and n-butanol fractions (EB) as well as compound 1 showed prominent free radical scavenging activity when assessed by the DPPH method. The methanolic extract showed moderate protection against DOX-induced alteration in cardiac oxidative stress markers; GSH and MDA, and cardiac serum markers; CK-MB and LDH activities. Additionally, histopathological study denoted mild protection against DOX-induced cardiotoxicity.

**Keywords:** Antioxidant; *Stachys schimperii*; Doxorubicin; Cardiotoxicity.

### 520. Studies on Flavanolignans from Cultured Cells of Silybum Marianum

Ahlam Elwekeel, Sameh Abou Zid, Nadia Sokkar and Ahlam Elfishway

*Acta Physiol Plant*, 34: 1445-1449 (2012) IF: 1.639

Callus and cell suspension cultures of *Silybum marianum* (L.) Gaertn. (Asteraceae) were established from in vitro germinated sterile plantlets. The cultures grew in Murashige and Skoog medium containing 1 mg l<sup>-1</sup> 2,4-dichlorophenoxyacetic acid (2,4-D) and 0.1 mg l<sup>-1</sup> kinetin. A reversed phase-high performance liquid chromatography method for determination of flavanolignans in plant material was developed using an isocratic solvent system comprising acetonitrile and water containing 0.5% (v/v) phosphoric acid.

Silychristin was the major flavanolignan produced by the cultured cells followed by silydianin. Elicitation of cultured *S. marianum* cells with 100  $\mu$ g ml<sup>-1</sup> yeast extract increased silychristin production from 0.11 to 0.23 mg g<sup>-1</sup> fresh weight. Free radical

scavenging activity was tested for the cultured cells using 1,1'-diphenyl picryl hydrazyl (DPPH) radical.

Extract prepared from the cultured cells of *S. marianum* showed 48% inhibition compared to 55% inhibition of the extract prepared from the fruits. Cytotoxic activity was tested using liver carcinoma cell line (HEPG2). Cultured cells and fruit extracts showed a significant cytotoxic activity of  $IC_{50} = 1.01$  and  $0.47 \mu\text{g}$ , respectively. Extract of *S. marianum* cultured cells ameliorated the adverse effects of carbon tetrachloride-induced hepatic injury in rats and returned the altered levels of biochemical markers to near normal levels.

**Keywords:** *Silybum marianum*; Cell culture; Elicitation; Antioxidant; Cytotoxicity; Hepato-Protective.

### 521. Bioactive Anthraquinones from Endophytic Fungus *Aspergillus Versicolor* Isolated from Red Sea Algae

Usama W. Hawas, Ahmed Atef El-Beih and Ali M. El-Halawany

*Arch Pharm Res*, 35: 1749-1756 (2012) IF: 1.592

The marine fungus *Aspergillus versicolor* was isolated from the inner tissue of the Red Sea green alga *Halimeda opuntia*. The fungus was identified by its morphology and 18s rDNA. Cultivation of this fungal strain led to a new metabolite named isorhodoptilometrin-1-methyl ether (1) along with the known compounds emodin (2), 1-methyl emodin (3), evariquinone (4), 7-hydroxyemodin 6,8-methyl ether (5), siderin (6), arugosin C (7), and variculanol (8). The structures were elucidated on the basis of NMR spectroscopic analysis and mass spectrometry. The biological properties of ethyl acetate extract and compounds 1-3 and 6-8 were explored for antimicrobial activity, anti-cancer activity and inhibition of Hepatitis C virus (HCV) protease.

**Keywords:** *Halimeda opuntia*; *Aspergillus versicolor*; Anthraquinones; Hcv N3/4A protease.

### 522. Phenolics from *Phaleria Nisidai* with Estrogenic Activity

Christopher Kitalong, Ali M. El-Halawany, Riham Salah El-Dine, Chao-mei Ma and Masao Hattori

*Rec Nat Prod*, 296-300 (2012) IF: 1.508

The methanol extract of *P. nisidai* leaves yielded a benzophenone rhamnoside, iriflophenone 2-O- $\alpha$ -L-rhamnopyranoside (1) in addition to genkwanin 5-O- $\beta$ -D-primeveroside (2) and mangiferin (3). The isolated compounds as well as the derived aglycones of 1 and 2 assigned as compounds 4 and 5, respectively, were tested for their estrogenic activity on ER $\alpha$  using an estrogen receptor competitive binding screen. Compounds 1, 4 and 5 showed almost the same binding ability to ER $\alpha$  with  $IC_{50}$  of  $630 \mu\text{M}$ ,  $700 \mu\text{M}$  and  $800 \mu\text{M}$ , respectively.

Virtual docking with ER $\alpha$  revealed that compound 1, 4 and 5 strongly hydrogen bond with amino acids Glu353, Arg349, Gly521 and His524, in the estrogen receptor ligand binding domain, similar to that of mammalian estrogen 17 $\beta$ -estradiol.

**Keywords:** *Phaleria nisidai*; Estrogenic activity; ER; Benzophenone; Mangiferin.

### 523. Potent Insecticidal Secondary Metabolites from the Medicinal Plant *Acanthus Montanus*

Elham Amin, Mohamed M. Radwan, Seham S. El-Hawary, Magda M. Fathy, Rabab Mohammed, James J. Becnel and Ikhlal Khan

*Rec Nat Prod*, 1-9 (2012) IF: 1.508

*Acanthus montanus* (Nees) T. Anders. (Family: Acanthaceae) is a small shrub with sparse branches and soft stems, widespread in Africa, the Balkans, Romania, Greece and Eastern Mediterranean. Documented evidence showed that the leaves of the plant possess spasmolytic, analgesic, anti-inflammatory and antipyretic activities. In our ongoing research project, aimed at identifying new natural compounds with insecticidal activity, the alcohol extract of the aerial parts of *A. montanus* exhibited a significant activity against adult *Aedes aegypti*. Phytochemical study of the plant has resulted in isolation of nine compounds, eight of which exhibit variable degrees of insecticidal activity.  $\beta$ -sitosterol-3-O- $\beta$ -D-glucoside (1) exhibited potent mosquitocidal activity (100% mortality) against adult *Aedes aegypti* at 3.1 ppm concentration, followed by palmitic acid (2) (90%), linaroside (3) (80%), and acetoside (9) (70%) respectively. It is noteworthy that this is the first report of insecticidal activity of  $\beta$ -sitosterol-3-O- $\beta$ -D-glucoside, linaroside and acetoside.

**Keywords:** Acanthaceae; *Acanthus Montanus*; Adult *Aedes Aegypti*;  $\beta$ -Sitosterol Glucoside; Palmitic Acid; Protocatechuic Acid; Shikimic Acid.

### 524. In Vitro Cytotoxic Screening of Selected Saudi Medicinal Plants

Hussein Almehdar, Hossam M. Abdallah, Abdel-Moneim M. Osman and Essam A. Abdel-Sattar

*Journal of Natural Medicines*, 66: 406-412 (2012) IF: 1.389

Many natural products from plants have been identified to exert anticancer activity. It might be expected to be a challenge to look at the Saudi plants in order to discover new sources for new molecules which may have anticancer activity. The methanolic extracts of forty species of plants traditionally used in Saudi Arabia for the treatment of a variety of diseases were tested in vitro for their potential anticancer activity on different human cancer cell lines. The cytotoxic activity of the methanolic extracts of the tested plants were determined using three human cancer cell lines, namely, breast cancer (MCF7), hepatocellular carcinoma (HEPG2), and cervix cancer (HELA) cells. In addition, human normal melanocyte (HFB4) was used as normal nonmalignant cells. Sulforhodamine B colorimetric assay was used to evaluate the in vitro cytotoxic activity of the different extracts. The growth inhibition of 50% ( $IC_{50}$ ) for each extract was calculated from the optical density of treated and untreated cells.

Doxorubicin, a broad-spectrum anticancer drug, was used as the positive control. Nine plant extracts were chosen for further fractionation based on their activity and availability.

Interesting cytotoxic activity was observed for *Hypoestes forskalii*, *Withania somnifera*, *Solanum glabratum*, *Adenium obesum*, *Pistacia vera oleoresin*, *Caralluma quadrangula*, *Eulophia petersii*, *Phragmanthera austroarabica*, and *Asparagus officinalis*. Other extracts showed poor activity.

**Keywords:** Plant extracts; *In Vitro* cytotoxic activity; Sulforhodamine B assay; *Caralluma quadrangula*; *Hypoestes forskalii*.

### 525. Enhanced Accumulation of Flavonolignans in *Silybum Marianum* Cultured Roots by Methyl Jasmonate

Ahlam Elwekeel, Ahlam Elfishway and Sameh AbouZid

*Phytochem Lett*, 5: 393-396 (2012) IF: 1.222

Root cultures of *Silybum marianum* (L.) Gaertn. (Asteraceae) were established from in vitro germinated sterile plantlets. The cultures grew in hormone-free Murashige and Skoog medium. The flavonolignan content in the cultured roots was determined by HPLC using 30% acetonitrile in acidified water (0.5% phosphoric acid). The major flavonolignans produced by the cultured roots were silychristin (74.2 mg g<sup>-1</sup> fresh weight (FW)) and silydianin (8.1 mg g<sup>-1</sup> FW). The flavonolignan precursor taxifolin was also detected in the cultured roots (40.8 mg g<sup>-1</sup> FW). Addition of methyl jasmonate to 7-days-old root cultures for 48 h increased the content of the produced flavonolignans and taxifolin to approximately 300% of the control cultures. Methyl jasmonate also enhanced about sixfold the accumulation of a compound identified as 3,30,5,50,7-pentahydroxyflavanone.

**Keywords:** *Silybum Marianum*; Root Culture; Silychristin; Silydianin; Taxifolin; Pentahydroxyflavanone; Methyl Jasmonate.

### 526. Simultaneous Determination of Saponins and Flavonoids from Aerial Parts of *Zygophyllum Coccineum* L

Elham Amin, Yan-Hong Wang, Bharathi Avula, Seham S. El-Hawary, Magda M. Fathy, Rabab Mohammed and Ikhlas Khan

*J Aoac Int*, 95: 757-762 (2012) IF: 1.199

Triterpenoid saponins are a class of glycosides with a wide range of bioactivities, which make them an interesting research candidate. *Zygophyllum coccineum* is an Egyptian desert plant rich in triterpenoid saponins. Reviewing the relevant literature, no data concerning the HPLC or UPLC analysis of *Zygophyllum* content were found. The present work presents two methods, HPLC-UV and UPLC-UV-ELS/MS, for the simultaneous determination of ten compounds in the alcohol extract of *Z. coccineum*. The HPLC method uses C18 column material and water/acetonitrile (both contain 0.1% trifluoroacetic acid) gradient system. The separation was achieved within 32.0 minutes. Considering run time of analysis, a more advanced and reliable LC method was conducted. The newly developed UPLC method simultaneously detects and quantifies the ten compounds, using Acquity UPLC Shield RP18 column, and reagent alcohol: acetonitrile (80:20) / water (both contain 0.05% formic acid) gradient system, within 13.0 min. The detection was achieved using UV, ELS, and MS. The methods were used to analyze another species, *Z. simplex* and results revealed a great variation in the secondary metabolite pattern between both species.

**Keywords:** *Z. coccineum*; *Z. simplex*; Triterpenoid saponins; Flavonoids; Hplc-Uv; Uplc-Uv-Elsd/Ms.

### 527. Cytotoxic Compounds from the Leaves of *Gaillardia Aristata* Pursh. Growing in Egypt

Maha M. Salama, Zeinab A. Kandil and Wafaa T. Islam

*Nat Prod Res*, 26: 2057-2062 (2012) IF: 1.009

Ten compounds, neopulchellin (1), 6 $\alpha$ -hydroxyneopulchellin (2),  $\beta$ -sitosterol-3-O- $\beta$ -D-glucoside (3), apigenin (4), quercetin (5),

eupafolin (6), kaempferol-3-methoxy-7-O- $\alpha$ -L-rhamnoside (7), apigenin-7-O- $\beta$ -D-glucopyranoside (8),  $\alpha$ -amyryrin (9) and  $\beta$ -sitosterol (10), were isolated from the leaves of *Gaillardia aristata* by applying bioassay guided fractionation. The cytotoxicity was traced against two human cancer cell lines (breast (MCF7) and colon (HCT116)). The highest cytotoxicity was revealed by compounds 1 and 2 (isolated from chloroform extract); with IC<sub>50</sub> values of 0.43, 0.32 mgmL<sup>-1</sup> against MCF7 and 0.46, 0.34 mgmL<sup>-1</sup> against HCT116, respectively. Compounds 9 and 10 (isolated from the n-hexane extract) exhibited lower IC<sub>50</sub> values of 3.05, 2.35  $\mu$ g mL<sup>-1</sup> against MCF7 and 3.05, 2.35  $\mu$ g mL<sup>-1</sup> against HCT116, respectively, while compounds 4–7 obtained from the ethyl acetate extract revealed the lowest cytotoxicity. Identification of the aforementioned compounds was carried out on the basis of their physico-chemical properties and spectral analysis (UV, EI/MS, 1D and 2D).

**Keywords:** Cytotoxic compounds; *Gaillardia aristata*; 6 $\alpha$ -hydroxyneopulchellin; Kaempferol-3-methoxy-7-O- $\alpha$ -L-rhamnoside.

### 528. Chemical and Biological Study of the Seeds of *Eragrostis Tef* (Zucc.) Trotter

Taha S. El-Alfy, Shahira M. Ezzat and Amani A. Sleem

*Nat Prod Res*, 26: 619-629 (2012) IF: 1.009

The chemical study of the red type of the seeds of *Eragrostis tef* (Zucc.) Trotter (Poaceae) led to the isolation of seven compounds from its ethanol extract; namely  $\beta$ -sitosterol (1),  $\beta$ -amyryrin-3-O-(2'-acetyl( glucoside (2),  $\beta$ -sitosterol-3-O- $\beta$ -D-glucoside (3), naringenin (4), naringenin-4'-methoxy-7-O- $\alpha$ -L-rhamnoside (5), eriodictyol-3',7-dimethoxy-4'-O- $\beta$ -D-glucoside (6) and isorhamnetin-3-O-rhamnoglucoside (7) which are reported for the first time in the genus *Eragrostis*. This is the first report for the isolation of compounds (2) and (6) in nature. The isolated compounds were identified using different spectroscopic methods (EIMS, UV, 1H NMR, 13C NMR, HMQC and HMBC). The proximate analysis revealed the high nutritive value of the seeds: carbohydrates (57.27 %), protein (20.9 %), essential amino acids (8.15 %) with major Leucine and Lysine (1.71 and 1.35 %, respectively), vitamin B1 (1.56 mg/100g), potassium and calcium (32.4 and 9.63 %, respectively). The seeds yielded 22 % w/w of fixed oil rich in unsaturated fatty acids (72.46 %), among which oleic acid was predominant (32.41 %), followed by linolenic acid (23.83%). The ethanolic extract and fixed oil of the seeds exhibited anti-hyperlipidemic and anti-hyperglycemic activities. Oral administration of the fixed oil for 10 days resulted in a rise in serum calcium level in rats.

**Keywords:** Tef; *Eragrostis tef*; Antihyperglycemic; Antihyperlipidemic.

### 529. Hepatoprotective Constituents of *Torilis Radiata* Moench. (Apiaceae)

Shahira M. Ezzat, Hossam M. Abdallah, Ghada A. Fawzy and

Shohda A. El-Maraghy

*Nat Prod Res*, 26: 282-285 (2012) IF: 1.009

Investigation of the aqueous ethanolic extract (AE) of the aerial parts of *Torilis radiata* Moench yielded two triterpenes (Lupeol acetate 1 and  $\alpha$ -Amyryrin 2), a sterol (Spinasterol 3) from its n-

hexane fraction (HF); a flavone (Acacetin 4), a coumarin (Scopoletin 5), a phenolic acid (Ferulic acid 6) from the chloroform fraction (CF) and a flavone glycoside (Luteolin-7-O-glucoside 7) from the n-butanol fraction (BF). the hepatoprotection of AE and its fractions was assessed in terms of the reduction in histological damage, accompanied with restoring the liver enzymes (alanine amino transferase (ALT), aspartate amino transferase (AST), lactate dehydrogenase, (LDH), reduction in the inflammatory markers (tumor necrosis-  $\alpha$  (TNF- $\alpha$ ), nitric oxide (NO), N-acetyl-  $\beta$ -D-glucosaminidase (NAG) and myeloperoxidase (MPO) in serum, also restoring the oxidant balance through decreasing the serum and hepatic malondialdehyde (MDA) levels along with increasing the activity of hepatic catalase (CAT), glutathione peroxidase (GSHPx) and the non enzymatic antioxidant; glutathione (GSH).

**Keywords:** Antioxidant; Anti-Inflammatory; Hepatoprotective; *Torilis radiata*.

### 530. Bioguided Isolation of Pentacyclic Triterpenes from the Leaves of *Alstonia Scholaris* (Linn.) R. Br. Growing in Egypt

El-Askary H.I., El-Olemy M.M., Salama M.M., Sleem A.A. and Amer M.H.

*Nat Prod Res*, 26: 1755-1758 (2012) IF: 1.009

Ethanollic and aqueous extracts of the leaves and flowers of *Alstonia scholaris* were evaluated for their antioxidant activity by investigating their effect on blood glutathione levels in alloxan-induced diabetic rats. the ethanolic extract of the leaves was the most active; therefore, its cytotoxicity against HepG2 cells was also tested. Promising GI<sub>50</sub> values of 1.96, 4.34 and 4.65 mgmL<sup>-1</sup> were observed for the extract, its chloroform and ethyl acetate fractions, respectively. the chloroform active subfraction I (GI<sub>50</sub> = 2.97 mgmL<sup>-1</sup>) yielded betulin (1), betulinic acid (2) and ursolic acid (3) upon purification. Compounds 1–3 were identified using spectroscopic techniques and by comparison with reported data. GLC of unsaponifiable and saponifiable fractions of the hexane extract revealed  $\beta$ -sitosterol (7.37%) and n-tetracosane (54.4%) to be the major sterol and hydrocarbon components, respectively. Linoleic acid (48.89%) was the predominant fatty acid.

**Keywords:** *Alstonia scholaris*; Antioxidant; Apocynaceae; Bioguided; Cytotoxicity; Hepg2; Triterpenoids.

### 531. A New Alkaloid and A New Diterpene from *Cleome Paradoxa* B. Br. (Cleomaceae)

Azza R. Abdel-Monem

*Nat Prod Res*, 26: 264-269 (2012) IF: 1.009

A new alkaloid, paradoxonine, and its enol tautomer, paradoxenoline, in addition to a new cembranoid diterpene, paradoxenoic acid, were isolated from the chloroformic fraction of the methanolic extract of *Cleome paradoxa* B.Br. the structures of the isolated compounds were established based on their spectral data, including MS, <sup>1</sup>HNMR, <sup>13</sup>CNMR, COSY, HMBC and HMQC. This is the first report on isolation of alkaloids from family Cleomaceae.

**Keywords:** *Cleome paradoxa* B.Br.; Alkaloids; Morpholine; Oxazine; Cembranoid; Diterpenes.

### 532. Molluscicidal and Mosquitocidal Activities of the Essential Oils of *Thymus Capitatus* Hoff. Et Link and *Marrubium Vulgare* L.

Maha M. Salama, Eman E. Taher and Mohamed M. El-Bahy

*Rev. Inst. Med. Trop. Sao Paulo*, 54 (5):281-286 (2012) IF: 1

Steam distillation of essential oils of aerial parts of *Thymus capitatus* and *Marrubium vulgare* L. collected at North cost of Egypt yielded 0.5% and 0.2%, respectively. Results of Gas chromatography-mass spectrometry analyses of the two samples identified 96.27% and 90.19% of the total oil composition for *T. capitatus* and *M. vulgare*, respectively. the two oil samples appeared dominated by the oxygenated constituents (88.22% for *T. capitatus* and 57.50% for *M. vulgare*), composed of phenols, mainly carvacrol (32.98%) and thymol (32.82%) in essential oil of *T. capitatus*, and thymol (34.55%) in essential oil of *M. vulgare*. It was evaluated the molluscicidal activity of *T. capitatus* and *M. vulgare* essential oils on adult and eggs of *Biomphalaria alexandrina* as well as their mosquitocidal activity on *Culex pipiens*. the LC<sub>50</sub> and LC<sub>90</sub> of *T. capitatus* essential oil against adult snails was 200 and 400 ppm/3hrs, respectively, while for *M. vulgare* it was 50 and 100 ppm/3hrs, respectively. Moreover, *M. vulgare* showed LC<sub>100</sub> ovicidal activity at 200 ppm/24 hrs while *T. capitatus* oil showed no ovicidal activity. It was verified mosquitocidal activity, with LC<sub>50</sub> and LC<sub>90</sub> of 100 and 200 ppm/12hrs respectively for larvae, and 200 and 400 ppm/12hrs respectively for pupae of *C. pipiens*.

**Keywords:** Vector control; Plant products; *Thymus capitatus*; *Marrubium vulgare*.

### 533. Isolation of New Cytotoxic Metabolites from *Cleome Droserifolia* Growing in Egypt

Shahira M. Ezzat and Amira Abdel Motaal

*Z. Naturforsch C.*, 266-274 (2012) IF: 0.772

The sulforhodamine B (SRB) assay was used to assess the cytotoxicity of the aqueous (AqEx) and ethanolic (AlEx) extract, of the aerial parts of *Cleome droserifolia* (Forssk.) Del. against two human cancer cell lines, breast (MCF7) and colon (HCT116) adenocarcinoma. AqEx exhibited higher cytotoxic activity, thus its four subfractions, namely n-hexane (HxFr), chloroform (ClFr), ethyl acetate (EtFr) and n-butanol (BuFr), were also tested. Purification of the more active ClFr and EtFr yielded nine compounds. Six terpenoids, guai-7(11),8-diene (C<sub>1</sub>), 1-hydroxy-guai-3,10(14)-diene (C<sub>2</sub>), 18-hydroxy-dollabela-8(17)-ene (C<sub>3</sub>), (24E)- stigmasta-5,8-dien-3 $\beta$ -ol (C<sub>4</sub>), teucladiol (6-hydroxynardol) (1 $\alpha$ ,5  $\beta$ -guai-10 (14) -ene-4 $\beta$ ,6 $\beta$ -diol) (C<sub>5</sub>), buchariol (4,10-epoxy-6 $\alpha$ -hydroxyguaiane) (C<sub>6</sub>), were isolated from ClFr and three flavonol glycosides, isorhamnetin-3-O- $\beta$ -D-glucoside (F<sub>1</sub>), quercetin-3'-methoxy-3-O-(4''-acetylramnoside)-7-O- $\alpha$ -rhamnoside (F<sub>2</sub>), kaempferol-4'-methoxy-3,7-O-dirhamnoside (F<sub>3</sub>), were isolated from EtFr. Compounds C<sub>3</sub> and F<sub>2</sub> are new in nature. the isolated compounds were identified using various spectroscopic methods (UV, IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR, HMQC, HMBC and COSY). Compounds C<sub>1</sub>, C<sub>3</sub>, F<sub>2</sub> and F<sub>3</sub>, showed significant cytotoxic activities against the two tested cell lines comparable to those of the anticancer drug doxorubicin®. the new compound C<sub>3</sub> was the most active as it had the lowest IC<sub>50</sub> values (1.9  $\pm$  0.08 and 1.6  $\pm$  0.09  $\mu$ g/ml, corresponding to 6.5 and 5.4  $\mu$ M, against MCF7 and HCT116 cells, respectively.

**Keywords:** Cytotoxic; *Cleome droserifolia*; Flavonols; Terpenes.

### 534. Chemical Composition and Biological Activities of the Essential Oil of *Mentha Suaveolens* Ehrh

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*Z Naturforsch C*, 67 c: 571-579 (2012) IF: 0.772

Hydrodistilled oils of the fresh aerial parts of *Mentha suaveolens* Ehrh. cultivated in Egypt were prepared from samples collected along the four seasons. the percentage yields of these essential oils were 0.50%, 0.52%, 0.60%, and 0.47% of the dry weight for winter, spring, summer, and autumn samples. GC/MS analyses of all samples revealed a qualitative and quantitative variability in the oil composition. the total number of compounds identified was 46 among which 15 were common in all samples. the oxygenated compounds constituted about 45%, 46%, 63%, and 44% of the total composition of the oils for winter, spring, summer, and autumn samples, respectively. Carvone was the major constituent in spring, summer, and autumn samples (about 31%, 56%, and 35%, respectively), while limonene (ca. 26%) was the major constituent of the winter sample followed by carvone (ca. 25%). the essential oil of the highest yield (full-flowering summer sample), with the highest oxygenated constituents and carvone contents, was screened for certain biological activities. It exhibited analgesic and acute anti-inflammatory activities (75% and 82% relative to indomethacin). It also showed a potent *in vivo* antioxidant activity (96% relative to vitamin E). in addition, it exerted moderate cytotoxic, hepatoprotective, and *in vitro* antioxidant activities. Moreover, the oil had a potent antifungal activity against *Candida albicans* (MIC = 4 µg/ml), *Saccharomyces cerevisiae* (MIC = 5.2 µg/ml), and *Aspergillus niger* (MIC = 6.8 µg/ml).

**Keywords:** *Mentha suaveolens*; Essential oil; Seasonal variations.

### 535. Evaluation of the Potential Cardioprotective Activity of Some Saudi Plants Against Doxorubicin Toxicity

Osama M. Ashour, Ashraf Abdel-Naim, Hossam M. Abdallah, Ayman A. Nagy, Ahmed M. Mohamadin and Essam A. Abdel-Sattar

*Z. Naturforsch C.*, 297-307 (2012) IF: 0.772

Doxorubicin (DOX) is an anthracycline antibiotic widely used as a chemotherapeutic agent in the treatment of several tumours. However, its cardiac toxicity limits its use at maximum therapeutic doses. Most studies implicated increased oxidative stress as the major determinant of DOX cardiotoxicity. the local Saudi flora is very rich in a variety of plants of quite known folkloric or traditional medicinal uses. *Tribulus macropterus* Boiss., *Olea europaea* L. subsp. *africana* (Mill.) P. S. Green, *Tamarix aphylla* (L.) H. Karst., *Cynomorium coccineum* L., *Cordia myxa* L., *Calligonum comosum* L' Hér, and *Withania somnifera* (L.) Dunal are Saudi plants known to have antioxidant activities. the aim of the current study was to explore the potential protective effects of methanolic extracts of these seven Saudi plants against DOX-induced cardiotoxicity in rats. Two plants showed promising cardioprotective potential in the order *Calligonum comosum* > *Cordia myxa*. the two plant extracts showed potent *in vitro* radical scavenging and antioxidant properties. They significantly protected against DOX-induced alterations in cardiac oxidative stress markers (GSH and MDA) and cardiac serum markers (CK-MB and LDH activities).

Additionally, histopathological examination indicated a protection against DOX-induced cardiotoxicity. in conclusion, *C. comosum* and *C. myxa* exerted protective activity against DOX-induced cardiotoxicity, which is, at least partly, due to their antioxidant effect.

**Keywords:** Saudi plants; Doxorubicin; Cardioprotection.

### 536. Quality Control of Certain Slimming Herbal Products Present in the Egyptian Market

Mostafa Abdel Kawi, Eman Haggag, Amira Abdel Motaal and Nermin Abdel Wahab

*Life Science Journal*, 9 (3): 2273-2285 (2012) IF: 0.073

The evaluation of two commercial slimming herbal teas was carried out by comparing them to prepared standard herbal mixtures. Quality control of the herbal tea preparations was conducted through microscopical identification of their diagnostic elements, GC/MS of the volatile oil constituents, HPLC quantitative estimation of the main active constituents as well as the bioactivities of the teas. It was revealed that the percents of scopoletin and esculetin in commercial herbal tea 1 (senna, liquorice, chicory, nettle, marjoram, celery and calendula) were 0.19 and 0.41%, respectively, which was somehow similar to those in the prepared standard tea (0.18% and 0.17%). The commercial herbal tea 2 (senna, chicory and fennel) contained 0.17% esculetin while its prepared standard tea contained 0.73%. the major constituents of the essential oil of herbal tea 1 were  $\alpha$ -terpinene (2.03%), terpin-4-ol (5.83%), E-anethol (1.99%),  $\alpha$ -terpineol (1.01%) and limonene (35.47%), while the major compounds in the prepared standard tea were  $\gamma$ -terpinene (6.48%), terpin-4-ol (21.12%),  $\gamma$ -terpineol (8.33%) and carvacrol (32.89%). While in herbal tea 2 the major volatile constituents were limonene (5.07%), fenchone (9.17%), methyl chavicol (30%) and E-anethol (52.80%), compared to limonene (1.94%), fenchone (4.28%), methyl chavicol (51.59%) and Eanethol (34.18%) found in its standard herbal preparation (1). Herbal tea 1 decreased the plasma levels of total cholesterol, triglycerides and total lipids by 13.76, 7.71 and 21.87%, respectively, while their prepared standard tea decreased the levels by 30.12, 13.62 and 13.73% in experimentally induced hypercholesteremic rats after 8 weeks of treatment. Herbal tea 2 decreased the levels of total cholesterol, triglycerides and total lipids by 23.11, 8.95 and 20.55%, respectively, while their prepared standard teas caused a reduction of 27.35, 12.92 and 26.84%. on the other hand, herbal tea 1 decreased the glucose levels by 20% in normoglycemic rats in 150 minutes, and by 8.26% in STZ-induced diabetic rats after 30 days, while their prepared standard teas caused 23.73 and 4.52% reduction, respectively. the herbal tea 2 decreased the glucose levels in normoglycemic and hyperglycemic rats by 15.60 and 10.30%, while their prepared standard teas decreased the levels by 28.64 and 8.30%, respectively.

**Keywords:** Drug evaluation; Senna; Liquorice; Chicory; Nettle; Marjoram; Celery; Calendula; Fennel; Hypocholesteremic; Hypoglycemic and antidiabetic activity.

### 537. Estrogenic Activity of Citrus Medica L. Leaves Growing in Egypt

Taha S. El-Alfy, Mona H. Hetta, Nemat Z. Yassin, Rehab F. Abdel Rahman and Esraa M. Kadry

*Journal of Applied Pharmaceutical Science*, 2: 180-185 (2012)

The estrogenic activity of petroleum ether extract of Citrus medica L. leaves as well as the chemical constituents responsible for the biological activity was studied. The petroleum ether extract proved to retain high estrogenic activity in immature female rats. The extract was saponified and its components (saponifiable part 23% and the unsaponifiable matter 77%) were identified using GC/MS technique. The extract proved to be safe (LD<sub>50</sub> < 2g/kg.bw). Oral administration of petroleum ether extract of C. medica in ovariectomized immature female Wistar rats for 7 days in a dose of 400 mg/kg resulted in significant increase in the uterine weight (g) (1.7±0.11) when compared with ovariectomized control rats (1.3±0.07). GC/MS analysis of both saponifiable and unsaponifiable matters revealed the presence of thirty three components (28 hydrocarbons and 5 sterols) in the unsaponifiable fraction, the major hydrocarbon was n-Heneicosane (16.7%) while the major sterol was  $\beta$ -sitosterol (4.03%) and 15 components in the saponifiable matter its major component was hexadecanoic acid (19.93%). As a conclusion petroleum ether extract of Citrus medica L. leaves possess a significant estrogenic activity.

**Keywords:** Citrus medica; Gc/Ms; Toxicity; Estrogenic effect.

### 538. Chemical and Biological Study of Manilkara Zapota (L.) Van Royen Leaves (Sapotaceae) Cultivated in Egypt

Nesrin M. Fayek, Azza R. Abdel Monem, Mohamed Y. Mossa, Meselhy R. Meselhy and Amani H. Shazly

*Pharmacognosy Research*, 4: 85-91 (2012)

**Background:** Manilkara zapota (L.) Van Royen is an evergreen tree, native to the tropical Americas and introduced to Egypt as a fruiting tree in 2002. No previous study was reported on the plant cultivated in Egypt.

**Materials and Methods:** In this study, the leaves of the plant cultivated in Egypt were subjected to phytochemical and biological investigations.

The lipoidal matter was analyzed by GLC. Five compounds were isolated from the petroleum ether and ethyl acetate fractions of the alcoholic extract of the leaves by chromatographic fractionation on silica gel and sephadex, the structures of these compounds were identified using IR, UV, MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR. The LD<sub>50</sub> of the alcoholic and aqueous extracts of the leaves was determined and their antihyperglycemic, hypocholesterolemic and antioxidant activities were tested by enzymatic colorimetric methods using specific kits.

**Results:** Unsaturated fatty acids represent 32.32 % of the total fatty acids, oleic acid (13.95%), linoleic acid (10.18 %) and linoleic acid (5.96 %) were the major ones. The isolated compounds were identified as lupeol acetate, oleanolic acid, apigenin-7-O- $\alpha$ -L-rhamnoside, myricetin-3-O- $\alpha$ -L-rhamnoside and caffeic acid.

This is the first report about isolation of these compounds from Manilkara zapota except myricetin-3-O- $\alpha$ -L-rhamnoside, which was previously isolated from the plant growing abroad. The LD<sub>50</sub> recorded 80 g/Kg b. wt. for both the tested extracts, so they could

be considered to be safe. They exhibited antihyperglycemic, hypocholesterolemic and antioxidant activities.

**Conclusion:** The observed biological activities were attributed to the different chemical constituents present in the plant mainly its phenolic constituents.

**Keywords:** Antihyperglycemic; Hypocholesterolemic; Antioxidant; Flavonoids; Manilkara zapota (L.) Van royen; Triterpenes.

### 539. Antihyperglycemic Effect of Meryta Denhamii Seem. Fruits and Phytochemical Study of Their Saponin Content

Enas H. Abdel Rahman, Azza R. Abdel Monem and Amany A. Sleem

*Pharmacognosy Journal*, 4: 56-59 (2012)

In this study Meryta denhamii Seem. fruits (Araliaceae) were tested for the antihyperglycemic effect against alloxan induced hyperglycemia in rats using metformin as standard drug. The alcoholic extract and n-butanol fraction (saponins rich fraction) of the fruits exhibited significant antihyperglycemic effect (42.8 and 38.4 % of change, respectively, comparing to 67.1% for metformin). The n-butanol fraction was subjected to chemical study which resulted in isolation of four monodesmosidic oleanane saponins.

Their structures were established based on their MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectral data as 3-O- $\beta$ -D-glucopyranosyl] oleanolic acid, 3-O-[ $\alpha$ -D-glucuronopyranosyl] oleanolic acid, 3-O-[ $\beta$ -D-glucopyranosyl-(1-3)- $\alpha$ -L-arabinofuranosyl] oleanolic acid and 3-O-[ $\alpha$ -L-arabinofuranosyl-(1-4)- $\beta$ -D-glucuronopyranosyl] oleanolic acid.

**Keywords:** Meryta Denhamii Seem. Fruits; Triterpenoid Saponins; Oleanane Saponins; Antihyperglycemic.

### 540. Polyphenolics Content and Biological Activity of Plectranthus Amboinicus (Lour.) Spreng Growing in Egypt (Lamiaceae)

Seham S El-hawary, Rabie H El-sofany, Azza R Abdel-Monem, Rehab S Ashour and Amany A Sleem

*Pharmacognosy Journal*, 4: 45-54 (2012)

**Background:** Volatile oil, terpenoids, mainly diterpene and polyphenolic compounds including flavonoids and phenolic acids were previously isolated from different Plectranthus species. Plectranthus amboinicus (Lour.) Spreng growing abroad was subjected to phytochemical study resulted in isolation of several flavonoids, also the plant exhibited antioxidant, diuretic, anti-inflammatory, cytotoxic and antimicrobial activities.

**Materials and methods:** In this study ethyl acetate fraction of Plectranthus amboinicus (Lour.) Spreng leaves growing in Egypt was fractionated and chromatographed on silica gel and sephadex to isolate its phenolic constituents. The isolated compounds were identified using UV, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR. Total phenolics and tannins content of the leaves, stems and roots of Plectranthus amboinicus (Lour.) Spreng were determined using Folin-Ciocalteu and Folin-Denis reagents, respectively. Phenolic compounds of the stems and roots were identified using UPLC-MS analysis. Leaves, stems and roots of this plant were tested for antioxidant, anti-inflammatory, analgesic, diuretic, cytotoxic and antimicrobial activities.

**Results:** the isolated compounds were identified as 3-methoxy genkwanin, crismaritin, p-coumaric acid, caffeic acid, taxifolin, rosmarinic acid, apigenin and 5-O-methyl-luteolin. the stems showed the highest concentration of the total polyphenolics followed by the leaves then the roots (9.6, 8.4 and 5.4 mg/g of gallic acid equivalents, respectively), while the roots recorded the highest tannins content followed by the leaves then the stems (126, 90 and 81 µg/g of tannic acid equivalents, respectively). UPLC-MS analysis revealed the presence of caffeic acid, rosmarinic acid, coumaric acid and chrysoeriol in the stems and roots, while luteolin, quercetin and eriodictiol were detected only in the stems. the different extracts of the three organs exhibited antioxidant, anti-inflammatory, analgesic, diuretic, cytotoxic and antimicrobial activities with variable potency.

**Keywords:** Plectranthus amboinicus; Lamiaceae; Phenolic compounds; Antioxidant; Anti-Inflammatory; Analgesic; Diuretic; Cytotoxic; Antimicrobial.

#### 541. Phytochemical Screening, DNA Fingerprinting, and Nutritional Value of Plectranthus Amboinicus (Lour.) Spreng

Seham S. El-hawary, Rabie H. El-sofany, Azza R. Abdel-Monem and Rehab S. Ashour

*Pharmacognosy Journal*, 4: 10-13 (2012)

In this study Plectranthus amboinicus (Lour.) Spreng was subjected to phytochemical and genetic investigation, so that it could be properly identified. the results of phytochemical screening of the different organs of the plant (leaves, stems and roots) revealed the presence of steam volatile substances, sterols and / or triterpenes, flavonoids, carbohydrates and / or glycosides, catechol tannins in the three organs under investigation. A DNA sample of the plant was analyzed by Random Amplified Polymorphic DNA (RAPD) technique using eleven oligonucleotide primers. the analysis of RAPD data achieves the use of B-19 and B-6 primers for selective discrimination of this plant. Also, the nutritional value, including the total carbohydrates, total soluble sugars, proteins, amino acids and vitamins content, of the leaves, stems and roots was determined. the roots recorded the highest values of the total carbohydrates, total soluble sugars and proteins content (66.04%, 23.33% and 17.58%, respectively), followed by the leaves (48.12%, 4.74% and 16.45%, respectively) then the stems (44.62%, 3.10% and 9.52%, respectively). the three organs under investigation contain essential amino acids in moderate amounts compared to the WHO daily recommended doses. They are rich in vitamins and can be used as a vitamins supplement.

**Keywords:** Plectranthus amboinicus; Dna fingerprinting; Phytochemical screening; Nutritional value.

#### 542. Chemical and Biological Assessment of African Olive Leaf Extract

Essam A Abdel-Sattar, Hossam M Abdallah, Alaa Khedr and Ashraf B Abdel-Naim

*Research Journal of Pharmaceutical, Biological and Chemical Sciences*, 3: 155-172 (2012)

Since the leaves of the Mediterranean olive have been recommended in the literatures as a remedy for the treatment of diabetes and hypertension, as well as they also contain antioxidant

agents, we decided to investigate the possible biological effects of chemically standardized African olive leaf extract (OLE) of *Olea europaea* subspecies *africana* growing wild in Saudi Arabia. Chemical standardization of oleuropein in African OLE using HPLC showed a high percentage reached up to 30%. Total phenols were 36 mg/g calculated as gallic acid equivalents (GAE) while the total amount of flavonoids was 1.35 mg/g calculated as rutin equivalents (RE).

The in vitro antioxidant activity of African OLE showed an IC50 of 60.2 µg/ml using diphenylpicrylhydrazine (DPPH) assay. the biological analysis of OLE included screening for potential antihypertensive and hypoglycemic activity.

Daily treatment for six weeks with African OLE (200 mg/kg) resulted in partial mitigation of L-N-nitroarginine methyl ester (L-NAME) induced hypertension relative to the untreated group. OLE was tested at three dose levels (100, 300, 500 mg/kg) for anti-hyperglycemic activity.

OLE exhibited blood glucose-lowering activity against streptozotocin (STZ) induced hyperglycemia in rats. the highest dose of OLE (500 mg/kg) showed a significant decrease in blood-glucose level by 69.6% at the 4th week of treatment compared to the untreated diabetic group.

There fore, OLE showed protective effects against L-NAME-induced hypertension and STZ-induced diabetes. the mechanisms underlying the observed anti-hyperglycemic activity can be attributed, at least partly, to enhance skeletal muscle uptake of glucose, inhibition of hepatic gluconeogenesis, insulinomimetic effect and antioxidant activity.

**Keywords:** *Olea africana*; African olive; Anti-Hyperglycemic; Antihypertensive; Antioxidant; Hplc.

#### 543. Antidiabetic Activity of Standardized Extracts of Balanites Aegyptiaca Fruits using Cell-Based Bioassays

Amira Abdel Motaal, Sherif Shaker and Pierre S. Haddad

*Pharmacognosy Journal*, 4: 27-31 (2012)

The antidiabetic activities of different extracts and fractions of *Balanites aegyptiaca* were tested in cultured C2C12 skeletal muscle cells and 3T3-L1 adipocytes. an 18-h treatment with 200 µg/mL of the sugars fraction (A1) showed the highest activity as it increased basal glucose uptake by 52% in muscle cells; which is twice the activity of 100 nM insulin [insulin equivalent (IE) = 2.0 ± 0.07]. the dichloromethane (E) and ethyl acetate (F) successive extracts exerted 37 and 41% increase in the glucose uptake, respectively.

Only E and F accelerated the triglyceride accumulation in pre-adipocytes undergoing differentiation, comparably with 10 µM rosiglitazone [rosiglitazone equivalent (RE) was 1.6 ± 0.3 and 0.7 ± 0.1, respectively]. Gas chromatography (GC) analysis of A1 revealed the presence of xylose, rhamnose, sorbitol, fructose, galactose and glucose.

The active extracts E and F were standardized by high-performance liquid chromatography (HPLC) to contain 0.031 and 0.239% of rutin, 0.007 and 0.004% of isorhamnetin, respectively.

**Keywords:** Balanites; C2c12; Diabetes; Fruit; Sugars; 3T3µL1.



#### 544. Four Butyrolactones and Diverse Bioactive Secondary Metabolites from Terrestrial *Aspergillus Flavipes* Mm2: Isolation and Structure Determination

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*Organic and Medicinal Chemistry Letters*, 1,2: 1-8 (2012)

The chemical constituents and biological activities of the terrestrial *Aspergillus flavipes* MM2 isolated from Egyptian rice hulls are reported. Seven bioactive compounds were obtained, of which one sterol: ergosterol (1), four butyrolactones: butyrolactone I (2), aspulvinone H (3), butyrolactone-V (6) and 4,4'-dihydroxypulvinone (7), along with 6-methylsalicylic acid (4) and the cyclopentenone analogue; terrien (5). Structures of the isolated compounds were deduced by intensive studies of their 1D & 2D NMR, MS data and comparison with related structures. The strain extract and the isolated compounds (1-7) were biologically studied against number of microbial strains, and brine shrimp for cytotoxicity. In this article, the taxonomical characterization of *A. flavipes* MM2 along with its upscale fermentation, isolation and structural assignment of the obtained bioactive metabolites, and evaluate their antimicrobial and cytotoxic activities were described.

**Keywords:** *Aspergillus flavipes* Mm2; Butyrolactones; Biological studies.

#### 545. Antihyperglycemic and Antioxidant Activities and Chemical Composition of *Conyza Dioscoridis* (L.) Desf. Dc. Growing in Egypt

Soheir M. El Zalabani, Mona H. Hetta, Samir A. Ross, Amira M. Abo Youssef, Mohamed A. Zaki and Ahmed S. Ismail

*Australian J. of Basic and Applied Sciences*, 6: 257-265 (2012)

The antihyperglycemic activity of total EtOH 70% extracts of leaf, flower and root of *Conyza dioscoridis* (L.) Desf. was tested on Streptozotocin – induced diabetic rats using 50mg/kg orally and 10mg/kg of Gliclazide. The root extract exerted the most significant decrease in serum glucose ( $106.45 \pm 8.25$  nmol/ml) and malondialdehyde ( $2.20 \pm 0.38$  nmol/ml) and the most significant increase in serum insulin ( $6.53 \pm 0.83$  ng/ml) and blood glutathione ( $44.25 \pm 4.58$  mg %) levels, ( $P < 0.05$ ), results were comparable to the standard. The antioxidant activity of the roots showed 76.5% of inhibition versus 88.2% of the standard. Thirteen compounds were isolated and identified using spectroscopic techniques (UV,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, DEPT and 2D NMR) to be: cholesterol (1),  $\beta$ -sitosterol (2),  $\alpha$ -amyrin (3), conyzin (4), lupeol acetate (5),  $\beta$ -sitosterol glucoside (6), gallic acid (7), p-caffeic acid (8), syringic acid (9), rutin (10), quercitrin (11), quercetin (12) and kaempferol (13). Compounds (6) and (8) are newly reported in the species.

**Keywords:** *Conyza dioscoridis*; Ld50; Antihyperglycemic; Antioxidant; Constituents.

#### 546. Genetic Profiling, Chemical Characterization and Biological Evaluation of Two *Conyza* Species Growing in Egypt

Soheir M. El Zalabani, Mona H. Hetta, Ahmed S. Ismail

*Journal of Applied Pharmaceutical Science*, 2: 54-61 (2012)

The present report is a comparative investigation of two *Conyza* species growing wild in Egypt namely, *Conyza dioscoridis* (L.)

Desf. and *Conyza bonariensis* (L.) Cronquist. It comprises a genetic and chemical characterization of the plants, as well as an evaluation of their biological activities. The DNA fingerprints of the two species were established based on a polymerase chain reaction (PCR) procedure using ten decamer primers. Further characterization of the plants was performed via determination of pharmacopoeial constants, phytochemical screening and estimation of phenolic content (total phenolics, tannins and flavonoids). The ethanol (70%) extracts of *C. dioscoridis* (EECD) and *C. bonariensis* (EECB) were subjected to acute toxicity study to determine their LD50; the anti-inflammatory, antimicrobial and cytotoxic activities were then evaluated.

Screening for potential cytotoxicity was carried out both by Brine Shrimp Lethality Test and Sulphorodamine-B assay on three human cell lines viz., breast carcinoma (MCF7), colorectal carcinoma (HCT116) and cervical carcinoma (HELA) cell lines. The DNA profiling revealed a similarity index of 88.89% between the investigated species. The variability observed among the pharmacopoeial constants constitute a valuable differential criterion; the total ash, acid insoluble ash, water soluble ash and crude fiber values obtained for *C. bonariensis* exceeded (17, 5, 10 and 3.5%, respectively) those for *C. dioscoridis*; meanwhile, the moisture content was higher (10%) in the latter. The phytochemical screening of EECD and EECB revealed the presence of flavonoids, steroids, terpenoids and tannins in both species. Estimation of phenolic contents (total phenolics, tannins and flavonoids expressed as gallic acid, tannic acid and rutin equivalents, respectively) showed that EECD contains higher amounts of all these constituents when compared to EECB (1.17 vs. 0.96 mg/g, total phenolics; 2.43 vs. 1.83 mg/g, tannins and 0.62 vs. 0.29 mg/g, flavonoids). EECD and EECB were found to be safe (LD50 upto 0.5g/kg).

Throughout evaluation of the antimicrobial activity against a set of microbial strains and potential cytotoxicity against MCF7, EECD appeared more efficient (MIC: 200-400  $\mu\text{g/ml}$  and IC50: 2.97  $\mu\text{g/ml}$ , respectively); meanwhile, the effect of EECB was more significant on HCT116 and HELA (IC50: 21 and 5.4  $\mu\text{g/ml}$ , respectively). Results of in-vivo assessment of the anti-inflammatory activity showed that the inhibitory effect of EECD was more prominent than that of EECB (74.20% vs. 59.0%). However, the effect of the extracts was reversed in the Brine Shrimp Lethality test (30% vs. 40% lethality, respectively).

**Keywords:** *Conyza dioscoridis*; *Conyza bonariensis*; DNA profiling; Chemical characterization; Bioactivities.

#### 547. Lipoidal Content and Anti-Inflammatory Activity of *Adenanthera Pavonina* L. Leaves

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*Journal of Applied Sciences Research*, 8: 207-214 (2012)

The dried powdered leaves of *Adenanthera pavonina* L. were successively extracted with solvents of increasing polarities (petroleum ether, chloroform, ethyl acetate and aqueous ethanol). The total ethanol extract of the powder was also prepared. The petroleum ether extract was fractionated into unsaponifiable matter (USM) and fatty acids (FA). The FA fraction was methylated to give FAME fraction. GC/MS analysis of the USM revealed the identification of fifty compounds represented 80.1 % of the total USM, with squalene (16.38%) as the major compound followed by n- hentriacontane (14.61%), phytol (10.29%) and 2,2-diethoxy ethanamine (8.34%). Oxygenated compounds represented 27.22 % of the total USM.

GC/MS analysis of FAME fraction revealed the identification of twenty four compounds represented 88.49 % of the total fraction, with methyl hexadecanoate (19.25%) as the major compound followed by methyl 9,12,15- octadecatrienoate (12.69 %), methyl eicosanoate (10.14%), methyl-9- octadecenoate (10.06%) and methyl 9,12-octadecadienoate (9.23%). the unsaturated FA represented 32.52 % of the total fraction. Column chromatographic fractionation of the petroleum ether extract resulted in the isolation of the sterol fraction which was analyzed by GLC and isolation for the first time of three triterpenoid compounds, which were identified as 22-hydroxy hopan-3-one, 24-methylene cycloartanol and betulinic acid. the LD50 of the total ethanol extract was determined. The acute anti- inflammatory activity of the total ethanol and successive extracts was evaluated by the carrageenan induced rat hind paw oedema test, which revealed significant effects of all extracts. the most potent effect was exhibited by 100 mg / kg b.wt. of the total ethanol extract (91.27 % potency) in comparison with indomethacin (100 % potency).

**Keywords:** Adenanthera bavonina; Unsaponifiable matter; Fatty acids; Triterpenes; Sterols; Antiinflammatory activity.

#### 548. Phytochemical Investigation of Caralluma Wissmannii O. Schwart

Abdelaziz M. Dawidar, Ahmed Y. Mubarak, Mamdouh Abdel-Mogib and Essam Abdelsattar

*Research Journal of Pharmaceutical, Biological and Chemical Sciences*, 3 (2): 884-892 (2012)

The chromatographic investigation of Caralluma wissmannii O. Schwart. led to the isolation of two new pregnane glycosides (5, 6) and five known compounds (1-4, 7). the new pregnane glycosides were identified using spectral means (NMR and MS) as 12-tigiloyl-tayloron 3 $\beta$ -D-thevetopyranosyl-(1 $\rightarrow$ 4)- $\beta$ -D-cymaropyranosyl- (1 $\rightarrow$ 4)-  $\beta$ -D-cymaropyranoside 5, 12-tigiloyl-tayloron 3 $\beta$ -D-thevetopyranosyl-(1 $\rightarrow$ 4)- $\beta$ -D-cymaropyranoside 6. the known compounds were identified as 3,4-seco-lup-20(29)-en-3-oic acid methyl ester 1, lupeol 2, stigmasterol 3,  $\beta$ - sitosterol 4, and luteolin 3',4'-di-O- $\beta$ -D-glucopyranoside 7. This is the first report on the phytochemical investigation of C. wissmannii.

**Keywords:** Asclepiadaceae; Caralluma wissmannii; Seco-Triterpenoid; Pregnane glycosides; Flavone glycoside.

#### 549. Activity of Chorisia Insignis Hbk. Against Larynx Carcinoma and Chemical Investigation of its Polar Extracts

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*Journal of Applied Sciences Research*, 8 (11): 5564-5571 (2012)

The chemical composition of the ethyl acetate and n-butanol fractions of the 70% ethanol extract of Chorisia insignis HBK. leaves (Family Bombacaceae) was studied. Ten compounds were identified from the nbutanol fraction, 3,4,5-trihydroxy cyclohexan-1-ol (1 $\rightarrow$ 1)-rhamnoside and phenyl ester of 3,5-dimethyl gallic acid were isolated by PPC for the first time from the plant, while kampferol 5,7,4'-trimethyl ether 3-O- $\alpha$ -Lrhamnopyranosyl-(1 $\rightarrow$ 6 $\rightarrow$ 6 $\rightarrow$ )-O- $\beta$ -D-glucuronide, dihydroquercetin 5,7,3',4'-tetramethyl ether 3-O-glucuronide, quercetin, 5,4',5'-trihydroxy-7,3'-dimethoxy 2,3-dihydroflavonol, quercetagenin-5,6,7,3',4'-pentamethyl ether 3-O- $\beta$ -D-glucuronide, 5,8,5'-trihydroxy-6,7,3',4'-tetramethoxy 3-O-glucuronyl dulcitol, dihydroquercetin 3-O-  $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 6 $\rightarrow$ 6 $\rightarrow$ )-O- $\beta$ -D-glucopyranoside and quercetin 5,7,3'-trimethyl ether 3-O- $\alpha$ -

Lrhamnopyranosyl-(1 $\rightarrow$ 6 $\rightarrow$ 6 $\rightarrow$ )-O- $\beta$ -D-glucopyranoside analyzed using HPLC/MS. HPLC/MS-MS technique was applied to investigate the ethyl acetate fraction and seven compounds were identified as: 5,6,7,3',4',5'- hexahydroxy-dihydroflavonol-3-O-glucuronide, 5,6,7,3',4',5'-hexahydroxy-dihydroflavonol-3-O- $\beta$ -D- $\Delta^{1,3}$ - octadienyl-glucuronide, kampferol 5,7,4'-trimethyl ether 3-O-ethylene glycol, 3,5,4'-trimethoxy-7-isobutyl flavone, 3,5,4'-trimethoxy-7-isobutyl dihydroflavone, dihydroquercetin-4'-methyl ether 3-O- $\beta$ -D-n-hexyldiglucuronide and quercetin-4'-methyl ether 3-O  $\beta$ -D-n-hexyl-diglucuronide. the potential cytotoxicity of the total alcohol extract and the successive fractions was determined against different human cell lines. All showed significant cytotoxic activity against the larynx cell line except the chloroform fraction.

**Keywords:** Chorisia insignis; Cytotoxicity; Hplc/ms; phenyl ester of 3,5-dimethyl gallic acid; 3;4;5- Trihydroxy cyclohexan-1-Ol (1 $\rightarrow$ 1)-Rhamnoside.

#### 550. Polyphenol Metabolism Provides A Screening Tool for Beneficial Effects of Onobrychis Viciifolia (Sainfoin)

Jana Thill, Ionela Regos, Mohamed Farag, Asma F. Ahmad, Justyna Kusek, Ana Castro, Karin Schlangen, Christine Hayot Carbonero, Ilya Z. Gadjev, Lydia M.J. Smith, Heidi Halbwirth, Dieter Treutter and Karl Stich

*Phytochemistry*, 82: 67-80 (2012) IF: 3.351

Onobrychis viciifolia (sainfoin) is a traditional fodder legume showing multiple benefits for the environment, animal health and productivity but weaker agronomic performance in comparison to other legumes. Benefits can be mainly ascribed to the presence of polyphenols. the polyphenol metabolism in O. viciifolia was studied at the level of gene expression, enzyme activity, polyphenol accumulation and antioxidant activity. A screening of 37 accessions regarding each of these characters showed a huge variability between individual samples. Principal component analysis revealed that flavonols and flavan 3-ols are the most relevant variables for discrimination of the accessions. the determination of the activities of dihydroflavonol 4-reductase and flavonol synthase provides a suitable screening tool for the estimation of the ratio of flavonols to flavan 3-ols and can be used for the selection of samples from those varieties that have a specific optimal ratio of these compounds for further breeding.

**Keywords:** Onobrychis viciifolia (Sainfoin); Chemometrics; Pca; Flavonoids enzymes; Flavonoid genes.

#### 551. Comparative Metabolite Profiling and Fingerprinting of Medicinal Licorice Roots Using A Multiplex Approach of Gc–Ms, Lc–Ms and 1D Nmr Techniques

Farag M.A., Porzel A. and Wessjohann L.A.

*Phytochemistry*, 76: 60-72 (2012) IF: 3.351

Glycyrrhiza glabra, commonly known as licorice, is a popular herbal supplement used for the treatment of chronic inflammatory conditions and possesses anticancer and antiviral activities. This species contains a plethora of phytochemicals including terpenoids, saponins, flavonoids, polyamines and polysaccharides. the full complement of bioactive compounds has yet to be elucidated, a step necessary in order to explain its

medicinal use. There are over 30 species in the *Glycyrrhiza* genus world-wide, most of which have been little characterized in terms of phytochemical or pharmacological properties. Here, large scale multi-targeted metabolic profiling and fingerprinting techniques were utilized to help gain a broader insight into *Glycyrrhiza* species chemical composition. UV, MS and NMR spectra of extracted components were connected with NMR, MS, and multivariate analyses data from *Glycyrrhiza glabra*, *Glycyrrhiza uralensis*, *Glycyrrhiza inflata* and *Glycyrrhiza echinata*. Major peaks in <sup>1</sup>H NMR and MS spectra contributing to the discrimination among species were assigned as those of glycyrrhizin, 4-hydroxyphenyl acetic acid, and glycosidic conjugates of liquiritigenin/isoliquiritigenin. Primary metabolites profiling using GC-MS revealed the presence of cadaverine, an amino acid, exclusively found in *G. inflata* roots. Both LC-MS and NMR were found effective techniques in sample classification based on genetic and/or geographical origin as revealed from derived PCA analysis.

**Keywords:** *Glycyrrhiza glabra*; Licorice; Metabolomics; Quality control; Nmr; Ms; Chemometrics.

### 552. Diversity of Phenolic Profiles in the Fruit Skin of *Prunus domestica* Plums and Related Species

Treutter D, Wang D, Farag MA, Baires GD, Rühmann S and Neumüller M.

*Journal of Agricultural and Food Chemistry*, 60: 12011-12019 (2012) IF: 2.823

The fruits of the European plum *Prunus domestica* exhibit a great diversity in appearance including skin colors. This study attempts to elucidate the phenylpropanoid and flavonoid profiles of 28 plum varieties belonging to *P. domestica* and related species as well as hybrids. A total of 49 phenolic compounds extracted from the fruit skin were quantitatively evaluated in an HPLC-DAD-based metabolomic study. The total phenolic contents of the cultivars varied among 0.4-29.9 mg/g fresh weight. The predominant anthocyanins were glycosides of cyanidin and peonidin, and rutin was the principal flavonol, whereas neochlorogenic acid and *n*-chlorogenic acid were the main hydroxycinnamic acids. Aside from these major phenolic classes, a group of tentatively identified flavones and several acylated flavonoids were also found. Principal component analysis revealed that anthocyanins and hydroxycinnamic acids contributed most to variety separation. The heterogeneity between the different varieties was also assessed using hierarchical cluster analysis of sample phenolics profile. A simple separation of species could not be found confirming the close relationship among them.

**Keywords:** Phenylpropanoid; Flavonoid; Rosaceae; Plum; Metabolome; Chemotaxonomy.

### 553. Volatiles Profiling in Medicinal Licorice Roots Using Steam Distillation and Solid-Phase Microextraction (Spme) Coupled to Chemometrics

Mohamed A. Farag and Ludger A. Wessjohann

*J Food Science*, 77: 1179-1184 (2012) IF: 1.658

Licorice (*Glycyrrhiza glabra* L.) is a plant of considerable commercial importance in traditional medicine and for the flavor and sweets industry. Although *Glycyrrhiza* species are very

competitive targets for phytochemical studies, very little is known about the volatiles composition within that genus, although such knowledge can be suspected to be relevant for understanding the olfactory and taste properties. To provide insight into *Glycyrrhiza* species aroma composition and for its use in food and pharmaceutical industry, volatile constituents from *G. glabra*, *G. inflata*, and *G. echinata* roots were profiled using steam distillation and solid-phase microextraction. Two phenols, thymol and carvacrol, were found exclusively in essential oil and headspace samples of *G. glabra*, and with highest amounts for samples that originated from Egypt. In *G. echinata* oil, (2E, 4E)-decadienal (21%) and  $\beta$ -caryophyllene oxide (24%) were found as main constituents, whereas 1 $\alpha$ , 10 $\alpha$ -epoxyamorpho-4-ene (13%) and  $\beta$ -dihydroionone (8%) predominated *G. inflata*. Principal component and hierarchical cluster analyses clearly separated *G. echinata* and *G. inflata* from *G. glabra*; with phenolics and aliphatic aldehydes contributing mostly for species segregation.

**Keywords:** Essential oil; Gc/MS; *Glycyrrhiza glabra* L.; *Glycyrrhiza inflata*; *Glycyrrhiza echinata*.

### Dept. of Pharmacology and Toxicology

### 554. Comparative Study of the Cardioprotective Effects of Local and Remote Preconditioning in Ischemia/Reperfusion Injury

Lamiaa A. Ahmed, Hesham A. Salem, Amina S. Attia, Azza M. Agha

*Life Sciences*, 90: 249-256 (2012) IF: 2.527

**Aims:** Though the cardioprotective effects of local or remote preconditioning have been estimated, it is still unclear which of them is more reliable and provides more cardioprotection. The present investigation was directed to compare, in one study, the cardioprotective effects of different cycles of local or remote preconditioning in ischemia/reperfusion (I/R)-induced electrophysiological, biochemical and histological changes in rats. **Main methods:** Rats were randomly assigned into 10 groups. Groups 1 and 2 were normal and I/R groups, respectively. Other groups were subjected to 1, 2, 3, 4 cycles of local or remote preconditioning before myocardial I/R (40 min/10 min). Heart rate and ventricular arrhythmias were recorded during I/R progress. At the end of reperfusion, plasma creatine kinase-MB (CK-MB) activity and total nitrate/nitrite (NOx) were determined. In addition, lactate, adenine nucleotides, thiobarbituric acid reactive substances (TBARS), reduced glutathione (GSH) and myeloperoxidase (MPO) activity were estimated in the heart left ventricle. Histological examination was also performed to visualize the protective cellular effects of the effective cycle of local or remote preconditioning. **Key findings:** In general, local preconditioning was more effective than remote preconditioning in reducing ventricular arrhythmias, CK-MB release, lactate accumulation and elevated MPO activity as well as preserving adenine nucleotides. Concerning the most effective group in each therapy, 3 cycles of local preconditioning provided more cardioprotection than that of remote preconditioning in the histological examination.

**Significance:** Despite being invasive, local preconditioning provided more effective cardioprotection than remote preconditioning in ameliorating the overall electrophysiological, biochemical and histological changes.

**Keywords:** Ischemia; Local; Myocardial; Preconditioning; Remote; Reperfusion.

### 555. Thymoquinone: Novel Gastroprotective Mechanisms

Mahmoud-Awny Magdy, El-Abhar Hanan and El-Maraghy Nabila

*Eur J Pharmacol*, (2012) IF: 2.516

Ample of evidence proved the gastroprotective effect of thymoquinone (TQ), the main constituent of *Nigella sativa* oil; however the full mechanistic cassette on the gastric ulcer etiopathogenesis is not fully elucidated. The aim of the present work is to unveil some of the possible mechanisms. Animals were injected with vehicle TQ (10 & 20 mg/kg), omeprazole (10 & 20 mg/kg) or their combination (10 mg/kg). Thirty minutes later, pyloric ligation was carried out and followed consequently with ischemia for another 30 min, abided by reperfusion for 120 min. The ischemia/reperfusion insult increased the gastric acid secretion, acid output, and pepsin, as well as the gastric mucosal content/ activity of lipid peroxide, proton pump and myeloperoxidase, along with ulcer index. However, content/ activity of gastric mucin, reduced glutathione, total nitric oxide, and superoxide dismutase were decreased.

TQ, especially the high dose level, corrected the altered parameters in a comparable manner to that of the reference drug used, omeprazole. In addition, when the low doses were combined they add to each other to reach the effect of the high dose of either drug. These results showed that apart from its known antioxidant properties, TQ has novel gastroprotective mechanisms via inhibiting proton pump, acid secretion and neutrophil infiltration, while enhancing mucin secretion, and nitric oxide production.

**Keywords:** Thymoquinone; Mucin; Proton pump; Nitric oxide; Myeloperoxidase; Ischemia/reperfusion.

### 556. Protective Effects of Magnesium Supplementation on Metabolic Energy Derangements in Lipopolysaccharide-Induced Cardiotoxicity in Mice

Lamiaa A.Ahmed

*European Journal of Pharmacology*, 694: 75-81 (2012) IF: 2.516

Metabolic derangements and bioenergetic failure are major contributors to sepsis-induced multiple organ dysfunctions. Due to the well known role of magnesium (Mg) as a cofactor in many enzymatic reactions that involve energy creation and utilization, the present investigation was directed to estimate the cardioprotective effect of Mg supplementation in lipopolysaccharide (LPS)-induced metabolic energy changes in mice. Oral doses of Mg aspartate (20 or 40 mg/kg) were administered once daily for 7 days. Mice were then subjected to a single intraperitoneal injection of LPS (2 mg/kg). Plasma was separated 3 h after LPS injection for determination of creatine kinase-MB activity. Animals were then sacrificed and the hearts were separated for estimation of tissue thiobarbituric acid reactive substances, reduced glutathione, lactate, pyruvate, adenine nucleotides, creatine phosphate and cardiac Na<sup>+</sup>,K<sup>+</sup>-ATPase activity. Finally, electron microscopic examination was performed to visualize the protective effects of Mg pretreatment on mitochondrial ultrastructure. In general, the higher dose of Mg was more effective than the lower dose in ameliorating creatine kinase-MB elevation and the state of oxidative stress, lactate accumulation, pyruvate reduction as well as preserving creatine phosphate, adenine nucleotides and Na<sup>+</sup>,K<sup>+</sup>-ATPase activity.

Moreover, the higher dose of Mg provided a significant cardioprotection against the mitochondrial ultrastructural changes. Mg therapy can afford a significant protection against metabolic energy derangements and mitochondrial ultrastructural changes induced by LPS cardiotoxicity in mice.

**Keywords:** Cardiotoxicity; Energy; Lipopolysaccharide; Magnesium.

### 557. Stw 5 Is Effective in Dextran Sulfate Sodium-Induced Colitis in Rats

Walaa Wadie, Heba Abdel-Aziz, Hala F. Zaki, Olaf Kelber, Dieter Weiser and Mohamed T. Khayyal

*Int. J. Colorectal Dis*, 27: 1445-1453 (2012) IF: 2.385

Purpose an herbal preparation, STW 5, used clinically in functional dyspepsia and irritable bowel syndrome, has been shown to possess properties that may render it useful in inflammatory bowel disease (IBD). the present work was conducted to study its effectiveness in a rat model of IBD.

Methods an experimental model reflecting ulcerative colitis in man was adopted, whereby colitis was induced in Wistar rats by feeding them 5 % dextran sulfate sodium (DSS) in drinking water for one week. STW 5 and sulfasalazine (as a reference standard) were administered orally daily for 1 week before colitis induction and continued during DSS feeding. the animals were then sacrificed, and the severity of colitis was evaluated macroscopically and microscopically. Colon samples were homogenized for determination of reduced glutathione, tumor necrosis factor- $\alpha$ , and cytokineinduced neutrophil chemoattractant-3 as well as myeloperoxidase, glutathione peroxidase, and superoxide dismutase. in addition, colon segments were suspended in an organ bath to test their reactivity towards carbachol, KCl, and trypsin. Results STW 5 and sulfasalazine were both effective in preventing the shortening of colon length and the increase in both colon mass index and total histology score as well as the changes in biochemical parameters measured except changes in dismutase activity. DSS-induced colitis led to marked depression in colonic responsiveness to the agents tested ex vivo, an effect which was normalized by both drugs. Conclusions the findings point to a potential usefulness of STW 5 in the clinical setting of ulcerative colitis.

**Keywords:** Dss Colitis; Colonic Responsiveness; Stw 5.

### 558. Angiotensin Antagonists and Renal Ischemia/Reperfusion: Possible Modulation by L-Carnitine

Maha A. Rabie, Hala F. Zaki, Ashraf K. Bahgat and Hekma A. Abd El-Latif

*Bulletin of Faculty of Pharmacy, Cairo University*, 50: 7-16 (2012) IF: 2

**Introduction:** Ischemia/reperfusion (I/R) injury and therapy with angiotensin antagonists were shown to exert significant effects on the kidney. the study aimed to investigate the protective effect, if any, of L-carnitine on the initial nephrotoxic effects of ramipril or losartan on I/R insult in rats.

**Methods:** I/R was induced through bilateral renal ischemia for 60 min followed by 60 min of reperfusion. Groups I and II received both 1% Tween 80 p.o. and saline i.p. and served as sham-operated and I/R control groups, respectively. Groups III-VII

received 2 weeks pretreatment with ramipril (1 mg/kg; p.o.), losartan (10 mg/kg; i.p.), L-carnitine (200 mg/kg; i.p.) and L-carnitine plus either ramipril or losartan, respectively. Chosen markers included kidney function tests, oxidative stress and inflammatory biomarkers as well as histological assessment of kidney sections.

**Results:** I/R increased plasma creatinine and urea levels but decreased albumin level; meanwhile, it increased the kidney tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) content, myeloperoxidase (MPO) and plasma lactate dehydrogenase (LDH) activities. Moreover, I/R decreased kidney carnitine, glutathione, and total nitrate/nitrite contents as well as superoxide dismutase activity. Both ramipril and losartan elevated creatinine and urea levels; meanwhile, they lowered raised LDH, TNF- $\alpha$  and MPO as compared to I/R-control group. L-carnitine alone or combined with either agent decreased creatinine and urea levels, LDH and MPO activities as well as TNF- $\alpha$  content as compared to ramipril or losartan monotherapy.

**Conclusions:** L-carnitine can protect the kidney from the initial deleterious effects of either ramipril or losartan in rats subjected to I/R most probably by virtue of its antioxidant and anti-inflammatory effects.

**Keywords:** L-Carnitine; Ischemia/Reperfusion; Losartan; Oxidative Stress; Ramipril.

### 559. Possible Modulation of the Antidiabetic Effect of Rosiglitazone by Buspirone

Wafaa R. Mohamed, Gamal A. El Sherbiny, Hala F. Zaki and Mostafa E. El Sayed

*Bulletin of Faculty of Pharmacy, Cairo University*, 50: 73-79 (2012) IF: 2

Diabetes mellitus (DM) is a group of metabolic disorders characterized by chronic hyperglycemia resulting from relative or absolute insulin deficiency with or without insulin resistance. As anxiolytics may have influence on glycemic control in diabetics, the present study was conducted to investigate the possible influence of buspirone in streptozotocin-induced DM and its possible interactions with rosiglitazone, an insulin sensitizer. Diabetes was induced by streptozotocin (50 mg/kg i.p.). Rats were classified into five groups namely: normal control, diabetic control, rosiglitazone (10 mg/kg p.o.), buspirone (20 mg/kg i.p.) or combination of both rosiglitazone and buspirone, respectively. All groups received daily treatments for 2 weeks after induction of DM including the normal group which received 1% Tween 80. There was no significant interaction between rosiglitazone and buspirone on the levels of serum glucose, insulin and C-peptide or liver glycogen content. Similarly, no interaction was observed between rosiglitazone and buspirone on oxidative stress parameters including serum malondialdehyde and blood glutathione levels or blood superoxide dismutase activity. In conclusion, the present study revealed that co-administration of buspirone with rosiglitazone does not produce serious reactions and buspirone can be safely administered as an anxiolytic in diabetic patients treated with rosiglitazone.

**Keywords:** Diabetes; Anxiety; Rosiglitazone; Buspirone; Insulin; Oxidative Stress.

### 560. Diverse Effects of Variant Doses of Dexamethasone in Lithium–Pilcarpine Induced Seizures in Rats

Muhammad Y. Al-Shorbagy, Bahia M. El Sayeh and Dalaal M. Abdallah

*Can. J. Physiol. Pharmacol*, 90: 13-21 (2012) IF: 1.953

Corticosteroids are used in the management of several epileptic ailments; however, their effectiveness in combating seizures remains controversial, with pro- and anti-convulsive effects ascribed. The current study aimed to address the modulatory effect of dexamethasone (DEX) utilizing 3 dose levels (5, 10, and 20 mg/kg body mass of male Wistar rat) in the rat lithium–pilcarpine (Li-PIL) epilepsy model. Li-PIL induced seizures that were associated with neuronal cell loss in the CA3 region, and increased prostaglandin (PGE)<sub>2</sub>, tumor necrosis factor (TNF)- $\alpha$ , interleukin (IL)-10, nitric oxide, and neutrophil infiltration in the hippocampus. However, Li-PIL compromised the oxidant–antioxidant balance of the hippocampus.

Effective anticonvulsant activity was only observed with 10 mg DEX/kg body mass, which reduced seizure production and incidence, as well as neuronal cell loss in the CA3 region. At this anticonvulsant dose, enhancements in the antioxidant system and IL-10, as well as suppression of altered inflammatory markers were observed. Conversely, doubling the dose showed a tendency to shorten seizure latency, and neither affected seizure incidence nor CA3 neuronal cell loss. These effects were associated with an increase in levels of PGE<sub>2</sub> and TNF- $\alpha$ . The present study found a lack of protection at 5 mg DEX/kg body mass, an anticonvulsant effect at 10 mg/kg, and a loss of protection at 20 mg/kg in the Li-PIL epilepsy model, which indicates that there is an optimal dose of DEX for preventing the induction of seizures.

**Keywords:** Convulsion; Lithium–Pilcarpine; Dexamethasone; Inflammation; Cytokines; Nitric Oxide; Oxidative Stress; Rats.

### 561. Potential Protective Effect of Taurine Against Dibromoacetonitrile-Induced Neurotoxicity in Rats

Rabab H. Sayed, Hesham A. Salem and Bahia M. El-Sayeh

*Environmental Toxicology and Pharmacology*, 34: 849-857 (2012) IF: 1.469

Dibromoacetonitrile (DBAN) is a disinfection by-product of water chlorination. Epidemiological studies indicate that it might present a potential hazard to human health. The present study aimed to investigate the possible neurotoxicity of DBAN in rats and possible protection by taurine. Based on initial dose–response experiment, DBAN (60 mg/kg) was administered orally for 7 days. DBAN administration significantly impaired behavior of rats. Further, DBAN produced significant decrease of monoamines,  $\gamma$ -aminobutyric acid (GABA), glutamate contents, acetylcholinesterase (AChE) and aspartate aminotransferase (AST) activities, in rat brain. On the other hand, a significant increase in malondialdehyde (MDA), nitric oxide (NO) contents and lactic dehydrogenase (LDH) activity was observed. Co-administration of taurine (200 mg/kg, i.p.) with DBAN mitigated most tested parameters. In conclusion, the present study indicates that DBAN has the propensity to cause significant oxidative damage in rat brain. However, taurine has a promising role in attenuating the obtained hazardous effects of DBAN.

**Keywords:** Dibromoacetonitrile; Water Disinfection by-Product; Neurotoxicity; Oxidative Stress; Taurine.

### 562. Cardioprotective Effects of Ozone Oxidative Preconditioning in an in Vivo Model of Ischemia/Reperfusion Injury in Rats

Ahmed, Lamiaa A.; Salem, Hesham A.; Mawsouf, Mohamed N.; Attia, Amina S.; Agha, Azza M.

*Scandinavian Journal of Clinical & Laboratory Investigation*, 72: 345-354 (2012) IF: 1.156

**Background:** Several studies have demonstrated the beneficial effects of ozone oxidative preconditioning in several pathologies characterized by cellular oxidative and inflammatory burden. The present study was designed to investigate the cardioprotective effects of oxidative preconditioning in ischemia/reperfusion (I/R) injury.

**Methods:** Rats were randomly assigned into five groups. Groups 1 and 2 were normal and I/R groups, respectively. Two of the other groups received two different doses of ozone therapies by rectal insufflations. The last group received vehicle (oxygen). Rats were subjected to myocardial I/R (40min/10min). Heart rate and ventricular arrhythmias were recorded during I/R progress. At the end of reperfusion, plasma creatine kinase-MB (CK-MB) activity and total nitrate/nitrite ( $\text{NO}_x$ ) were determined. In addition, lactate, adenine nucleotides, thiobarbituric acid reactive substances (TBARS), reduced glutathione (GSH) and myeloperoxidase (MPO) activity were estimated in the heart left ventricle. Histological examination was also performed to visualize the protective cellular effects.

**Results:** Both doses of ozone therapy were equally protective in reducing CK-MB release. However, the higher dose was more effective in reducing oxidative stress, lactate accumulation, elevated MPO activity and plasma  $\text{NO}_x$  as well as preserving myocardial adenine nucleotides. Histological examination also revealed better improvement with a higher dose of ozone therapy compared to the I/R group.

**Conclusion:** Ozone therapy can afford significant cardioprotection against biochemical and histological changes associated with I/R injury.

**Keywords:** Arrhythmias; Ischemia; Ozone; Preconditioning; Reperfusion.

### 563. Potential Protective Effect of Honey Against Paracetamol-Induced Hepatotoxicity

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*Archives of Iranian Medicine*, 15: 674-680 (2012) IF: 0.972

**Background:** Paracetamol overdose causes severe hepatotoxicity that leads to liver failure in both humans and experimental animals. The present study was undertaken to investigate the protective effect of honey against paracetamol-induced hepatotoxicity in Wistar albino rats. Silymarin served as a standard reference hepatoprotective drug.

**Methods:** Hepatoprotective activity was assessed by measuring biochemical parameters such as the activities of liver function enzymes as serum alanine aminotransferase (ALT) and serum aspartate aminotransferase (AST). Equally, comparative effects of honey on oxidative stress biomarkers such as malondialdehyde (MDA), reduced glutathione (GSH) and glutathione peroxidase (GPx) were also evaluated in the rat liver homogenates. Considering the fact that the initial event in paracetamol-induced hepatotoxicity is a toxic-metabolic injury leading to hepatocyte

death, activation of the innate immune response and upregulation of inflammatory cytokines, the effect of honey on serum level and hepatic content of interleukin-1 $\beta$  (IL-1 $\beta$ ) was also estimated.

**Results:** Paracetamol caused marked liver damage as evident by significant increase in activities of serum AST and ALT as well as IL-1 $\beta$  level. Paracetamol also resulted in a significant decrease in liver GSH content and GPx activity parallel to an increase in IL-1 $\beta$  and MDA contents.

Pretreatment with honey and silymarin prior to the administration of paracetamol significantly prevented the increase in the serum levels of hepatic enzyme markers, reduced oxidative stress and inflammatory cytokines. The histopathological evaluation of the livers also revealed that honey reduced the incidence of liver lesions induced by paracetamol.

**Conclusion:** Honey can be used as an effective hepatoprotective agent against paracetamol induced liver damage.

**Keywords:** Paracetamol; Honey; Hepatotoxicity; Silymarin; Antioxidant.

### 564. Modulation of the Antidiabetic Effect of Glimepiride by Diazepam in Diabetic Rats

W.R. Mohamed, G.A. El Sherbiny, H.F. Zaki and M.E. El Sayed

*British J. of Pharmacology and Toxicology*, 3: 190-196 (2012)

Anxiolytic drugs may influence glycemic control in diabetic subjects, so the present study was conducted to investigate the effect of glimepiride, a commonly used oral hypoglycemic, diazepam, a commonly used anxiolytic, and their combination in STZ-induced diabetic rats. Diabetes was induced by streptozotocin (50 mg/kg i.p.).

Rats were divided into 5 groups namely: normal control, diabetic control, glimepiride (10 mg/kg p.o.), diazepam (5 mg/kg i.p.) or combination of both glimepiride and diazepam, respectively.

All groups received daily treatments for 2 weeks including the normal group which received 1% Tween 80.

Diazepam significantly improved the effect of glimepiride on the levels of serum glucose, insulin, C-peptide and liver glycogen content. In addition, combination of diazepam with glimepiride significantly improved the effect of the latter on oxidative stress biomarkers including serum lipid peroxides, blood glutathione levels and blood superoxide dismutase activity of diabetic rats. In conclusion, the present study revealed that diazepam increased the antidiabetic and the antioxidant actions of glimepiride which may be of considerable value in the treatment of diabetes mellitus where both reduction of associated anxiety and tight glycemic control are needed.

**Keywords:** Anxiety; Diabetes; Diazepam; Glimepiride; Insulin; Oxidative Stress.

### 565. Protective Effects of Combined Therapy of Gliclazide with Curcumin in Experimental Diabetic Neuropathy in Rats

Hanan Naeim Attia, Nouf Mohammed AL-Rasheed, Nawal Mohammed AL-Rasheed, Yousreya Ali Maklad and Amany A.E. Ahmed and Sanaa Abdel Baky Kenawy

*Behavioural Pharmacology*, 23: 153-161 (2012) IF: 2.72

Diabetic neuropathy is the most common chronic complication of diabetes. the aim of the present study was to evaluate the protective effects of curcumin against neuropathy in gliclazide-treated diabetic rats. Diabetes was induced by an intraperitoneal injection of streptozotocin (45 mg/kg).

Diabetic animals were given gliclazide (10 mg/kg, orally) alone or combined with curcumin (100 mg/kg, orally) or gabapentin (30 mg/kg, intraperitoneally as a positive control). Behavioral responses to thermal (hot plate and tail flick) and mechanical (tail pinch) pain, and some biochemical tests (serum glucose, C-peptide, peroxyntirite, lipid peroxides, and tumor necrosis factor- $\alpha$ ) were assessed after 5 consecutive weeks of daily treatment. Combined treatment of curcumin with gliclazide significantly increased hot-plate and tail-flick latencies in comparison with that of the diabetic control group.

The threshold of mechanical hyperalgesia was also significantly elevated. Serum glucose and C-peptide levels were significantly increased in the combined treatment compared with the diabetic control group, whereas serum levels of peroxyntirite, lipid peroxide, and tumor necrosis factor- $\alpha$  production were significantly decreased.

The data suggest that the combination of curcumin with gliclazide may protect against the development of diabetic neuropathy, with favorable effects with respect to the gliclazide/gabapentin combination.

**Keywords:** Curcumin; Diabetes; Gabapentin; Gliclazide; Neuropathy; Pain; Rat.

### 566. Protection by Low-Dose C Radiation on Doxorubicin-Induced Nephropathy in Rats Pretreated with Curcumin, Green Tea, Garlic or L-Carnitine with Curcumin, Green Tea, Garlic or L-Carnitine

Rasha R. Radwan, Esmat A. Shaban, Sanaa A. Kenawy and Hesham A. Salem

*Bulletin of Faculty of Pharmacy, Cairo University*, 50: 133-140 (2012) IF: 2

The protective potentials of a single exposure to 0.3 Gy of c radiation alone or with previous treatment with certain natural products with antioxidants activity, namely curcumin (50 mg/kg, i.p.), green tea (300 mg/kg, p.o.), garlic (100 mg/kg, p.o.) or L-carnitine (40 mg/kg, i.p.) against doxorubicin (DOX)-induced nephropathy in rats were studied. Natural products were administered daily for 14 successive days followed by single i.p. injection of DOX (5 mg/kg). Rats were subjected to whole body c radiation, 1 day before DOX administration. Serum levels of creatinine, urea, uric acid, low density lipoprotein (LDL-C), high density lipoprotein (HDL-C) cholesterols, total proteins and albumin as well as renal concentrations of reduced glutathione (GSH), thiobarbituric acid reactive substances (TBARS), nitric oxide (NO) and calcium (Ca) were determined. Irradiation

provided significant protections against DOX-induced changes in all measured parameters, except renal Ca content. All the test natural products significantly improved radiation-induced protection against renal lipid peroxidation. L-Carnitine markedly augmented the protection toward changes in renal GSH, NO and Ca concentrations. Curcumin increased the protection toward changes in serum albumin and renal GSH and NO concentrations, while garlic increased the protection toward changes in serum LDL-C level. It could be concluded that low-dose c radiation could provide prophylaxis against DOX-induced nephropathy which might be augmented by the use of certain natural antioxidants.

**Keywords:** Antioxidant; Doxorubicin; Radiation; Nephropathy.

### 567. Effect of Nigella Sativa and Wheat Germ Oils on Scopolamine-Induced Memory Impairment in Rats

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*Bulletin of Faculty of Pharmacy, Cairo University*, 50: 81-88 (2012) IF: 2

**Aim:** to investigate the possible memory enhancing effects of Nigella sativa oil (NSO) and wheat germ oil (WGO) on scopolamine-induced amnesic rats.

**Methods:** Male Wistar rats received either saline or scopolamine (16 mg/kg, i.p.). the other three groups were pretreated with NSO (1 ml/kg, p.o.), WGO (170 mg/kg, p.o.) or donepezil used as a reference drug (10 mg/kg, p.o.) for 14 days before scopolamine injection. Cognitive and biochemical measurements were then assessed. Principal.

**Results:** NSO and WGO treated rats significantly reversed scopolamine-induced deficit of spatial and non-spatial working memory impairment in the T maze alternation task and object recognition test, respectively. Administration of NSO prior to scopolamine showed a significant decrease in malondialdehyde (MDA) and increase in Glutathione (GSH) brain contents to be similar to that observed in donepezil group. It did not alter cholinesterase activity and showed a significant decrease in brain tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) content to be similar to donepezil-treated rats. Scopolamine-demented rats pretreated with WGO did not change MDA brain content significantly as compared to scopolamine and donepezil groups. WGO-treated rats showed a significant increase in GSH to a level similar to that observed in the donepezil group, it showed a significant decrease in cholinesterase activity as compared to scopolamine group and significantly elevated brain TNF- $\alpha$  content when compared to donepezil group.

**Keywords:** Nigella Sativa Oil; Wheat Germ Oil; Scopolamine; Memory Impairment; Rats.

### 568. Antihypertensive and Cardioprotective Effects of Pumpkin Seed Oil

Aliaa E.M.K. El-Mosallamy, Amany A. Sleem, Omar M.E. Abdel-Salam, Nermeen Shaffie and Sanaa A. Kenawy

*J Med Food*, 15: 180-189 (2012) IF: 1.408

Pumpkin seed oil is a natural product commonly used in folk medicine for treatment of prostatic hypertrophy. in the present study, the effects of treatment with pumpkin seed oil on hypertension induced by the nitric oxide synthase inhibitor Nx-

nitro-l-arginine methyl ester hydrochloride (l-NAME) (50 mg/kg/day) in rats were studied and compared with those of the calcium channel blocker amlodipine. Pumpkin seed oil (40 or 100 mg/kg), amlodipine (0.9 mg/kg), or vehicle (control) was given once daily orally for 6 weeks. Arterial blood pressure (BP), heart rate, electrocardiogram (ECG) changes, levels of serum nitric oxide (NO) (the concentrations of nitrite/nitrate), plasma malondialdehyde (MDA), blood glutathione, and erythrocytic superoxide dismutase activity were measured. Histopathological examination of heart and aorta was conducted as well. l-NAME administration resulted in a significant increase in BP starting from the second week.

Pumpkin seed oil or amlodipine treatment significantly reduced the elevation in BP by l-NAME and normalized the l-NAME-induced ECG changes—namely, prolongation of the RR interval, increased P wave duration, and ST elevation. Both treatments significantly decreased the elevated levels of MDA and reversed the decreased levels of NO metabolites to near normal values compared with the l-NAME-treated group.

Amlodipine also significantly increased blood glutathione content compared with normal (but not l-NAME-treated) rats. Pumpkin seed oil as well as amlodipine treatment protected against pathological alterations in heart and aorta induced by l-NAME. In conclusion, this study has shown that pumpkin seed oil exhibits an antihypertensive and cardioprotective effects through a mechanism that may involve generation of NO.

**Keywords:** Amlodipine; Arterial blood pressure; Nx-Nitro-L-arginine methyl ester hydrochloride; Pumpkin.

### 569. Can Trimetazidine, Vinpocetine or Isosorbide Dinitrate Ameliorate Cyclosporine-Induced Nephrotoxicity in Rats?

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*Journal of Pakistan Medical Student*, 2: 32-39 (2012)

**Background:** the present study was conducted to investigate the effect of concurrent administration of trimetazidine (a mitochondrial stabilizing anti-anginal agent), vinpocetine (a phosphodiesterase-1 inhibitor) and isosorbide dinitrate (a NO donor) on nephrotoxicity induced by cyclosporine A (CsA) treatment.

**Methods:** Female albino rats were divided into eight groups. Group1 rats were treated with corn oil and served as normal control. Group2 received CsA (15mg/kg, s.c. for 4 weeks) and served as control. Groups 3 and 4 received CsA along with trimetazidine (5 & 10mg/kg, p.o). Groups 5 and 6 received CsA along with vinpocetine (5 & 10mg/kg, p.o). Groups 7 and 8 received CsA along with isosorbide dinitrate (3.6, and 7.2mg/kg p.o). Blood urea nitrogen (BUN), serum creatinine, serum uric acid and blood glucose were measured. Creatinine clearance (Ccr) and proteinuria were estimated. Reduced glutathione (GSH), lipid peroxides, nitric oxide (NO), and hydroxyproline contents were measured in kidney tissues.

**Results:** Injection of CsA increased BUN, serum creatinine, and blood glucose levels as well as renal hydroxyproline content. It also decreased Ccr and renal NO content. Only isosorbide dinitrate (3.6mg/kg) could partially improve CsA-dependent changes in renal function as shown by decrease in elevated serum creatinine and renal hydroxyproline content as well as improvement of Ccr. However, administration of isosorbide dinitrate at a higher dose (7.2mg/kg) along with CsA deteriorated

the renal function reflected by decreased Ccr and renal NO content associated with proteinuria, increased BUN and uric acid levels.

**Conclusion:** the current study demonstrates that isosorbide dinitrate at the dose of 3.6mg/kg could protect against CsA-induced nephrotoxicity, whereas both trimetazidine and vinpocetine are of unclear utility

**Keywords:** Cyclosporine; Nephrotoxicity; Trimetazidine; Vinpocetine; Isosorbide.

## Faculty of Physical Therapy

### Dept. of Physical Therapy for Basic Science

### 570. the Efficacy of Forward Head Correction on Nerve Root Function and Pain in Cervical Spondylotic Radiculopathy: A Randomized Trial

Aliaa A Diab and Ibrahim M Moustafa

*Clinical Rehabilitation*, 26 (4): 351-361 (2012) IF: 2.123

To investigate the effect of forward head posture correction on pain and nerve root function in cases of cervical spondylotic radiculopathy.

**Design:** A randomized controlled study with six months follow-up.

**Setting:** University research laboratory.

**Subjects:** Ninety-six patients with unilateral lower cervical spondylotic radiculopathy (C5–C6 and C6– C7) and craniovertebral angle measured less than or equal to 50° were randomly assigned to an exercise or a control group.

**Interventions:** the control group (n/48) received ultrasound and infrared radiation, whereas the exercise group (n/48) received a posture corrective exercise programme in addition to ultrasound and infrared radiation.

**Main outcome measures:** the peak-to-peak amplitude of dermatomal somatosensory evoked potentials, craniovertebral angle, visual analogue scale were measured for all patients at three intervals (before treatment, after 10 weeks of treatment, and at follow-up of six months).

**Results:** There was a significant difference between groups adjusted to baseline value of outcome at 10 weeks post-treatment for craniovertebral angle, pain, C6 and C7 peak-to-peak amplitude of dermatomal somatosensory evoked potentials  $P=0.000, 0.01, 0.000, 0.001$  respectively and at follow-up for all previous variables ( $P=0.000$ ).

**Conclusion:** Forward head posture correction using a posture corrective exercise programme in addition to ultrasound and infrared radiation decreased pain and craniovertebral angle and increased the peak-to-peak amplitude of dermatomal somatosensory evoked potentials for C6 and C7 in cases of lower cervical spondylotic radiculopathy.

**Keywords:** Forward Head; Radiculopathy; Randomized Controlled Trial.



### 571. The Role of Forward Head Correction in Management of Adolescent Idiopathic Scoliotic Patients: A Randomized Controlled Trial

Aliaa A Diab

*Clinical Rehabilitation*, 26 (12): 1123-1132 (2012) IF: 2.123

To investigate the effectiveness of forward head correction on three-dimensional posture parameters and functional level in adolescent idiopathic scoliotic patients.

**Design:** A randomized controlled study with three-month follow-up.

**Setting:** University research laboratory.

**Subjects:** Seventy-six adolescent idiopathic scoliotic patients with Cobb angle ranged from 10° to 30° and craniovertebral angle less than 50° were randomly assigned to a study or a control group.

**Interventions:** All the patients (n = 76) received traditional treatment in the form of stretching and strengthening exercises. In addition, patients in the study group (n = 38) received a forward head posture corrective exercise programme.

**Outcome measures:** Craniovertebral angle, Functional Rating Index and posture parameters, including: lumbar lordosis, thoracic kyphosis, trunk inclination, trunk imbalance, lateral deviation, surface rotation and pelvis torsion were measured before treatment, after 10 weeks, and at three-month follow-up.

**Results:** There was a significant difference between the study and control groups adjusted to baseline values at 10 weeks post treatment with respect to the following parameters: craniovertebral angle (P = 0.006), trunk inclination (P = 0.005), lordosis (P = 0.01), kyphosis (P = 0.001), trunk imbalance (P = 0.001), lateral deviation (P = 0.001), pelvic torsion (P = 0.004) and surface rotation (P = 0.013). at three-month follow-up, there were still significant differences in all the previous variables (P < 0.005). in contrast, while there was no significant difference with respect to Functional Rating Index at 10 weeks (P = 0.8), the three-month follow-up showed a significant difference (P = 0.001).

**Conclusion:** A forward head corrective exercise programme combined with conventional rehabilitation improved three-dimensional scoliotic posture and functional status in patients with adolescent idiopathic scoliosis.

**Keywords:** Forward Head; Scoliosis; Randomized controlled trial.

### 572. Lumbar Lordosis Rehabilitation for Pain and Lumbar Segmental Motion in Chronic Mechanical Low-Back Pain: A Randomized Trial

Aliaa A. Diab and Ibrahim M. Moustafa

*Journal of Manipulative and Physiological Therapeutics*, 247-252 (2012) IF: 1.358

The purpose of this study was to investigate the effects of lumbar extension traction with stretching and infrared radiation compared with stretching and infrared radiation alone on the lumbar curve, pain, and intervertebral movements of patients with chronic mechanical low back pain (CMLBP).

**Methods:** This randomized clinical study with 3-month follow-up was completed at the Cairo University research laboratory. Eighty patients (age ranged from 40 to 50 years) with CMLBP and a hypolordotic lumbar spine were randomly assigned to traction or a comparison group. the comparison group (n = 40) received stretching exercises and infrared radiation, whereas the traction group (n = 40) received lumbar extension traction in addition to

stretching exercises and infrared radiation. the absolute rotatory angle, intervertebral movements, and visual analog scale were measured for all patients at 3 intervals.

**Results:** the results revealed a statistically significant difference between the groups at 2 follow-up time points compared with the baseline values for the translational and sagittal rotational movements of L3-L4, L4-L5, L5-S1, and L2-L3(posttreatment) and absolute rotatory angle (P b .01). There were no statistically significant changes in pain (P = .1 and .3) and L1-L2 (P = .072 and .076) or L2-L3 (at follow-up; P = .3), and there was no significant difference between all the previous variables adjusted to the groups' baseline outcome interaction (P N .01).

**Conclusion:** Lumbar extension traction with stretching exercises and infrared radiation was superior to stretching exercises and infrared radiation alone for improving the sagittal lumbar curve, pain, and intervertebral movement in CMLBP.

**Keywords:** Randomized trial; Traction; Lordosis; Low back Pain.

### The National Cancer Institute

*Dept. of Clinical Pathology*

#### 573. Golgi Protein 73 (Gp73) as A Novel Serum Marker for Early Detection of Hepatocellular Carcinoma in Egyptian Patients

Mona A El Shafie, Amal M Fawzy, Elhamy Abd Al Monem, Sherif Abbass, Doaa M Zakaria and Sherif El Baz

*Life Science*, 9 (2): 823-830 (2012) IF: 0.073

Serum Golgi protein 73 (sGP73) is a novel and promising biomarker for detection of hepatocellular carcinoma (HCC). However, there are few reports on the predictive values levels of GP73 in diagnosis of liver cirrhosis (LC), HCC and the relationship of this level to clinicopathologic features of patients.

**Methods:** This study included 66 patients, 31 of them were proved HCC and 35 patients have LC, additionally, 20 apparently healthy subjects were included as a control group. Clinical examination, abdominal ultrasonography, Triphasic C.T to patients with focal lesion. Liver function tests, complete blood cell count and serum AFP were measured. Des-γ- carboxyprothrombin (DCP) and Golgi Protein 73 (GP73) were determined by an ELISA technique. Correlations with clinical parameters were done.

**Results:** the serum levels of AFP, DCP and GP73 were significantly elevated in LC and more elevated in HCC cases as compared to controls. the sensitivity and specificity of GP73 for HCC were superior to those of AFP and DCP especially in early detection of HCC, GP73 had a sensitivity of 87% and a specificity of 95% at the optimal cut-off value of 7.62 ng/ml. the area under the receiver-operating characteristic curve (AUROC) was 0.87. DCP give a sensitivity of 80.6% and specificity of 85% at a cut-off 32.64 ng/ml, while, AFP had a sensitivity of 77.4% and a specificity of 60% at a cut-off 28.51 ng/ml. However, when GP73 used in combination with AFP, they lead to an enhanced the sensitivity of HCC detection up to 90.3% and the area under receiver-operating characteristic curve (AUROC) was 0.83. A significant correlation was found between serum GP73 level and prognostic markers of LC (AST, ALT, serum albumin and child score) and more aggressive tumor characters (tumor size and vascular invasion).

**Conclusion:** the serum level of GP73 may be implicated in development of LC and disease progression to HCC. In

combination with AFP, it had an overall performance that was better than AFP alone in early detection of HCC. Future study was needed to be confirmed in larger cohorts of patients to determine if these markers are true indicators of early HCC.

**Keywords:** Hcc; Golgi Protein 73; Dcp; Afp; Elisa.

#### 574. Detection of Ck19 Mrna in the Blood of Breast Cancer Female Egyptian Patients and Its Relation to Established Prognostic Parameters

Amal F. M. Said, Iman I. H. Abulkheir, Amany Helal and Dalia B. Mohammad

*Life Science*, 9 (1): 561-571 (2012) IF: 0.073

Purpose Breast cancer is a leading cause of cancer-related deaths in women Worldwide. the clinical course of this disease is highly variable and clinicians continuously search for prognostic parameters that can accurately predict prognosis. peripheral blood cytokeatin-19 (CK-19) mRNA-positive cells and its correlation with well established prognostic factors including pathologic parameters, hormonal status and biologic marker; HER 2/ neu in breast female Egyptian cancer patients was studied .

**Patients and Methods:** A total of 60 peripheral blood specimens were collected for study. Patients were forty newly diagnosed breast cancer and 10 patients with benign breast lesions .The10 apparently healthy donors and patients with benign lesions were used as the control group.

They were analyzed for the presence of CK-19 mRNA-positive cells using nested reverse transcription polymerase chain reaction assay (RT-PCR). Immunohistochemical staining for HER 2/neu, estrogen and progesterone receptors were carried out for all cases. the association with known prognostic factors and the effect of CK-19 mRNApositive cells on patients' prognosis was investigated.

**Results:** CK-19 mRNA-positive cells were detected in the blood of 14 patients (35%) of the 40 patients.

There was statistically significant association between the presence of CK19 mRNA-positive cells and the patients' tumor size and histologic grade of the tumor, stage of disease and the involved lymph nodes P = <0.001, 0.006 , 0.007 and 0.005 respectively. CK-19 mRNA-positive cell detection also showed high significance with HER2 expression receptor (p=0.001). None of the patients with CK 19 positive cells expressed dual ER & PR positivity being both negative and either negative.

There was no statistically significantly association between the detection of CK19 mRNA-positive cells and patient's age, menstrual status or pathologic type.

**Conclusion:** Peripheral-blood CK-19 mRNA-positive cells might constitute a biologically active subset of breast cancer patients with high tumor burden and bad prognosis.

**Keywords:** Cancer Breast; Peripheral-Blood; Ck-19; Rt-Pcr; Prognostic Factors.

#### Dept. of Medical Oncology

#### 575. Geographic Distribution of Hematopoietic Cancers in the Nile Delta of Egypt

Herzog CM, Dey S, Hablas A, Khaled HM, Seifeldin IA, Ramadan M, El-Hamzawy H, Wilson ML and Soliman AS.

*Ann Oncol.*, 23 (10): 2748-2755 (2012) IF: 6.425

Previous evidence indicated that incidence rates of non-Hodgkin's lymphoma (NHL) are high in Egypt although little is known about risk factors.

**Materials and Methods:** Using data from the population-based cancer registry of Gharbiah governorate in Egypt, we assessed the 1999-2005 incidence of hematopoietic cancers (HCs) based on the ICD-O3 by age- and sex-specific urban-rural distribution.

**Results:** NHL showed the highest incidence among all HCs (11.7 per 100 000). Urban incidence of HCs was higher than rural incidence. Incidence rates of Hodgkin's lymphoma (HL) and NHL were high especially among urban males up to the 64-year age category. Rural incidence of HL and NHL was high below age 20. Among the districts of the governorate, we observed NHL incidence pattern similar to that observed for hepatocellular carcinoma because of the possible link to hepatitis C virus for both cancers. Comparison to the published HCs data from Algeria, Cyprus, and Jordan showed the highest NHL rate in Egypt than the other countries in the region.

**Conclusions:** Future studies should define the role of environmental exposures in hematopoietic carcinogenesis in this population. in-depth studies should also investigate the role of access to health care in the urban-rural variation of HC distribution in this population.

#### 576. Systematic Review of Purine Analog Treatment for Chronic Lymphocytic Leukemia: Lessons for Future Trials

CLL Trialists' Collaborative Group (CLLTCG)

*Haematologica*, (2012) IF: 6.424

A systematic review of purine analogs revealed heterogeneity between trials in treatment effects on response and progression free survival, but not survival, perhaps partly due to variations in analytical methods. in addition, combination treatments required evaluation. Therefore, individual patient data were sought for all randomized trials in untreated chronic lymphocytic leukemia which involved a purine analog, but which did not include antibody therapies. Sixteen trials were found, addressing seven comparisons. Eight trials, with 2,753 patients, showed that single agent purine analog improved progression free survival (odds ratio=0.71; 95% confidence interval I=0.63- 0.79). Heterogeneity remained substantial. Three trials, with 1,403 patients, showed that progression free survival was further improved by the addition of cyclophosphamide (odds ratio=0.54; 0.47-0.62). Fewer data were available on the addition of other drugs to purine analog, and none showed clear benefit. Two trials, with 544 patients, suggested cladribine improved progression free survival compared to fludarabine (odds ratio=0.77; 0.63-0.95). No differences were seen in overall survival for any comparisons. in conclusion, purine analogs, particularly combined with cyclophosphamide, significantly improve progression free survival but not survival. Some groups, such as the elderly, may not see the same benefits and maximizing doses may be important

for all treatments, including chlorambucil. Longer follow up, consistent definitions and detailed reporting of trials should be encouraged.

**Keywords:** Purine analog; Combination therapy; CII, Review; cyclophosphamide.

### 577. Response to Chemotherapy is Predictive in Relation to Longer Overall Survival in an Individual Patient Combined-Analysis with Pleural Mesothelioma

Jaine K. Blayney, Giovanni L. Ceresoli, Bruno Castagneto, Mary E.R. O'Brien, Baktiar Hasan, Richard Sylvester, Robin Rudd, Jeremy Steele, Sara Busacca, Camillo Porta, Luciano Mutti, Kenneth 'Byrne, Paula Scullin, Rabab Gaafar, Paul Baas, Jan Van Meerbeeck and Dean A. Fennell

*Eur. J. Cancer*, 48: 2983-2992 (2012) IF: 5.536

There is currently no early predictive marker of survival for patients receiving chemotherapy for malignant pleural mesothelioma (MPM). Tumour response may be predictive for overall survival (OS), though this has not been explored. We have thus undertaken a combined-analysis of OS, from a 42day landmark, of 526 patients receiving systemic therapy for MPM. We also validate published progression-free survival rates (PFSRs) and a progression-free survival (PFS) prognostic-index model.

**Methods:** Analyses included nine MPM clinical trials incorporating six European Organisation for Research and Treatment of Cancer (EORTC) studies. Analysis of OS from landmark (from day 42 post-treatment) was considered regarding tumour response. PFSR analysis data included six non-EORTC MPM clinical trials. Prognostic index validation was performed on one non-EORTC data-set, with available survival data.

**Results:** Median OS, from landmark, of patients with partial response (PR) was 12.8months, stable disease (SD), 9.4months and progressive disease (PD), 3.4months. Both PR and SD were associated with longer OS from landmark compared with disease progression (both  $p < 0.0001$ ).

PFSRs for platinum-based combination therapies were consistent with published significant clinical activity ranges. Effective separation between PFS and OS curves provided a validation of the EORTC prognostic model, based on histology, stage and performance status.

**Conclusion:** Response to chemotherapy is associated with significantly longer OS from landmark in patients with MPM.

### 578. Cancer Education for Medical Students in Developing Countries: Where Do We Stand and How to Improve?

Mohamed Amgada, Emad Shash, and Rabab Gaafar

*Crit Rev Oncol Hematol*, 84: 122-129 (2012) IF: 4.411

This article is a review of the literature regarding the state of oncology education for medical students in developing countries, and possible solutions to the problems at hand.

**Methods:** Ovid Medline, PubMed, ERIC, the Cochrane CENTRAL Register of Controlled Trials (CENTRAL) and Google Scholar were searched using the terms oncology, undergraduate, cancer, education and teaching.

**Results:** the search resulted in 40 relevant articles in total. Ten articles showed that there is a lack of adequate knowledge in the scientific, clinical and psychological aspects of oncology and palliative care amongst students and physicians in developing countries.

Eight articles describe the relevance and usefulness of summer schools, workshops and trainings. the rest of them discuss possible methods of addressing the issue, the most important of which is the inclusion of a clinical oncology rotation in the undergraduate syllabus.

**Conclusion:** Graduated physicians and medical students are a long way from reaching the standard knowledge and skills required in oncology. Thus, there is a pressing need to reform the undergraduate medical curricula in developing countries in order to increase cancer awareness for better graduated future physicians.

**Keywords:** Cancer; Developing; Education; Oncology; Review; Undergraduate; Medical; Students.

### 579. A Randomized, Phase 2 Study Comparing Pemetrexed Plus Best Supportive Care Versus Best Supportive Care as Maintenance Therapy After First-Line Treatment with Pemetrexed and Cisplatin for Advanced, Non-Squamous, Non-Small Cell Lung Cancer

Nabil Mubarak, Rabab Gaafar, Samir Shehata, Tarek Hashem, Dani Abigeres, Hamdy A Azim, Gamal El-Husseiny, Hamed Al-Husaini and Zhixin Liu

*Bmc Cancer*, 12 (423): 1-11 (2012) IF: 3.011

Maintenance therapy for non-small cell lung cancer (NSCLC) aims to extend disease control after first-line chemotherapy with active and well-tolerated agents. the utility of continuation maintenance therapy requires further research.

**Methods:** This multicenter, randomized, phase 2 study compared continuation maintenance therapy with pemetrexed (500 mg/m<sup>2</sup> every 21days) and best supportive care (BSC) versus BSC alone in patients with advanced, non-squamous NSCLC who had not progressed after 4 cycles of induction chemotherapy with pemetrexed (500 mg/m<sup>2</sup>) and cisplatin (75 mg/m<sup>2</sup>). the primary endpoint was progression-free survival (PFS) from randomization, was analyzed using a Cox model, stratified for the tumor response at the end of induction therapy, at a one-sided alpha of 0.2. Secondary endpoints: response and disease control rates, overall survival (OS), one year survival rates, and treatment-emergent adverse events (TEAEs).

**Results:** A total of 106 patients commenced induction therapy, of whom 55 patients were randomized to maintenance pemetrexed/BSC (n=28) or BSC (n=27). Although the median PFS time for maintenance phase for both arms was 3.2?months, the one-sided p-value for the PFS HR comparison was less than the prespecified limit of 0.2 (HR=0.76, two-sided 95% confidence interval [CI]: 0.42 to 1.37; one-sided p-value=0.1815), indicating that PFS was sufficiently long in the pemetrexed/BSC arm to warrant further investigation. Similar PFS results were observed for the overall study period (induction plus maintenance) and when the PFS analysis was adjusted for sex, baseline disease stage, and the ECOG PS prior to randomization. the median OS for the maintenance phase was 12.2?months (95%CI: 5.6 to 20.6) for the pemetrexed/BSC arm and 11.8?months (95% CI: 6.3 to 25.6) for BSC arm. the one-year survival probabilities were

similar for both arms for the maintenance phase and the overall study period. Both the induction and continuation maintenance therapies were generally well-tolerated, and similar proportion of patients in each arm experienced at least 1 grade 3/4 TEAE (pemetrexed/BSC, 17.9%; BSC, 18.5%).

**Conclusions:** Continuation pemetrexed maintenance therapy resulted in promising PFS with an acceptable safety profile in a Middle Eastern population with advanced non-squamous NSCLC and is worthy of further investigation.

### 580. Does Fasting During Ramadan Trigger Non-Adherence to Oral Hormonal Therapy in Breast Cancer Patients?

Ahmed Abdelmabood Zeeneldin and Ayman Abdelsamee Gaber

*Journal of the Egyptian National Cancer Institute*, 24: 133-137 (2012) IF: 2

To estimate the effect of fasting during Ramadan (the ninth lunar month) on adherence to oral hormonal therapies (OHT) among breast cancer (BC) patients.

**Patients and Methods:** During Ramadan 2010, 139 BC patients were interviewed at the Egyptian National Cancer Institute. They were asked about fasting as well as intake of OHT in Ramadan and in the preceding month.

**Results:** the median age was 50 years and most patients were postmenopausal with good performance status and non-metastatic disease. the median number of fasting days was 18% and 93% of patients were fasting 80% or more of Ramadan. Tamoxifen and aromatase inhibitors were used in 64% and 36%, respectively. Adherence to OHT during Ramadan and its preceding month were 94.2% and 95.7%, respectively ( $p=0.77$ ). In univariate analysis, non-adherence prior to Ramadan and shorter duration of OHT were predictors of non-adherence during Ramadan ( $P<0.001$ ,  $0.003$ , respectively). Fasting, age, performance status, presence of metastases and type of hormonal therapy were not good predictors of adherence.

**Conclusions:** While most of patients receiving OHT for BC are fasting during Ramadan, this does not negatively impact compliance with treatment.

**Keywords:** Breast; Cancer; Fasting; Ramadan; Egypt.

### 581. Fasting Among Muslim Cancer Patients During the Holy Month of Ramadan.

Ahmed A. Zeeneldin, and Fatma M. Tahab

*Ann Saudi Med*, (2012) IF: 1.071

Muslims constitute more than 20% of the world's population and have a significant share of its cancer cases. Many Muslim cancer patients witness the fasting month of Ramadan but we do not know which individuals elect to fast.

**Design and Setting:** Cross-sectional study conducted among Muslim cancer patients at the National Cancer Institute (NCI), Egypt, during Ramadan, Hijri 1430 (the month of fasting) August-September 2009.

**Subjects and Methods:** One-hundred and two patients being treated at the NCI were interviewed. The most common diagnoses were breast cancer (31%), acute leukemia (24%), colorectal cancer (7%), non-Hodgkin lymphoma (5%), bladder cancer (4%), lung cancer (4%), and laryngeal cancer (4%). The two sexes were equally represented and so were metastatic and nonmetastatic

diseases. The outpatient:inpatient ratio was 3:1. Treatments being received by these patients included chemotherapy, radiotherapy, hormonal therapy, and nonspecific therapy in 42%, 31%, 10%, and 17%, respectively. Other concomitant diseases were present in 22% of the patients.

**Results:** While 40% of patients did not fast at all during Ramadan, 36% and 24% were partial and complete fasters, respectively. Female patients, those with performance status (PS) 0 to 1, those whose disease was a nonmetastatic solid tumor, and those receiving non-intravenous chemotherapy as outpatients were more likely to be fasting than their corresponding counterparts. Being a female, having PS 0 to 1, and receiving treatment as an outpatient were the only factors that were significant on multivariate analysis. Only 46% of patients sought the treating oncologist advice on whether they could fast.

**Conclusions:** Most cancer patients fast during Ramadan, but only half of them discuss the issue with their oncologists. We hope that our study stimulates more research on this topic.

**Keywords:** Egypt; Cancer; Fasting; Ramadan.

### 582. Past and Future Trends in Cancer and Biomedical Research: A Comparison Between Egypt and the World Using Pubmed-Indexed Publications

Ahmed A Zeeneldin, Fatma M Taha and Manar M Moneer

*Biomed Central Research Notes*, (2012)

PubMed is a free web literature search service that contains almost 21 millions of abstracts and publications with almost 5 million user queries daily. The purposes of the study were to compare trends in PubMed-indexed cancer and biomedical publications from Egypt to that of the world and to predict future publication volumes.

**Methods:** The PubMed was searched for the biomedical publications between 1991 and 2010 (publications dates). Affiliation was then limited to Egypt. Further limitation was applied to cancer, human and animal publications. Poisson regression model was used for prediction of future number of publications between 2011 and 2020.

**Results:** Cancer publications contributed 23% to biomedical publications both for Egypt and the world. Egyptian biomedical and cancer publications contributed about 0.13% to their world counterparts. This contribution was more than doubled over the study period. Egyptian and world's publications increased from year to year with rapid rise starting the year 2003. Egyptian as well as world's human cancer publications showed the highest increases. Egyptian publications had some peculiarities; they showed some drop at the years 1994 and 2002 and apart from the decline in the animal: human ratio with time, all Egyptian publications in the period 1991-2000 were significantly more than those in 2001-2010 ( $P<0.05$  for all). By 2020, Egyptian biomedical and cancer publications will increase by 158.7% and 280% relative to 2010 to constitute 0.34% and 0.17% of total PubMed publications, respectively.

**Conclusions:** The Egyptian contribution to world's biomedical and cancer publications needs significant improvements through research strategic planning, setting national research priorities, adequate funding and researchers' training.

**Keywords:** Egypt; Pubmed; Biomedical research; Cancer research; Bibliometric.

### 583. Colorectal Carcinoma in Gharbiah District, Egypt: Comparison Between the Elderly and Non-Elderly

Ahmed A Zeeneldin, Magdy M Saber, Ibrahim A Seif El-din and Sara A Frag

*Journal of Solid Tumors*, 2 (3): 0-0 (2012)

**Objective:** This work was conducted to study colorectal carcinoma (CRC) in Gharbiah district, Egypt and to verify the effect of age on the treatments and their outcomes.

**Methods:** Between 2000 and 2002, 293 cases with CRC were identified in the Gharbiah population based cancer registry (GPBCR); 159 of whom were treated at Tanta Cancer Center (TCC). Patients were grouped into elderly and non-elderly (> and < 65 years, respectively).

**Results:** CRC was the 6th cancer in Egypt, representing 4% of the total cancers and 53% of GIT cancers. the median age was 53 years with male predominance. Colon cancers were more common than rectal cancers. Most patients had tumors that were localized, low grade and adenocarcinoma (AC). Constipation, abdominal pains and bleeding per rectum were the commonest complaints. Surgery, radiotherapy and chemotherapy were adopted in 84%, 28% and 72% of patients, respectively. the median OS and PFS were 23 and 25 months (95%CI: 17-29 and 11.8-18.2), respectively. Compared to non-elderly, elderly patients were more likely to have rectal tumors, non-AC histology, non-metastatic disease; more comorbidities were less likely to receive chemotherapy particularly in the adjuvant setting ( $P < 0.05$  for all). the OS and PFS of elderly patients were not statistically different from the non-elderly.

**Conclusions:** Within the limits of this retrospective trial, elderly patients with CRC tend to have more rectal and non-metastatic cancers. They were more likely to have comorbidities and less likely to receive chemotherapy. However, the OS and DFS were comparable to non-elderly.

**Keywords:** Egypt; Elderly; Gharbiah population-based cancer registry; Colon rectum neoplasms; Treatment; Survival.

### 584. Tamoxifen in Advanced Hepatocellular Carcinoma: A Retrospective Cohort Study

Zeeneldin AA, and Saadeldin MR

*Mediterranean Oncology Journal*, 1: 40-44 (2012)

**Background:** Hepatocellular carcinoma (HCC) is a common cancer worldwide as well as in Egypt with hepatitis B and C, alcohol and aflatoxins being the commonest risk factors. Tamoxifen was initially reported to confer a marginal survival benefit in advanced HCC. However, later reports declined any benefit.

**Aims:** to study the impact of tamoxifen on overall survival (OS) and progression-free survival in Egyptian patients with advanced HCC.

**Methods:** This retrospective cohort study was conducted at Tanta Cancer Center (TCC), Egypt where 236 advanced HCC cases were treated with tamoxifen 10 mg PO BID.

**Results:** the median OS was 7.2 (95% CI: 6.1-8.3) months. the 1-year OS rate was 30%. Tamoxifen produced partial responses and clinical stabilization in 8% and 61% of cases, respectively. the median PFS was 4.9 (95% CI: 3.9-5.9) months. During univariate analysis, it was shown that absence of fatigue, Child-Pugh A, single tumors, absence of nodal and distant metastases, all had significantly better OS and PFS than their counterparts.

Multivariate analysis showed that only Child-Pugh class and multiplicity of lesions were independent predictors of OS and PFS.

**Conclusions:** This large retrospective study showed that use of tamoxifen in advanced HCC produced survival figures comparable to the randomized controlled trials that declared lack of survival benefit. Thus further use of tamoxifen in this setting is discouraged.

**Keywords:** Hepatocellular carcinoma; Tamoxifen; Egypt; Retrospective study.

### 585. Cytogenetic Profile of Locally Advanced and Metastatic Schistosoma-Related Bladder Cancer and Response to Chemotherapy

Magdy Sayed Aly, Hussein Mostafa Khaled, Mohamed Emara and Tarek D. Hussein

*Cancer Genet*, 205 (4): 156-162 (2012)

Bladder cancer is a common malignancy in developing countries in which bladder infection with the parasite *Schistosoma haematobium* is prevalent. Several epidemiological, histopathological, and clinical characteristics of schistosoma-associated bladder cancer suggest that it is distinct from bladder cancer seen in other places in the world.

The aim of this study was to extend establishing the cytogenetic profile of this type of malignancy in advanced and metastatic cases, and to demonstrate its relation to the end results of systemic therapy. Fluorescence in situ hybridization was applied to interphase nuclei to detect numerical chromosome changes in 41 patients with bladder cancer. Numerical chromosome aberrations were detected in 27 of 41 cases (66%). in 17 (41%) cases, a gain of chromosome 7 was observed, while losses in chromosomes 9 and 17 were detected in 20 (49%) and 18 (44%) cases, respectively. Loss of chromosome Y was detected in 7 of the 32 male patients included in this study (22%). There was a statistically significant association between stage of the disease and overall survival; Bajorin score and time to disease progression and overall survival; and between response to systemic therapy and time to disease progression and overall survival.

The only chromosomal abnormality that had a significant relationship with overall survival was the gain of chromosome 4. When the genetic basis of schistosoma-associated bladder cancer is fully understood, new diagnostic and therapeutic strategies could be developed, which in turn may promote better clinical management and survival.

**Keywords:** Genetics; Bladder cancer; Squamous cell carcinoma; Transitional cell carcinoma; in situ hybridization; Schistosomiasis.

### 586. Inflammatory Breast Cancer: Is It Really A Separate Entity?

AS Bastawisy, RM Gaafar, SS Eisa, GM Amira and MH Helal

*E Cancer Medical Science*, 6 (250): (2012)

Inflammatory breast cancer (IBC) is the most aggressive form of primary breast carcinoma and is associated with a dismal outcome despite the availability of multi-modality treatment options.

**Patients and Methods:** This is a prospective case control study comparing two groups of newly diagnosed patients; the first with inflammatory breast cancer (IBC) and the second with locally advanced non inflammatory breast cancer (LABC). In both groups MIB1, ER, PR, Her2neu were assessed. Neo-adjuvant chemotherapy consisted of four cycles of FEC100 followed by modified radical mastectomy according to clinical response, postoperative chemotherapy with two courses of the same regimen followed by radiotherapy. Tamoxifen 20 mg po daily for 5 years in ER and/or PR positive tumours, starting after the completion of radiotherapy. Primary end points were a) comparison of MIB-1 score in both groups, b) comparison of clinical and pathological responses in both groups. Secondary endpoints were comparison of progression free survival and overall survival.

**Results:** From a total of 42 patients, 21 were stage III B (T4d, N0-2 M0) IBC and 21 were stage III B (T4a-c, N0-2, M0) LABC. Patients in the age range from 28 to 68 were included and followed from November 2007 until February 2010 with a median follow-up period of 22.5 months. Toxicity of both arms, mainly haematologic, nausea and vomiting, was in general acceptable with no treatment-related deaths. Of the patients with IBC 81.3% had a high MIB-1 score as compared with 43.8% of patients with LABC (P-value = 0.028). Objective clinical response to neo-adjuvant chemotherapy in the IBC arm was 57.1% (4.8% complete response (CR)) as compared with 81% (9.5% CR) in LABC (P-value = 0.09). Overall pathological response (complete pathological response (pCR)+partial pathological response (pPR)) was 35.3% in the IBC arm compared with 40% in LABC arm (P-value = 0.618). One year, 2 year and median progression free survival (PFS) were 55.87%, 37.71% and 21.7 months, respectively in the IBC arm compared with 85.71%, 66.67% in LABC (median PFS was not reached) (P-value = 0.072). One and 2 year overall survival (OS) were 69.82% and 51.20%, respectively in the IBC arm compared with 95.24% and 95.24% in LABC arm (P-value = 0.0038).

**Conclusions:** IBC should be considered as a separate entity. A high MIB-1 score is a potential molecular marker for IBC.

#### Dept. of Pediatrics Oncology

### 587. Hematopoietic Stem Cell Transplantation for Thalassemia

Yasser Elborai, Alain Uwumugambi and leslie Lehmann

*Immunotherapy*, 4 (9): 947-956 (2012) IF: 1.854

Thalassemia is an autosomal recessive disorder associated with defective synthesis of the  $\alpha$ - or  $\beta$ -chain of hemoglobin. For  $\beta$ -thalassemia major patients, therapeutic options are either monthly red cell transfusions and chelation therapy or allogeneic stem cell transplant. Patients undergoing transfusion therapy remain at risk for transmitted infections and iron overload with associated tissue damage. Stem cell transplant is the only curative approach and

success is inversely correlated with the degree of iron overload and hepatic damage. Overall outcomes following stem cell transplant with a matched sibling donor are excellent with over 90% of low-risk children becoming transfusion free. Hypertransfusion therapy and aggressive chelation in addition to hydroxyurea, azathioprine and fludarabine is a new approach for high-risk patients to decrease graft rejection by suppressing endogenous erythropoiesis pretransplant. The use of unrelated donors and novel approaches such as gene therapy are under current investigation

**Keywords:** Blood transfusion; Chelation; Gene therapy; Iron overload; Stem cell transplantation; Thalassemia.

#### Dept. of Radiation Oncology

### 588. Schistosomiasis and Bladder Cancer: Similarities and Differences from Urothelial Cancer.

Mohamed S Zaghloul and Iman Gouda

*Expert Rev Anticancer Thera*, 12 (6): 753-763 (2012) IF: 2.652

Through the years, schistosoma-associated bladder cancer was believed to be a unique entity of disease, different from urothelial cancer. As carcinogenesis is a highly complex process resulting from the accumulation of many genetic and epigenetic changes leading to alterations in the cell proliferation and regulation process, confirmation of their minute differences or similarities are extremely difficult.

In bladder cancer, many of these carcinogenic cascades were not fully documented in spite of the efforts undertaken. The control of schistosomiasis and the subsequent decrease in the intensity of infestation showed feature changes approaching that of urothelial tumors. However, schistosoma-associated bladder cancer still presents in more advanced stages than schistosoma-non-associated urothelial cancer.

Furthermore, many data were collected proving that, upon applying the same treatment protocol and management care, stage-by-stage comparison of the treatment end results were found to be similar in bladder cancer patients with the different etiologies.

**Keywords:** Bilharziasis; Biology; Bladder cancer; Chemotherapy; Cytogenetics; Pathology; Radical cystectomy; Radiotherapy; Schistosomiasis.

### 589. Pre-treatment Verification of Intensity-Modulated Radiation Therapy in Paediatric Patients: Adequate Estimation for Tolerance Limits

Ehab M. Attalla, Hassan Shafik, Hany Ammar, Ismail Eldesoky, Mohamed Farouk and Shima Shoier

*Chinese-German Journal of Clinical Oncology*, 11 (11): 621-625 (2012)

**Objective:** The objective of this work was to establish adequate tolerance limits based on a certain defined institutional indices and generate published data presenting our results to the radiotherapy community.

**Methods:** One hundred paediatric patients were treated using 6-MV X-ray beams produced by Siemens ONCOR Expression linear accelerator. The clinical step-and-shoot intensity-modulated radiation therapy (IMRT) treatment plans were designed using KonRad release 2.2.23. For two treatment sites (abdomen, head

and neck), the fluence maps generated by the treatment planning system were all delivered for the quality assurance (QA) which included absolute dose verification for all treatment fields, relative dose verification for each treatment field.

**Results:** The 724 fluence maps were analyzed at three different criteria using the gamma index tool. The 3% dose difference of local prescribed dose /3 mm was considered adequate. The passing rate for all fields of all plans always exceeded 70%. The dose differences between the measured and calculated doses ranged from -2.2% to +4% [mean and standard deviation (s): 1.4 ± 1.5] for the abdominal case, and from -3.3% to +5.6% (1.3 ± 1.6) for head and neck case with total confidence limit 0.046 (4.6%). The 14/100 (14%) of the absolute point dose measurements were out of ±3% from the dose predicted by the treatment planning system. Only two cases were below -3%, while 12 cases over +3%.

**Conclusion:** At 3% dose difference of local prescribed dose /3 mm criteria, a 75% passing a gamma criterion and 3% for absolute point dose can be achieved for abdomen and head and neck treatments site. We considered the tolerance limits based on these indices for IMRT QA adequate.

**Keywords:** Intensity-modulated radiation therapy (IMRT); Quality assurance (QA); Tolerance; Paediatric patient.

### 590. Dosimetric Study Comparing Photon and Electron Beams for Boosting the Tumor Bed in Early-Stage Breast Cancer

Mohamed Mahmoud, Soha Ahmed, Ehab M. Attalla, Hassan S. Abouelenein, Shaimaa Shoier and Mohsen Barsoum

*Chinese-German Journal of Clinical Oncology*, 11 (12): 710-715 (2012)

**Objective:** The aim of our study was to assess and compare the potential dosimetric advantages and drawbacks of photon beams and electron beams as a boost for the tumor bed in superficial and deep seated early-stage breast cancer.

**Methods:** We planned CTs of 10 women with early breast cancer underwent breast conservative surgery were selected. Tumor bed was defined as superficial and deep with a cut of point 4 cm, those with less than 4 cm were defined as superficial tumors representing 4 patients and those with depth of 4 cm or more were classified as deep tumors representing 6 patients. The clinical target volume (CTV) was defined as the area of architectural distortion surrounded by surgical clips. The planning target volume (PTV) was the CTV plus margin 1 cm. A dose of 10 Gy in 2 Gy fractions was given concurrently at the last week of treatment. Organs at risk (OARs) were heart, lungs, contra-lateral breast and a 5 mm thick skin segment of the breast surface. Dose volume histograms were defined to quantify the quality of concurrent treatment plans assessing target coverage and sparing OARs. The following treatment techniques were assessed: photon beam with 3D-conformal technique and a single electron beam.

**Results:** For superficial tumors better coverage for CTV and PTV with good homogeneity with better CI was found for the 3D conformal radiotherapy (3DCRT) but with no significant planning objectives over electron beam. For deep tumors, the 3DCRT met the planning objectives for CTV, PTV with better coverage and fewer hot spots with better homogeneity and CI. For superficial tumors, OARs were spared by both techniques with better sparing for the electron beam where as for deep tumors also OARs were well spared by both techniques.

**Conclusion:** Boosting the tumor bed in early stage breast cancer with optimized photon may be preferred to electron beam for both superficial and deep tumors. The OARs dose sparing effect may allow for a potential long-term toxicity risk reduction and better cosmesis.

**Keywords:** 3D Conformal radiotherapy; Electron beam; Organs at risk.

### 591. Supine Craniospinal Irradiation in Children: Patient Position Modification, Dose Uniformity and Early Adverse Effects.

M.S. Zaghoul, E. Eldebawy, E. Attalah, S. Ahmed, M. Nazmy and H. Aboel Anin

*Gulf J Oncology*, 1-15 (2012)

Different craniospinal irradiation techniques are complex. the homogeneity of the dose to the target and the normal tissues at risk affect both the control rate and the level of adverse effects.

**Patients and methods:** Thirty one patients were treated with CSI in the supine position. Custom-made Styrofoam was tailored for each patient to straighten the convexity and concavity of the spinal axis allowing better dose distribution uniformity during CSI technique. in the first 6 patients, CT simulation were performed twice: one time with the patient lying directly on the vacuum mattress without the foam (the conventional way) and the second while lying on the foam. Dose distribution was calculated using a 3D conformal planning. the gap between the fields was determined using isodose alignment method. All treatment portals were verified during the first 3 treatment sessions and once weekly thereafter using either cone-beam or portal image device. Weekly feathering (shifting of the junction between the 2 adjacent radiation fields) was routinely performed.

**Results:** the 95% dose distribution had better coverage with the foam (p=0.042) while the hot volume of 110% and 105% dosage were significantly lesser than conventional technique (both p=0.028). the organs at risk received nearly similar radiation doses in the 2 positions. the CSI led to minimal immediate adverse effects that were reversible. Weight loss was experienced by 55% of patients.

**Conclusion:** This modified technique of CSI is simple, ensuring better dose distribution to CSI target without increasing the dose to the surrounding organs at risk. It is tolerable and safe to apply.

**Keywords:** Craniospinal Irradiation; Supine; Medulloblastoma; Cns45 Leukemia; Conformal radiotherapy.

### 592. Re-Evaluation of the Value of Adjunctive Modern Radiotherapy in Muscle-Invasive Bladder Cancer

Mohamed Saad Zaghoul

*Journal of Solid Tumors*, 2 (3): 1-3 (2012)

The 5-year overall survival of T3 and T4 bladder cancer patients showed no difference between the pre- and post-operative radiotherapy; in overall survival, disease-free survival, local control and distant metastasis-free rates. It was estimated that both immediate postoperative complications and late serious gastrointestinal (GIT) sequelae were similar in both groups and of minimal amplitude. Late bowel complications were reported to be 4.5% in the post-operative setting and 2% in the pre-operative setting this was nearly similar to the percentages previously

reported (4% and 5% grade 3+4 late bowel toxicity in conventional and hyper fractionated postoperative radiotherapy groups). In another retrospective study, a total of 12% of the patients who received PORT experienced chronic intestinal complications of different grades compared with 8% in the cystectomy alone group. Four patients in each group (5.8% and 3.3%, respectively) needed surgery for intestinal late complications. on the other hand, much higher late GIT complications were reported by Reseinger et al. ( 37% late GIT complications with 22.5% of the irradiated patients suffered from grade 3+4 and required surgery). Such alarming and hindering results were mainly due to the usage of unusually large volume of irradiation to include the common iliac and lower para-aortic lymph nodes. The safe and similarly effective irradiation volume has to be restricted in its upper limit to include the internal and external iliac nodes (Just below the bifurcation of the common iliac vessels). This big difference in radiation volume led to the discrepancy in the reported late GIT and therefore the hesitancy of the oncology community to re-investigate the value of post-operative radiotherapy after radical cystectomy. Obviously, the pre-and post-operative radiotherapy were tolerable and safe. This report though being the first comparing these 2 modalities of radiation, yet it used a conventional 2D technique with 3 fields arrangement. This conventional technique entails bigger volume of intestine to be exposed to high radiation dose; being unable to conform the planning volume and minimize the dose to the organs at risk (OAR). Essentially this technique does not necessitate the use of any type of verification (Port film, Electronic Portal Imaging Device EPID or Cone-beam Computed Tomography CBCT).

**Keywords:** Blooder Cancer; Radiotherapy.

### 593. Bladder Cancer and Schistosomiasis: is there A Difference for the Association?

Mohamed S. Zaghloul and Iman Gouda

*Bladder Cancer -from Basic Science to Robotic Surgery, (2012)*

Bladder cancer represents a significant worldwide health problem with an estimated 386,300 new cases and 150,200 deaths in 2008 worldwide. the majority of bladder cancer occurs in males and there is a 14-fold variation in incidence internationally. the highest incidence rates are found in the countries of Europe, North America, and Northern Africa (Jemal et al.2011). Smoking and occupational exposures are the major risk factors in Western countries, whereas chronic infection with Schistosoma hematobium (SH) in developing countries, particularly in Africa and the Middle East, accounts for about 50% of the total burden. the majority of bladder cancers associated with schistosomiasis are squamous cell carcinoma.

#### Dept. of Surgical Oncology

### 594. Surgical Management of Primary Hyperparathyroidism Guided by Double-Phase Tc-99M-Mibi Scintigraphy

Abdel Hamid Hussein Ezzat, Tarek El. Baradie, Amr Attia, Magdy Kotb, Ahmad Zaher and I man Gouda

*Chinese-German J. of Clinical Oncology, 11 (1): 24-32 (2012)*

The aim of this work was to study the clinicopathological features of cases with primary hyperparathyroidism (PHPT) referred to

National Cancer Institute (NCI), Cairo University in the last six years and to study the role of nuclear medicine techniques in the initial diagnosis and preoperative localization directing surgical management of these cases.

**Methods:** This study included 27 patients with PHPT properly diagnosed and treated in the NCI, Cairo University from January 2005 to December 2010. Preoperative neck U/S and Tc-99m-MIBI scintigraphy were done in all cases. If preoperative localization detected a single lesion, unilateral exploration was done. Bilateral exploration was done if multiple foci of active parathyroid glands or no lesions were detected.

**Results:** This study included 27 patients (8 males and 19 females). the median age was 43 years (range from 19 to 68 years). All cases presented with bone disease in the form of bony pain in 23 patients, bony swellings in 15 patients and pathological fractures in 6 cases.

Twenty one patients (77.8%) had single adenoma, 5 cases (18.5%) had parathyroid hyperplasia, and only one case had double adenomas. the sensitivity of neck U/S in detecting single adenoma was 61.9% (13/21), with 81% positive predictive value (PPV) while the sensitivity of Tc-99m- MIBI scintigraphy was 90.5% (19/21) with 100% PPV. Based on preoperative localization tests, unilateral exploration was done in 19 patients with solitary adenomas. All cases in this group were cured with no reported case of persistent or recurrent hypercalcemia.

**Conclusion:** Presentation of PHPT may mimic malignant bone tumors but fortunately these patients were correctly diagnosed with bone scan which confirm the presence of metabolic bone disease rather than bone metastases.

This was followed by estimation of serum calcium and parathormone levels for confirmation. Unilateral exploration based on the combination of ultrasound and preoperative localization by Tc-99m-MIBI scintigraphy was effective and could replace the standard bilateral neck exploration in cases with solitary adenoma. Bilateral neck exploration was required for suspected bilateral disease, hyperplasia or non visualized parathyroids.

**Keywords:** Primary hyperparathyroidism; Tc-99 M; Mibi scintigraphy.

#### Dept. of Tumor Biology

### 595. Assessment of Health Related Quality of Life in Patients Receiving Stem Cell Therapy for End Stage Liver Disease: an Egyptian Study

Hosny Salama, Abdel-Rahamn N Zekri, Rasha Ahmed, Iman Medhat, El Sayed Abdallah, Tarneem Darwish, Ola S Ahmed and Abeer Bahnassy

*Stem. Cell. Res. Ther., 3 (49 ): 2-10 (2012) IF: 3.212*

This prospective cohort study aimed to assess the influence of stem cell therapy (SCT) on healthrelated quality of life (HRQOL) by using the SF-36 v2 and to elucidate the influence of objective clinical variables on subjective HRQOL.

**Methods:** the study included 100 chronic liver disease patients (50 received SCT, and 50 received supportive medical treatment (SMT)). Both groups completed a modified SF-36 v2 form before therapy and at 1-, 3-, 6-, and 12-month intervals. Fifty healthy Egyptian volunteers were enrolled in the study and completed the SF-36 v2 form once.

**Results:** Both SCT and SMT groups showed significantly lower pretherapy SF 36 v2 scores compared with healthy volunteers. in



SCT-treated patients, limited complications were encountered (SF-36 v2 scores showed significant improvement in all domains throughout the follow-up period) compared with the deterioration shown by SMT patients after therapy. A significant association was detected between SF-36 v2 scores and laboratory data in SCT patients during the first month after therapy. the grade of ascites improved during the follow-up in SCT compared with SMT patients. the mean survival time was 277.56 days (95% CI, 246.217 to 308.903) for SMT and 359.300 days (95% CI, 353.022 to 365.578) for SCT patients (log rank, 0.00). Stem celltreated patients showed no malignancies.

**Conclusions:** SCT positively affects health-related quality of life in cirrhosis patients. the survival rate was significantly improved after SCT.

### 596. Aberrant Expression of Cell Cycle Regulatory Genes Predicts Overall and Disease Free Survival in Malignant Pleural Mesothelioma Patients

Abeer A. Bahnassy, Abdel-Rahman N. Zekri, Amany A. Abou-Bakr, Mervat M. El-Defdar, Ahmad El-Bastawisy, Mona A. Sakr, Ghada M. El-sherif and Rabab M. Gaafar

*Experimental and Molecular Pathology*, 93 (1): 154-161 (2012) IF: 2.425

Malignant pleural mesothelioma (MPM) is a highly aggressive disease with a generally poor prognosis. Since escape from cell cycle checkpoint control is common in several solid tumors, the present study was performed to evaluate the role of some cell cycle regulatory genes in the development and progression of MPM.

**Patients and methods:** Aberrant expression of p14ARF, p16INK4A, p21waf, p27KIP, p53, mdm2 and Rb was assessed in 55 MPM cases from Egypt using immunohistochemistry and PCR techniques. Results were correlated with clinico-pathological prognostic factors, overall and disease free survival (OS&DFS).

**Results:** Altered expression of p14ARF, p16INK4A, p21waf, p27KIP1, Rb, p53 and mdm2 proteins was detected in 50.9%, 54.5%, 53.3%, 61.8%, 53.3%, 58.2%, and 50.8% of cases, respectively. SV40 infection significantly correlated with p14ARF, p16INK4A, p27kip1 and Rb aberrations ( $p = 0.014$ ,  $p = 0.02$ ,  $p = 0.01$ ,  $p = ? 0.01$ ). Asbestos exposure significantly correlated with p53, p21waf and mdm2 aberrations ( $p = 0.001$ ,  $p = 0.03$ ,  $p = 0.02$ ). on multivariate analysis PS ? 2, p27KIP1 and Rb aberrations were independent prognostic factors for OS ( $p = 0.016$ ,  $p = 0.011$ ,  $p = 0.003$ ) whereas on tumor recurrence, p27KIP1 and Rb aberrations were independent prognostic factors for DFS ( $p = 0.002$ ,  $p = 0.03$ ,  $p = 0.01$ ).

**Conclusions:** MPM is a complex disease characterized by multiple genetic aberrations; some of them involve cell cycle regulatory genes. p14ARF, p16INK4A, Rb and p27KIP1 seem to be involved in SV40-associated MPM whereas mdm2, p53 and p21WAF are related to asbestos exposure. in addition to recurrence and PS, only p27KIP1 and Rb could be used as molecular prognostic markers in MPM.

**Keywords:** Malignant pleural mesothelioma; Prognosis; P16; P14; P53; P21waf; P27; Rb.

### 597. Epstein-Barr Virus and Breast Cancer: Epidemiological and Molecular Study on Egyptian and Iraqi Women

Abdel-Rahman N. Zekri, Abeer A. Bahnassy, Waleed S. Mohamed, Fatma A. El-Kassem, Saja J. El-Khalidi, Mohamed M. Hafez and Zeinab K. Hassan

*Journal of the Egyptian National Cancer Institute*, 24, 123–131 (2012) IF: 2

The role of Epstein-Barr virus (EBV) in breast carcinogenesis is still controversial. Unraveling this relationship is potentially important for better understanding of breast cancer etiology, early detection and possibly prevention of breast cancer. the aim of the current study is to unravel the association between EBV and primary invasive breast cancer (PIBC) in two different Arab populations (Egyptian and Iraqi women).

**Patients and Methods:** the study was done on paraffin-embedded tissues of 40 Egyptian and 50 Iraqi patients with PIBC in addition to 20 normal breast tissues as controls for each group. Both controls and neoplastic tissues were assessed for the expression of EBV genes and proteins (EBNA-1, LMP-1, and EBER) as well as CD21 marker by immunohistochemistry (IHC), in situ hybridization (ISH) and PCR techniques.

**Results:** Our gold standard for EBV reactivity in breast cancer cases was positivity of both EBNA1 by PCR and EBER by in situ hybridization. EBV was detected in 18/40 (45%) and 14/50 (28%) of Egyptian and Iraqi women; respectively where  $p = 0.073$ , compared to 0/20 (0%) of their control groups ( $p < 0.05$ ). Regarding the association between EBV positivity and tumor grade, there was not any statistical significant difference between EBV presence and tumor grade in both populations where  $p = 0.860$  and  $p = 0.976$  and the calculated rank biserial correlation coefficient was 0.114 and 0.269 for Egyptian and Iraqi women respectively.

**Conclusion:** Our findings show that EBV might act as a promoter for the development of PIBC and it might contribute to increased tumor aggressiveness in Egyptian and Iraqi patients.

**Keywords:** Epstein-barr virus infection; Egyptian and iraqi women; Primary invasive breast cancer (PIBC).

### 598. Insulin-Like Growth Factor System in Egyptian Children with Acute Lymphoblastic Leukemia

Zakhary N.I., Boshra S.A., El-Sawalhi M.M., Fahim A.T. and Ebeid E.N.

*Genetic Testing and Molecular Biomarkers*, 16 (9): 1067-1072 (2012) IF: 1.11

Insulin-like growth factors (IGFs) and IGF-binding proteins (IGFBPs) have been reported to play an important role in tumor proliferation. This study aimed to investigate the validity of measuring IGFs and specific IGFBPs in the serum of Egyptian children with acute lymphoblastic leukemia (ALL) as additional markers in diagnosis and follow-up of the disease. IGF-I, IGF-II, IGFBP-2, and IGFBP-3 were determined in the sera of 33 ALL patients at time of diagnosis and after an intensification phase of chemotherapy (IPC) that lasts about 6 months as well as in 15 healthy children as a control group using enzyme-linked immunosorbent assay (ELISA) technique. at time of diagnosis, serum IGF-I, IGF-II, and IGFBP-3 were significantly lower than those in the control group. After IPC, serum IGF-I and IGF-II returned to their normal levels, while serum IGFBP-3 was still

decreased. on the other hand, serum IGFBP-2 was significantly higher than those in the control group at diagnosis, but returned to normal value after IPC. in conclusion, the changes in IGF system could be useful to support diagnosis and follow-up of children with ALL.

### 599. Hepatitis C Virus and Other Risk Factors in Hepatocellular Carcinoma

Schiefelbein E, Zekri A.R., Newton D.W., Soliman G.A., Banerjee M., Hung ChW, Seifeldin I.A., Lo A.C. and Soliman AS.

*Acta. Virol.*, 56 (3): 235-240 (2012) IF: 0.682

Hepatocellular carcinoma (HCC) increased in Egypt in the past years, becoming the most common cancer among men. Hepatitis B virus (HBV) and hepatitis C virus (HCV) are the known primary risk factors for HCC. This study describes the viral profile of HCC in a predominantly rural area in Egypt. We included 148 HCC cases and 148 controls from the Tanta Cancer Center and the Gharbiah Cancer Society in the Nile delta region. Serological (ELISA) and molecular (PCR) analysis for HBV and HCV infection were performed on plasma samples from each subject. Epidemiologic, environmental, and medical histories were collected by interviewing of subjects. Around 90.5% of cases and controls were from rural areas. HCV infection was high in both cases and controls (89.2% and 49.3%, for cases and controls respectively by serology). HCV was the most important HCC risk factor [OR 9.7 (95% CI: 3.3-28.0, P <0.01)], and HBV infection showed marginal tendency of increased risk [OR 5.4 (95% CI: 0.9-31.8, P <0.06)]. Ever worked in farming [OR 2.8 (95% CI: 1.1-7.2, P <0.03)] and history of cirrhosis [OR 3.6 (95% CI: 1.6-8.1, P <0.01)] or blood transfusion [OR 4.2 (95% CI: 0.99-17.8, P <0.05)] were also associated with increased HCC risk. This study in a predominantly rural area in Egypt supports previous reports from other parts of Egypt that HCV infection is the primary HCC risk factor in Egypt. Further understanding of the relationship between infection and other risk factors in the development of HCC could lead to targeted interventions for at-risk individuals.

**Keywords:** Hepatocellular carcinoma; Hepatitis; Rural; Risk factors; Egypt.

### 600. Molecular Prognostic Profile of Egyptian HCC Cases Infected with Hepatitis C Virus

Abdel-Rahman N Zekri, Zeinab K Hassan, Abeer A Bahnassy, Ghada MSherif, Dina ELdahshan, Mohamed Abouelhoda, Ahmed Ali and Mohamed M Hafez

*Asian Pacific J Cancer Prev*, 13: 5433-5438 (2012) IF: 0.659

Hepatocellular carcinoma (HCC) is a common and aggressive malignancy. Despite of the improvements in its treatment, HCC prognosis remains poor due to its recurrence after resection. This study provides complete genetic profile for Egyptian HCC. Genome-wide analyses were performed to identify the predictive signatures.

**Patients and Methods:** Liver tissue was collected from 31 patients with diagnosis of HCC and gene expression levels in the tumours and their adjacent non-neoplastic tissues samples were studied by analyzing changes by microarray then correlate these with the clinico-pathological parameters. Genes were validated in

an independent set by qPCR. the genomic profile was associated with genetic disorders and cancer focused on gene expression, cell cycle and cell death. Molecular profile analysis revealed cell cycle progression and arrest at G2/M, but progression to mitosis; unregulated DNA damage check-points, and apoptosis.

**Result:** Nine hundred fifty eight transcripts out of the 25,000 studied cDNAs were differentially expressed; 503 were up-regulated and 455 were down-regulated. A total of 19 pathways were up-regulated through 27 genes and 13 pathways were down-regulated through 19 genes. Thirty-seven genes showed significant differences in their expression between HCC cases with high and low Alpha Feto Protein (AFP ?600 IU/ml). the validation for the microarray was done by real time PCR assay in which PPP3CA, ATG-5, BACE genes showed down-regulation and ABCG2, RXRA, ELOVL2, CXR3 genes showed up-regulation. cDNA microarrays showed that among the major upregulated genes in HCC are sets.

**Conclusion:** the identified genes could provide a panel of new diagnostic and prognostic aids for HCC.

**Keywords:** Egyptian Hcc; Hepatitis C Virus; Gene Expression Profile; Microarrays.

### 601. MicroRNAs and Metastasis-Related Gene Expression in Egyptian Breast Cancer Patients

Mohamed M Hafez, Zeinab K Hassan, Abdel Rahman N Zekri, Ayman A Gaber, Salem S Al Rejaie, Mohamed M Sayed-Ahmed and Othman Al Shabanah

*Asian Pacific Journal of Cancer Prevention*, 13: 591-598 (2012) IF: 0.659

MicroRNAs (miRNAs) are a class of naturally occurring small noncoding RNAs that regulate gene expression, cell growth, differentiation and apoptosis by targeting mRNAs for translational repression or cleavage. the present study was conducted to study miRNAs in Egyptian breast cancer (BC) and their relation to metastasis, tumor invasion and apoptosis in addition to their association with the ER and PR statuses.

**Methods:** Real Time RT-PCR was performed to identify the miRNA expression level of eight miRNAs and eight metastatic-related genes in 40 breast cancer samples and their adjacent non-neoplastic tissues. The expression levels of each miRNA relative to U6 RNA were determined using the  $2^{-\Delta\Delta CT}$  method. Also, miRNA expression profiles of the BC and their corresponding ANT were evaluated. Results: the BC patients showed an up-regulation in miRNAs (mir-155, mir-10, mir-21 and mir-373) with an upregulation in MMP2, MMP9 and VEGF genes. We found down regulation in mir-17p, mir-126, mir-335, mir-30b and also TIMP3, TMP1 and PDCD4 genes in the cancer tissue compared to the adjacent non-neoplastic tissues. Mir -10b, mir -21, mir-155 and mir373 and the metastatic genes MMP2, MMP9 and VEGF were significantly associated with an increase in tumor size (P < 0.05). No significant difference was observed between any of the studied miRNAs regarding lymph node metastasis. Mir-21 was significantly over-expressed in ER-/PR- cases. Conclusion: Specific miRNAs (mir-10, mir-21, mir-155, mir-373, mir-30b, mir-126, mir-17p, mir-335) are associated with tumor metastasis and other clinical characteristics for BC, facilitating identification of individuals who are at risk.

**Keywords:** Breast cancer; Mirna; Gene expression; Metastasis risk; Egypt.

### 602. Stem Cell Transplantation as New Treatment Modalities in Primary Hyperoxaluria (A Case Report)

A. N. Zekri, H. Salama, M. Al Shabrawy, A. Bahnassy, O. S. Ahmed, A. Amer and R. Ahmed

*Stem Cell Discovery*, 2 (4): 176-179 (2012)

Primary hyperoxaluria-1 (PH1) is a potentially lethal disease caused by mutations of the gene expressing alanine: glyoxylateaminotransferase (AGXT) that lead to oxalate overproduction by hepatocytes. Clinical and animal studies had showed that stem cell transplantation is safe and partially effective minimally invasive substitute for liver transplantation in the treatment of patients with inherited liver-based metabolic disorders. In the present study we used allogeneic stem cell transplantation as a potential therapy in PH1.

**Methods:** 200 ml bone marrow were collected from mother after GCSF induction and in-vitro differentiation as previously reported by our group (Salama et al., 2010). This differentiated bone marrow cells were transfused to her child who aged 11 years old presented with recurrent bilateral renal stones and elevated blood urea and creatinine level diagnosed as PH1 after obtaining a written informed consent from his parents together.

**Result:** the child showed progressive improvement in his urinary oxaluria and kidney biochemical profile as well as reduction in the plasma oxalate level from  $\geq 200 \mu\text{mol/L}$  to  $4.0 \mu\text{mol/L}$  value with no new renal stone formation or calcium deposit during the 4 years follow-up period after the stem cell transplantation as evidenced by kidney X-ray, ultrasound and CT scan since the parents refuse to supply us with tissue biopsy from kidney or liver to be studied.

**Conclusion:** From this study we recommended a large study to confirm the value of using stem cells in treating patients with PH1.

**Keywords:** Allogeneic Stem Cell; Primary.

### 603. Repressed Induction of Interferon-Related Micrnas Mir-146A and Mir-155 in Peripheral Blood Mononuclear Cells Infected with Hcv Genotype 4.

Nada El-Ekiaby, Nabila Hamdia, Mohamed Negm, Rasha Ahmed, Abdel Rahman Zekri, Gamal Esmat and Ahmed Ihab Abdelaziz

*Febs Open Bio*, 2: 179-186 (2012)

MicroRNAs regulate the expression of many genes and subsequently control various cellular processes, such as the immune response to viral infections mediated by type I interferon (IFN). In this study, the expression pattern of two interferon-related microRNAs, miR-146a and miR-155, was examined in healthy and HCV-genotype-4-infected peripheral blood mononuclear cells (PBMCs) using qRT-PCR. In contrast to other viral infections, the expression pattern was similar in both healthy and infected PBMCs. This could be attributed to attenuation of IFN pathway by HCV, which was assessed by investigating the expression of MxA, an interferon-stimulated gene, that showed lower expression in HCV-infected PBMCs. To determine the site of interference of HCV in the IFN pathway, expression of both microRNAs was examined following stimulation of PBMCs with IFN- $\gamma$ 2a, an activator of the JAK/STAT pathway as well as with

imiquimod, a toll-like receptor-7 (TLR-7) agonist that promotes interferon release. IFN stimulation induced the expression of miR-146a and miR-155 in HCV-infected and healthy PBMCs. Stimulation with imiquimod led to a down-regulation of both microRNAs in infected PBMCs, while it increased their expression in healthy PBMCs, indicating that HCV might interfere with miR-146a and miR-155 expression at sites upstream of interferon release, specifically in the TLR-7 pathway. The pattern of expression of both miR-146a and miR-155 was very similar with a strong positive correlation, but showed no correlation to the patients' clinical or histopathological parameters or response to treatment. In conclusion, HCV infection might repress the induction of miR-146a and miR-155 by interfering with TLR-7 signaling.

**Keywords:** Hcv; Pbmcs; Mir-146A; Mir-155; Interferon; Tlr-7

### 604. Role of Glypican-3 in the Early Diagnosis of Hepatocellular Carcinoma Among Egyptian Patients

Nadia Iskandar Zakhary, Mervat Sayed Mohamed, Ola Khorshid, Remon Sobhy Azer and Naglaa Zayed

*Journal of Genetic Engineering and Biotechnology*, 10, 73-79 (2012)

The aim was evaluation of the role of glypican-3 (GPC3) in early diagnosis of hepatocellular carcinoma (HCC) among Egyptian patients associated with hepatitis C virus (HCV) where genotype 4a is prevalent, as well as differentiating HCC from benign chronic liver disease.

**Methods:** 80 individuals were enrolled in the study: 14 healthy volunteers, 18 patients with HCV, 18 patients with liver cirrhosis (LC) and 30 patients with HCC. Serum GPC3 and AFP levels were measured using ELISA technique.

**Results:** GPC3 at cut-off value of 3.8 ng/ml (100% specificity) have superior sensitivity than AFP at cut-off values of 151.0 ng/ml (100% specificity) in differentiating HCC from benign liver disease. The GPC3 sensitivity was 93.3% versus 83.3% for AFP while the combined use of both markers improved the sensitivity to 96.7%. For early detection of HCC with tumor size  $\leq 5$  cm, the GPC3

**Keywords:** Hcc; Gpc3; Afp; Hcv; Serum Marker.

### 605. 2-Potent Inhibitory Effects of P7 Inhibitors on Genotype 4 Hcv-Infected Peripheral Blood Mononuclear Cells

Maged A. Saleh, Radwa Y. Mekky, Nada El-Ekiaby, Nabila Hamdi, Rasha Ahmed, Abdel Rahman Zekri, Gamal Esmat and Ahmed I. Abdelaziz

*Recent Patents on Biomarkers*, 2 (3): 227-233 (2012)

Several patents were published for HCV p7 protein including a synthetic p7 model for drug design and screening of experimental compounds. Additionally, patents were published for identification and use of compounds as p7 inhibitors. HCV p7 protein is a viral ion channel (viroporin) that was found to be crucial for viral production through facilitating assembly and release. Accordingly, targeting the protein is expected to inhibit these stages in the HCV lifecycle. p7 inhibitors displayed effectiveness against recombinant replicons of different HCV genotypes with genotype-dependant responses, but they were

never tested on genotype 4 (GT-4). Our study focused on examining the effects of four p7 inhibitors; amantadine, rimantadine, N-nonyl-deoxyjirimycin (NN-DNJ) and hexamethylenamiloride (HMA) on HCV GT-4 for the first time which involves the majority of cases in Egypt and the Middle East-North Africa (MENA) region. HCV viral load was assessed after stimulation by p7 inhibitors for HCV-positive Peripheral Blood Mononuclear Cells (PBMCs) which are known to be extra-hepatic reservoirs for the virus. The compounds showed strong reduction of viral load without affecting cell viability in congruency with previous experimental work that alternatively used other HCV genotypes and cell lines.

**Keywords:** Amantadine; Hexamethylenamiloride (HMA); N-nonyl-deoxyjirimycin (NN-DNJ); p7; PBMCs; Rimantadine; Hepatitis C virus (HCV); Genotype 4, p7 inhibitors; Extra-hepatic reservoirs; Chronic liver disease.

### 606. The Role of Some Natural and Synthetic Compounds in Cancer Protection / Chemical Carcinogenesis

Nadia Iskandar Zakhary, Abdelfattah Badawi, Atef T Fahim and Rania Farag Ahmed El-Telbany

*Important Facts About Cancer Prevention*, (2012)

Chemoprevention is an innovative area of cancer research that focuses on the prevention of cancer through pharmacologic, biologic, and nutritional intervention. As originally described, this involves the primary prevention of initiation and the secondary prevention, delay, or reversal of promotion and progression. Several agents have demonstrated cancer preventive risk reduction in large phase three clinical trials in individuals with an increased risk of cancer. Other large trials are ongoing. There are several possible approaches to cancer prevention. Patients can decrease behaviors that put them at risk, be more vigilant in screening and surveillance, opt for surgical preintervention, and/or utilize "medicinal" approaches. The latter three areas in particular can benefit from the advances that nanotechnology can offer. This book was conceived with the idea of focusing on one of many worldwide research programs, and that is the role of different agents in the war against cancer. Metals and metal compounds have been used in medicine for several thousands of years. In this book, we present a selection of anticancer activities and cancer prevention potential for a selection of metal ions. This book comprises ten chapters dealing with variegated aspects of cancer and prevention. The chapters covered the role of many topics in cancer prevention as chemical carcinogenesis, some natural and synthetic compounds, metal ions, metals, trace elements, amino acids, surfactants, and nanotechnology.

### 607. Radiation-Induced Double-Strand Breaks Require Atm But Not Artemis for Homologous Recombination During S-Phase

Sabrina Kucher, Thorsten Rieckmann, Gabor Rohaly, Wael Y. Mansour, Ekkehard Dikomey, Irena Dornreiter and Jochen Dahm-Daphi.

*Nucleic Acids Res*, 40 (17): 8336-8347 (2012) IF: 8.026

Double-strand breaks (DSBs) are repaired by two distinct pathways, non-homologous end joining (NHEJ) and homologous recombination (HR). The endonuclease Artemis and the PIK

kinase Ataxia- Telangiectasia Mutated (ATM), mutated in prominent human radiosensitivity syndromes, are essential for repairing a subset of DSBs via NHEJ in G1 and HR in G2. Both proteins have been implicated in DNA end resection, a mandatory step preceding homology search and strand pairing in HR. Here, we show that during S-phase Artemis but not ATM is dispensable for HR of radiation-induced DSBs. In replicating AT cells, numerous Rad51 foci form gradually, indicating a Rad51 recruitment process that is independent of ATM-mediated end resection. Those DSBs decorated with Rad51 persisted through S- and G2-phase indicating incomplete HR resulting in unrepaired DSBs and a pronounced G2 arrest. We demonstrate that in AT cells loading of Rad51 depends on functional ATR/Chk1. The ATR-dependent checkpoint response is most likely activated when the replication fork encounters radiation-induced single-strand breaks leading to generation of long stretches of single-stranded DNA. Together, these results provide new insight into the role of ATM for initiation and completion of HR during S- and G2-phase. The DSB repair defect during S-phase significantly contributes to the radiosensitivity of AT cells.

**Keywords:** Atm; S-Phase; Dsb repair; Artemis.

### 608. Evaluating the Role of Curcum Powder as a Protective Factor Against Bladder Cancer- an Experimental Study

Hala El-Mesallamy, Tarek M Salman, Abeer M Ashmawey and Nada Osama

*Asian Pacific J. Cancer Prevention*, 13: 5287-5290 (2012)  
IF: 0.659

Throughout human history, plant products have been used for many purposes including as medicines. Herbal products and spices can be used as preventive agents against cancer due to their antimicrobial, antioxidant and antitumorigenic properties. This study was designed to evaluate the potential protective effect of curcum in rats administered nitrosamine precursors; dibutylamine (DBA) and sodium nitrate (NaNO<sub>3</sub>); and infected with *Escherichia coli* (E. coli) and also to monitor changes in nuclear factor the Kappa B p65 (NF- $\kappa$ B p56) pathway and its downstream products, Bcl-2 and interleukin-6 (IL-6), in parallel with nitrosamine precursors, E. coli and curcum treatment. Rats were divided into three groups (n=25 each; except of control group, n=20). Group I a normal control group, group II administered DBA/NaNO<sub>3</sub> in drinking water and infected with E. coli and group III was administered DBA/NaNO<sub>3</sub> in drinking water, infected with E. coli and receiving standard diet containing 1% curcum powder. Histopathological examination reflected that the curcum treated group featured a lower incidence of urinary bladder lesions, and lower levels of NF- $\kappa$ B, Bcl-2 and IL-6, than the group receiving nitrosamine precursor and infected with E. coli. These findings suggested that curcum may have a protective role during the process of bladder carcinogenesis by inhibiting the NF- $\kappa$ B pathway and its downstream products.

**Keywords:** Bladder Carcinogenesis; Curcum; E. Coli; Nf- $\kappa$ B P65; Bcl-2; Il-6.

### 609. Role of Chronic E. Coli Infection in the Process of Bladder Cancer - an Experimental Study

Hala El-Mosalamy, Tarek M Salman, Abeer M Ashmawey and Nada Osama

*Infectious Agents and Cancer*, 7 (19): 190-204 (2012)

Bladder cancer is a common malignancy in Egypt. A history of urinary tract infection can be considered as a risk factor for bladder cancer. Escherichia coli (E. coli) infection is responsible for 70% of urinary tract infection. This study aimed to evaluate the role of chronic E. coli infection during bladder carcinogenesis. in order to achieve this aim, we investigated the histopathological changes in bladder tissue and measured the level of nuclear factor kappa p65 (NF- κBp65), Bcl-2 and interleukin 6 (IL-6) in four groups each consisting of 25 male albino rats except of control group consisting of 20 rats. the first group was normal control group, the second group was infected with E. coli, the third group was administered nitrosamine precursor, and the fourth group was infected with E. coli and administered nitrosamine precursor.

**Results:** the histopathological examination revealed that E. coli infected group was able alone to produce some histopathological changes in bladder tissue and that nitrosamine precursor plus E. coli group showed highest incidences of urinary bladder lesions than the nitrosamine precursor group. NF- κBp65, Bcl-2 and IL-6 levels were significantly higher in nitrosamine precursor plus E. coli group than the other groups.

**Conclusion:** These findings suggested that urinary bladder infection by E. coli may play a major additive and synergistic role during bladder carcinogenesis.

**Keywords:** Bladder carcinogenesis; E. Coli; Nf- κBp65; Bcl-2; IL-6.

#### Dept. of Tumor Pathology

### 610. Diagnostic Accuracy of Fine Needle Aspiration Cytology in Thyroid Lesions

E.A. Sinna and N. Ezzat

*Journal of the Egyptian National Cancer Institute*, 24: 63-70 (2012) IF: 2

Evaluation of accuracy of fine needle aspiration cytology (FNAC) in the diagnosis of different thyroid lesions.

**Patients and methods:** This is a retrospective study of 296 diagnosed cases of thyroid nodules referred to cytology unit, pathology department, NCI, who underwent FNAC for diagnosis. The results were categorized according to the recent Bethesda classification into: insufficient for diagnosis, benign, atypical follicular lesion of undetermined significance, follicular neoplasm, suspicious for malignancy, and malignant sampling. the final histologic diagnosis and/or clinico-radiologic follow-up assessment for non-neoplastic lesions were considered the gold standard.

**Results:** the study included 296 cases presented with thyroid nodules who underwent diagnostic thyroid FNAC. Female to male ratio was 5.2:1, and the median age was 44 years. Ninety-eight cases (33.1%) were diagnosed as benign, 40 cases (13.5%) as follicular lesion of undetermined significance, 49 cases (16.5%) as follicular neoplasm, 30 cases (10.1%) as suspicious for malignancy, 58 cases (19.5%) as malignant, and 21 cases (7.1%) as unsatisfactory. Nodular hyperplasia represented the majority of benign cases (89.8%), while papillary carcinoma was the most frequent malignant lesion (72.4%). Cytologic diagnoses were compared with their corresponding final histologic ones.

FNAC achieved a sensitivity of 92.8, a specificity of 94.2%, a positive predictive value of 94.9%, a negative predictive value of 91.8%, a false positive rate of 7.2%, a false negative rate of 5.8%, and a total accuracy of 93.6%.

**Conclusion:** FNA cytology is a sensitive, specific, and accurate initial diagnostic test for the evaluation of patients with thyroid swellings.

**Keywords:** Fnac; Thyroid gland lesions; Accuracy.

### 611. The Validity of Immunocytochemical Expression of Cyclin D1 in Fine Needle Aspiration Cytology of Breast Carcinoma

Noha Ezzat and Nesreen Hafez

*Journal of the Egyptian National Cancer Institute*, 24 ( 3): 145-150 (2012) IF: 2

The aim of this work is to study the validity of cyclin D1 expression, a cell cycle regulatory protein, on (fine needle aspiration cytology) FNAC samples in patients with breast carcinoma using immunostaining technique.

**Patient and methods:** This is a study done on 70 patients with primary breast carcinoma, presented to Cytology Unit, Pathology Department, National Cancer Institute, Cairo University. They underwent preoperative FNAC and diagnosed as breast carcinoma. the cytologic and tissue section slides were subjected to cyclin D1 immunocytochemical staining. Only the nuclear immunoreactivity for cyclin D1 was considered specific. the rate of concordance, and discordance, and kappa value were calculated. Relation between cytologic expression of cyclin D1 and different clinicopathologic parameters was evaluated.

**Results:** Cyclin D1 immunocytochemical expression was observed in 53/70 cases (75.7%) in cytologic smears. in histologic sections of the corresponding cases, cyclin D1 was detected in 48/70 cases (68.6%). the concordance rate of cyclin D1 expression in the FNA and histologic sections was 87.1% while the discordance rate was 12.9%. Kappa showed a value of 0.65. A statistically significant relation was found between cyclin D1 immunocytochemical expression and hormonal status as well as nuclear grade.

**Conclusion:** Cyclin D1 immunocytochemical expression can be performed successfully on cytologic samples with a high concordance rate and agreement with histologic results. This can help in determining tumor biology, and plan for patients' treatment. the marker showed a significant relation with hormone receptor status and nuclear grade.

**Keywords:** Fnac; Breast carcinoma; Cyclin D1.

### 612. A Case of Synchronous Double Primary Breast Carcinoma and Osteosarcoma: Mismatch Repair Genes Mutations as A Possible Cause for Multiple Early Onset Malignant Tumors

Hytham Ahmed, Asmaa Salama, Salem Eid Salem and Abeer A. Bahnassy

*Am. J. Case. Rep.*, 13: 218-223 (2012)

Simultaneous or consequent development of multiple solid tumors might be faced in some patients, especially the young. These tumors might be related to certain hereditary cancer syndromes or certain genetic predispositions.

We present the case of a 19-year-old woman with metastatic breast cancer to the contralateral axillary lymph node, associated with simultaneous osteosarcoma of the left lower femur. As she did not fit into any of the familial cancer syndromes, genetic predisposition was suspected. We detected.

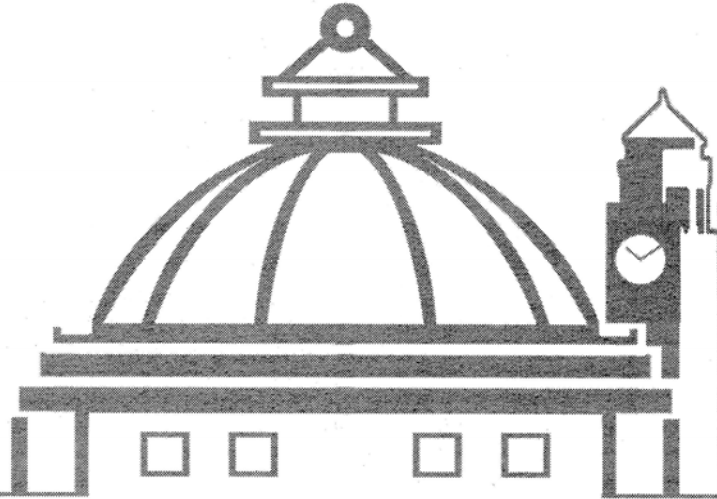
MLH1 and MSH2 promotor methylation (PM), microsatellite instability (MSI), and different mutational events in both tumors. BRCA1 gene mutations were detected in the breast tumor, with reduced mRNA expression of BRCA1&2. ERCC1, MLH1 and MSH2, especially in OS, and RRM1 was overexpressed in both tumors.

**Conclusions:** Aberrations in MMR genes could explain simultaneous or consequent development of multiple solid tumors, especially in a young patient. We recommend detecting these defects, close followup for those patients, and genetic counseling for their family members. Further studies in a larger population are essential to support our results.

**Keywords:** Osteosarcoma; Breast cancer; Double primary; Mismatch repair genes.



**International Publications Awards  
Cairo University**



# Authors' Index





## Authors' Index

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