

Abstracts

Abstracts of Theses Approved for the M.Sc., M.Med. and Phd. Degrees at the School of Medical Sciences, University Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia.

CONSTRUCTION OF VAC IV: TOWARDS THE DEVELOPMENT OF DNA VACCINE CANDIDATE AGAINST TUBERCULOSIS

Agustine Nengsih binti Said
MSc Immunology

**Department of Microbiology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.**

Introduction : Tuberculosis (TB) is the one of leading cause of death in the world, caused by a bacterium, *Mycobacterium tuberculosis*. The disease affects 1.7 billion people every year which is equivalent to one-third of the entire world population. The recent increase in the incidence of TB, particularly antibiotic-resistant TB underscores the need for an effective vaccine against this important disease. The only vaccine currently in use is the live, attenuated strain of *Mycobacterium bovis*, bacille Calmette-Guérin (BCG) that was produced in the early 1920s.

Objectives : In this study, a plasmid DNA encoding Mtb8.4, 30kDa (Ag85B) and 32kDa (Ag85A) genes of *M. tuberculosis* was constructed as an alternative vaccine candidate against TB.

Material & Methods : Using assembly polymerase chain reaction (PCR) method, the synthetic gene, designated as VacIV gene was constructed from overlapping oligonucleotides of the desired genes. The VacIV gene was successfully cloned into an eukaryotic expression vector, pVAX1[®] to produce a DNA vaccine candidate namely pVaxVacIV. The VacIV gene was also successfully expressed in *E. coli* expression system. The immunogenicity of this vaccine candidate was then tested in mice. Mice were immunized intramuscularly with the vaccine candidate. Control mice were immunized with the blank vector (pVAX1[®]). The splenocytes were cultured with antigens such as purified protein derivatives (PPD), rVacIV protein and Mtb8.4 synthetic peptide for lymphocytes transformation test (LTT) and cytokines assay.

Results : Sera were also collected to determine the level of serum IgG subclasses. Our results showed that lymphocytes from mice immunized with the pVaxVacIV secreted a higher gamma interferon (IFN- γ) but not the interleukin-4 (IL-4) levels compared to the lymphocytes from the control mice. Mice immunized with pVaxVacIV also showed high lymphocytes stimulation index and high ratio of IgG2a:IgG1 as compared to control group.

Conclusions : These results showed that the newly constructed DNA vaccine candidate, pVaxVacIV was immunogenic in mice and can be further developed as a potential vaccine candidate for TB.

Assoc. Prof. Dr. Mustafa Musa : Supervisor
Prof. Zainul F. Zainuddin : Co. Supervisor

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ACCURACY OF TRAUMA CERVICAL SPINE RADIOGRAPH INTERPRETATION AMONG EMERGENCY MEDICINE TRAINEES IN EMERGENCY DEPARTMENT HOSPITAL UNIVERSITI SAINS MALAYSIA

Dr. Abd. Kursi bin Abdul Latif
MMed Emergency Medicine

**Department of Emergency Medicine,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.**

Introduction : The emergency physician faces a great challenge in the diagnosis of cervical spine injuries, therefore radioimaging is use as an important aid for diagnostic purposes. The emergency physician must be prepared to manage patient with potential injuries to cervical spine efficiently and effectively and act accordingly. Standard cervical film trauma series is routinely performed in The Emergency Department after primary assessment has been made. Lateral and anterior-posterior view are performed in trauma case with suspected cervical spine injury. This study was performed to determine the accuracy of cervical spine radiograph interpretation among the emergency medicine trainees in Hospital Universiti Sains Malaysia.

Objectives : To determine the accuracy of two views of cervical spine trauma radiograph interpretation amongst Emergency Medicine trainees.

Methodology : This was a prospective descriptive analytical study of a 6 months period from December 2006 until May 2007 carried out at the Emergency Department Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan. Two views cervical spine radiograph film of trauma patients with suspected cervical spine injury were used and comparison were made between the emergency medicine trainees and radiologist as 'GOLD STANDARD'. Degree of agreement of ED trainees interpretation were also analysed. Data was analysed by using SPSS version 12.0. The degree of agreement were analysed by using Kappa statistic.

Results : There were a total of 162 patients cervical spine radiograph enrolled into the study during the study period. All final year emergency medicine trainees' interpretations were accurate as radiologist. They had achieved 97% to 99% accuracy. Strength of agreement among them with the radiologist interpretation were also high with Kappa value 0.88 to 0.97. The frequent difficulties in interpreting the x-rays were inadequate view of lateral cervical spine film. The prevalence of misinterpretation were also low at 0.5% to 2%.

Conclusions : There are high percentages of accurate interpretations among the emergency medicine trainees in cervical trauma radiographs. In a busy ED, their ability to interpret the radiographs and subsequently proceed with CT cervical spine injuries has improved the patient care without the presence of radiologist. It is without doubt that CT is the gold standard and it is the EPs judgment to take further actions in making their decision for advance imaging modalities.

Dr. Nik Hisamuddin Nik Abdul Rahman : Supervisor
Dr. Rashidi Ahmad : Co-Supervisor
Dr. Idzwan Zakaria : Co-Supervisor

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OUTCOME OF LEG PAIN AND LOWER LIMB WEAKNESS AFTER THE USE OF ANTI-ADHESION GEL IN SINGLE LEVEL LUMBAR DISCECTOMY.

Dr. Abdul Aziz bin Yahya
MMed Orthopaedic

**Department of Orthopaedic,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Introduction : Surgical treatment in a properly selected patient provides faster relieve for acute lumbar intervertebral disc herniation. However, up to 20% of patients may experience recurrent radiculopathy due to epidural fibrosis. The implantation of bioresorbable anti-adhesion gel (which mainly composed of carboxymethylcellulose and polyethylene oxide) on the dura may decrease the amount of fibrosis after surgery. Minimally invasive microdiscectomy is also believed to further decrease the amount of fibrosis formation. We will study the effectiveness of the anti-adhesion gel and minimal invasive microdiscectomy in improving the outcome of leg pain and lower limb weakness after single level lumbar discectomy over a period of 6 months.

Methodology : This is a cross sectional study, conducted from September 2002 to December 2006 at the Hospital Alor Setar, Kedah, Malaysia. In this study 57 patients who had radiculopathy symptoms such as leg pain and lower limb weakness underwent single level lumbar discectomy. 33 patients received anti-adhesion gel intraoperatively and 24 patients did not receive the gel. From the treated group 24 patients underwent open discectomy and 9 patients underwent minimally invasive microdiscectomy using the METRx microdiscectomy instrument system. All surgery were done by single orthopedic spine surgeon. Leg pain and lower limb weakness were assessed by visual analog scale and lower extremity motor score. Assessments were made preoperatively, 30 days, 90 days and 6 months post operation. All assessments were supervised by the operating surgeon.

Result : Surgical procedures were well tolerated by patients and no device related adverse events were noted throughout the study. All 33 patients who received the gel showed significant reduction of the leg pain and lower limb weakness compared to the control group. Whereas, the minimally invasive microdiscectomy showed comparable result to the open discectomy group.

Conclusion: In our study, anti-adhesion gel improved the outcome of leg pain and lower limb weakness after lumbar discectomy. Outcome of minimally invasive microdiscectomy is comparable to open discectomy.

**Prof. Dr. Zulmi Wan : Supervisor
Dato' Dr. Suresh Chopra : Co-Supervisor**

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**HUMAN BONE TISSUE ENGINEERING USING CORAL
AND DIFFERENTIATED OSTEOBLASTS FROM
MESENCHYMAL DERIVED STEM CELLS**

Dr. Asma' binti Hassan
PhD Biology Molecule

**Department of Anatomy,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Introduction : The future use of mesenchymal stem cells (MSC) for bone tissue engineering depends on the establishment of *in vitro* MSC cell culture; differentiation into osteoblasts and generation of new bone on coral scaffolds.

Objectives : The purposes of these studies were to develop a cultural method for the human bone marrow and cord blood mesenchymal stem cells to differentiate into osteoblasts phenotype followed by assessing their *in vitro* ability to proliferate and differentiate in the coral scaffolds.

Material & Methods : Mesenchymal stem cells of human were isolated, culture-expanded and then differentiated into osteoblasts.

Cellular morphology was analysed by light microscopy technique and the immune phenotype by MSC cell surface markers (CD105, CD166). Mesenchymal stem cells were cultured in MSC media containing 10 nM dexamethasone, 3.5 mM b- glycerophosphate and 50 mM L- ascorbic acid. Osteogenic differentiation was evaluated by means of histochemical stainings [alkaline phosphatase (ALP) and von Kossa] at day 7, 14 and 21 after osteogenic differentiation. Quantitative biochemical assays were analysed by alkaline phosphatase activity, calcium content and total protein assay. Immunocytochemical stainings against osteonectin (ON), osteopontin (OPN) and osteocalcin (OC) served as markers for- osteoblasts were each determined at 3 different time-points. Cell viability for differentiated osteoblasts in eluted corals (1, 10, 25, 50, 100 and 200 mg/ml) were assessed with dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide (MTT) assay. Cell proliferation and differentiation on coral scaffolds were analysed by using scanning electron microscopic (SEM).

Results : MSC surface markers expressed CD105 and CD166 which defined MSC in bone marrow. Cells from cord matrix persisted for a limited passage number with limited CD105 expression. Von Kossa stained for mineralised nodules on day 14 but ALP activity was minimal throughout osteogenic differentiation. Alkaline phosphatase expression increased with time and calcium assay correlated with the histochemical findings. Osteopontin reached a maximum on day 7 and gradually decreased until day 21 but the secretion of OC increased time dependently. Interestingly, ON showed a biphasic pattern with increased expression on day 7 and 21. The control cells cultured in the absence of osteogenic medium produced negligible expression of these markers. MTT assay showed significantly cell proliferation compared to control with administration of high coral concentration. SEM studies exhibited good cell coverage on coral surface with deposition of the matrix for all cell types that is the differentiated osteoblasts, MSC without osteogenic medium and osteoblast cell line.

Conclusions : The results suggest that coral is biocompatible material thus provides an attractive scaffold for bone tissue engineering.

**Prof. Abd. Rani Samsudin : Supervisor
Dr. Karima Akool Menkhi Al-Salih : Co-Supervisor**

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**THE STUDY OF CORRELATION OF QUALITY OF LIFE
ASSESSMENT WITH VISUAL FUNCTION AMONG
KELANTAN GLAUCOMATOUS PATIENTS**

Dr. Azreen Redzal bin Anuar
MMed Ophthalmology

**Department of Ophthalmology
School of Medical Sciences, University Sains Malaysia,
Health Campus, Kelantan, Malaysia.**

Introduction : Objective approaches of measuring the visual function impairment such as visual field and visual acuity are inadequate and do not totally reflects the true quality of life in the glaucoma patients. Currently, questionnaires are used as the health related quality of life instruments. Only few studies has been done to assess the correlation between the two.

Objective : To evaluate the reliability of the modified NEI VFQ 25 in the Kelantan glaucomatous patients and to correlate the modified NEI VFQ 25 and utility analysis to the visual field and visual acuity impairment.

Methodology : A cross sectional study was carried out from April to October 2006. Translation of the questionnaires by translation and back translation method was carried out first, followed by a pilot study on 30 glaucoma patients using the translated questionnaires. The process of reliability assessment on the questionnaires were done after the pilot study. There were 134 patients selected for the study. Ocular examination was carried out on the patients including the visual acuity assessment using the standard Snellen chart. After completion of the

ocular examination, the patients underwent an interview by in person approach using the modified NH VFQ 25 and utility analysis questionnaire. Lastly, the patients underwent the Esterman binocular visual field test using standard Carl Zeiss Humphrey Perimetry machine.

Results : Cronbach's a for the modified NEI VFQ 25 was 0.740, indicating moderate internal consistency. The total modified NEI VFQ 25 showed significant positive correlation with Esterman binocular visual field ($P<0.001$). A significant negative correlation noted between modified NEI VFQ 25 score with LogMAR visual acuity in the better eye ($P=0.009$) and also with LogMAR visual acuity in the worse eye ($P<0.001$). Modified NEI VFQ 25 subscale showed higher correlation with the visual acuity in worse eye compared to better eye. Modified NET VFQ 25 subscale showed low to strong correlation with Esterman binocular visual field. A significant negative correlation was noted between modified utility analysis with LogMAR visual acuity in the better eye ($P=0.010$) and also with LogMAR visual acuity in the worse eye ($P<0.001$). A significant positive correlation was noted between modified utility analysis with Esterman binocular visual field ($P<0.001$).

Conclusion : The validity and reliability of the modified NEI VFQ 25 were shown to be sufficient. This questionnaire is applicable to the Malay-speaking population as quality of life instrument. A significant correlation noted between modified NEI VFQ 25 with visual field and visual acuity of glaucoma patients. The modified utility analysis also showed significant correlation with visual field and visual acuity of glaucoma patients.

Assoc. Prof. Mohtar Ibrahim : Supervisor
Assoc. Prof. Dr. Wan Hazabbah Wan Hitam : Co Supervisor

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AN OUTCOME ANALYSIS OF CHILDREN WHO UNDERWENT SPINAL DYSRAPHISM REPAIR IN HOSPITAL UNIVERSITI SAINS MALAYSIA

Dr. Badrishah Idris
MSurgery (Neurosurgery)

Department of Neurosciences,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

Objective : To evaluate the impact of multiple factors and outcome (ambulatory function, and control of bowel and bladder) associated with spinal dysraphism following surgical repair.

Methodology : A retrospective chart review of children operated for spinal dysraphism in Hospital Universiti Sains Malaysia from 1 January 1990 to 31 December 2004 was conducted. Children who were solely operated before age 12 years old and who had been followed-up for at least 18 months post repair were included in the study.

Results : A total of 53 children with spinal dysraphism were included in the study. Open spinal dysraphism was 79.2% and closed spinal dysraphism 20.8%. 77.4% of patients with spinal dysraphism were ambulatory after two years following repair. Univariate analysis of the association of predictors with ambulatory status revealed that hydrocephalus, presence of shunt, motor and reflex score of SBNS, and status of difference between functional and anatomical level were significant factors of ambulatory status. By using multiple logistic regression, none of the significant predictors from the univariate analysis for ambulation function remained significant. The significant predictors from the univariate analysis of poor bladder control in this study were related to the type of spina bifida, presence of hydrocephalus, presence of sensation at SI and below, and functional level below L5 and above. From multivariate analysis, type of spinal dysraphism and functional level at L5 were found to be the significant predictors for poor bladder control.

Conclusion : Open spinal dysraphism was the more common operated spinal dysraphism in Hospital Universiti Sains Malaysia. This

study has demonstrated various factors that can affect the ambulatory function, and control of bowel and bladder in children with spinal dysraphism.

Prof. Jafri Malin Abdullah : Supervisor
Dr. Salmi Abdul Razak : Co-Supervisor

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A RANDOMISED CONTROLLED TRIAL OF THE EFFECT OF DISPLAYED PAIN SCORE ON ANALGESIC ADMINISTRATION IN ADULT TRAUMA PATIENTS AT THE EMERGENCY DEPARTMENT OF KUALA LUMPUR HOSPITAL

Dr. Cecilia Anthonysamy
MMed Emergency Medicine

Department of Emergency Medicine,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

Introduction : Pain is a common symptom experienced by trauma patients presenting to emergency departments. Yet only 38% of patients evaluated for major trauma received analgesic (Silka et al., 2004). The management of pain is often regarded as less important compared to arriving at diagnosis and treatment proper. Yet a physician's primary duty is to comfort, manage and reduce the suffering of a patient. Documentation of patient's pain score at triage has been recommended by JCAHO as a tool towards improving pain management in the ED.

Objectives : The objective of this study was to determine the effect of documentation and display of patients' self assessment of pain using numerical rating scale (NRS) on analgesic use among adult trauma patients at the emergency department at Kuala Lumpur Hospital.

Methodology : A randomized control trial was conducted recruiting 200 trauma patients who presented to the secondary triage and treated in the green zone of the emergency department in Kuala Lumpur Hospital. Only patients who had GCS of 15/15 were included. Convenient sampling was used. Pain score was done using NRS for all patients. They were randomized to have the pain score either displayed prominently in the trial group or not displayed in the control. Outcome measured were proportion of patients receiving analgesic and timing from triage to analgesic administration.

Results : The mean pain score was 5.7. 15 % of patients had mild pain, 48 % had moderate pain and 37 % had severe pain. 26.5 % (53) patients received analgesics. There was no significant difference in the proportion of patients, 29.7 % receiving analgesic when pain score was displayed, compared to 23.2 % when pain score was not displayed. p value was 0.3 by chi-square test. Within the trial group, the severity of pain was significantly associated with receiving analgesic ($p = 0.007$). Severity of pain did not have a confounder effect on the association of displayed pain score and analgesic administration. Mean time to receiving analgesic from triage was 81.3 minutes in the trial sample compared to 88.7 minutes in the control sample. There was no relationship between pain score and the timing to analgesic.

Conclusions : Display of pain score in the absence of other multi-prong intervention can not be enough to improve analgesic administration in emergency department.

Dr. Nik Hisamudin Nik Abd. Rahman : Supervisor
Dr. Rashidi Ahmad : Co. Supervisor

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DEVELOPMENT OF A DNA-BASED MOLECULAR METHOD FOR THE RAPID DETECTION OF ENTEROCOCCUS SPECIES AND ANTIMICROBIAL RESISTANCE GENOTYPES

Dr. Chan YeanYean
PhD Microbiology

Department of Microbiology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

Introduction : Enterococci have emerged as a significant cause of nosocomial infections in many parts of the world over the last decade. The most common enterococci strains present in clinical isolates are *E. faecalis* and *E. faecium*, which have acquired resistance to either gentamicin or vancomycin. The conventional culture test takes 2-5 days to yield complete information of the organism and its antibiotic sensitivity pattern.

Objectives : Hence, our present study was focused on developing a multiplex PCR assay for the rapid detection of vancomycin and bifunctional aminoglycoside resistant enterococci. This assay simultaneously detects 8 genes namely 16S rRNA of *Enterococcus* genus, *ddl* of *E. faecalis* and *E. faecium*, *acaA-aphD* that encodes high level gentamicin resistance (HLGR), multilevel vancomycin resistant genotypes such as *vanA*, *vanB*, *vanC* and *vanD* and one internal control gene.

Material & Methods : Unique and specific primer pairs were designed to amplify the 8 genes with the PCR products ranging from 150 to 1200 bp. The specificity of the primers were confirmed by DNA sequencing of the multiplex PCR products and BLAST analysis. The sensitivity and specificity of multiplex PCR assay was evaluated against the conventional culture method. The multiplex PCR was thermostabilized and an accelerated stability test was evaluated at room temperature, 37°C and 10°C. The analytical sensitivity of the assay was found to be 1 ng at the DNA level while the analytical specificity was evaluated with 43 reference enterococci and non-enterococcal strains and was found to be 100%. The thermostabilized multiplex PCR mix stored at 10°C was stable up to two and a half years by the accelerated stability test.

Results : The diagnostic accuracy was determined using a total of 543 samples from clinical isolates, poultry farms, water samples and stool samples, which showed that 3.9% of the samples were vancomycin resistant and 16.0% were bifunctional aminoglycoside resistant enterococci. The presence of an internal control in the multiplex PCR assay helped to rule out false negative cases. The multiplex PCR assay is robust and can give information about the 8 genes that are essential for the identification of the most common *Enterococcus* species and their antibiotic susceptibility pattern.

Conclusions : The PCR assay developed in this study can be used as an effective surveillance tool to study the prevalence of enterococci and their antibiotic resistance pattern in hospitals and farm animals.

Assoc. Prof. M. Ravichandran : Supervisor
Prof. Zainul F Zainuddin : Co-Supervisor

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HEARING IMPAIRMENT IN CHILDREN AND A1555G MITOCHONDRIAL DNA (MTDNA) GENE MUTATION SCREENING IN NON-SYNDROMIC SENSORINEURAL DEAFNESS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

Che Ismail Che Lah
MSc Human Genetic

Department of ORL-HNS,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia

Objectives : The main aim of the study was to screen for A1555G mitochondrial DNA mutation (mtDNA) amongst children with nonsyndromic sensorineural deafness at the Hospital Universiti Sains

Malaysia.

Patients & Methods : A total of 75 children with hearing impairment on follow-up the in Otorhinolaryngology-HNS Clinic, Hospital USM were selected. Data on the high risk factors and age at diagnosis were obtained. Subjects then were divided into either early detection (≤ 3 years old) or late detection (> 3 years old). Statistical analysis using Univariate Simple Logistic Regression was used to determine any significant relationship between age of diagnosis and other parameters such as aetiology, demographic and socio economic status.

Results : The average age of diagnosis was 54 months. There was a possible significant relationship between age of diagnosis and subjects with positive family history (OR=0.263, CI 95%, $p<0.05$). Generally the age of diagnosis was considerably late compared to the critical age for development of speech and language. This could effect the effectiveness of the rehabilitation program. The A1555G mtDNA mutation detection was performed using Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) technique with paired specific primer for nucleotide 1555 mtDNA. DNA mitochondrial from 75 subjects and 75 controls were extracted through salting-out procedure. Amongst the 150 samples analysed, mutation analysis using PCR RFLP technique had identified A1555G mtDNA mutation in one patient (1/75) and another one among the normal control subject (1/75).

Conclusions : Our findings showed that the frequency of this A1555G mutation in non syndromic sensorineural hearing loss patients and normal population was 1.3% respectively.

Assoc. Prof. Dr. DinSuhaimi Sidek : Supervisor
Prof. Dr. Mohd. Nizam Isa : Co-Supervisor
Dr. Narazah Mohd. Yusoff : Co-Supervisor

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AN EXPERIMENTAL STUDY ON INTRASTROMAL INJECTION OF AMPHOTERICIN B IN FUSARIUM SOLANI KERATITIS IN RABBITS

Dr. Che Mahiran binti Che Daud
MMed Ophthalmology

Department of Ophthalmology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia

Objectives : To compare the effectiveness between intrastromal injection of amphotericin B 0.15% (1.5mg/ml) and intrastromal injection of amphotericin B 0.0005% (5 µg/ml) and the safety of intrastromal injection Amphotericin B 0.0005% in *Fusarium solani* keratitis in rabbits.

Methodology : Fungal keratitis was induced with a standardized inoculum of *Fusarium solani* placed on the debrided cornea into the right eye of 18 New Zealand white rabbits. Rabbits in Group A (n were treated with topical 0.15% amphotericin B every hourly for 12 hours daily (control), while rabbits in Group B (n=6) were treated with intrastromal injection 0.15 % (1.5mg/ml) of amphotericin B and Group C rabbits (n=6) were treated with intrastromal injection 0.0005% (5µg/ml) of amphotericin B. The intrastromal injection was given at day 3, 6, 9 and 11. Serial clinical examination was conducted at day 3, 6, 9, 11 and 14 to look at the changes in the size of the epithelial defect, the depth of the ulcer, stromal infiltration, hypopyon and the presence of satellite lesion. The infected eyes were enucleated on the day 14 and sent for histopathology evaluation.

Results : The intrastromal injection of amphotericin B 0.0005% injection (group C) was found to be effective compared to intrastromal injection amphotericin B 0.15% ($p<0.001$) in treating *Fusarium* keratitis in rabbits. There was statistical significant difference in the size of epithelial defect ($p=0.02$) and satellite lesion ($p=0.02$) for the rabbits treated with intrastromal injection of amphotericin B 0.0005% compared to the intrastromal injection of amphotericin B 0.15%.

Histopathological examination also revealed absence of fungal load, the depth of ulcer limited to anterior two third, moderate inflammatory responses and mild granulation tissue in the group treated with intrastromal injection amphotericin B 0.0005%. These histopathological findings were consistent with serial clinical observation. There was no evidence of cornea! decompensation, severe punctate keratopathy and or cornea! melting in the group treated with intrastromal injection amphotericin B 0.0005%.

Conclusion : Intrastromal injection of amphotericin B 0.0005% (5µg/ml) was found to be effective and safe in treating *Fusarium solani* keratitis. Thus, after undergoing clinical trial it can be applied to the patient whose refractory to conventional therapy and can reduce the cost and shorten the hospital stay.

Dr. Liza Sharmini Ahmad Tajudin : Supervisor
Assoc. Prof. Dr. Mohtar Ibrahim : Co Supervisor

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**EFFECTS OF ESSENTIAL CITRUS SPP ON
CARDIOVASCULAR SYSTEM OF THE RATS AND
EFFECTS OF ANTIANXIETY AND ANTIDEPRESSION
IN MICE**

Che Rugayah Che Awang
MSc Pharmacology

**Department of Pharmacology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, Kelantan, Malaysia.**

Objectives : This study attempts to look at the effects of three essential oils from members of the *Citrus* family of plants on the cardiovascular system of the rats and to look at possible antianxiety and antidepressive effects of these oils. It's balmy smell suggest that these essential oils could produce relaxation possibly via its action on the central nervous system and subsequently may influence indirectly the cardiovascular system. The study focused on the effects of essential oils of *Citrus* spp on the blood pressure and heart rate of rats (the effect of direct aroma test via the nasal passage), and the antianxiety and antidepressive effects of these essential oils in mice.

Material & Methods : The results obtained may be correlated to the effects seen on human emotion (Elevated Plus-maze test and Behavioral Despair or Forced Swimming test). Essential oils of 3 members of the Citrus genus from the Rutaceae family were used. Specifically they are the *Citrus hystrix*, *D.C.* (wild lime or limau purut'), *Citrus microcarpa* (musk lime or 'limau kasturi') and *Citrus aurantifolia* (common lime or 'limau nipis'). These plants are traditionally used as medicaments by Malays, perhaps due to its strong and characteristic smell.

Results : Intranasal *C. hystrix* shows significant hypotensive ($p < 0.05$) on the blood pressure (systolic and diastolic) with sustained hypotensive for 5.30 ± 5.5 minutes, but for the heart rate of the rats, it is not significantly ($p > 0.05$) different. Results from our experiment showed the smelling of essential oils (0.1 ml) of *C. hystrix* and *C. microcarpa* conferred antianxiety and *C. aurantifolia* has antidepressive properties.

Conclusions : The thesis describes the effects of essential oils of the three *Citrus* spp and suggestions as to the possible mode of action of these oils on the cardiovascular system and the central nerve system.

Prof. Dr. Syed Mohsin Sahil Jamalullail : Supervisor
Dr. Abdul Razak Sulaiman : Co Supervisor

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**PRELIMINARY STUDY OF OSTEOPOROSIS AND
OSTEOPENIA AMONG POSTMENOPAUSAL WOMEN
IN MUKIM TASEK, DAERAH BADANG FROM**

NOVEMBER 006 TO NOVEMBER 2007

Dr. Emil Faszliq bin Mohd
MMed Orthopaedics

**Department of Orthopaedics,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.**

Objectives : This is a prospective cross sectional descriptive study with aims to identify the prevalence of Osteoporosis and Osteopenia in early postmenopausal women in Mukim Tasek, Daerah Badang. Systematic sampling of the population in Mukim Tasek, Kota Bharu was conducted from June 2007 to November 2007.

Patients & Methods : A total of 54 women post menopause age 45-65 years old, who were disease free and with intact uterus were recruited.

Results : Mean menopausal age at 50.56 ± 2.93 years. Prevalence of osteoporosis is 14% and osteopenia 30%. The weight, height and primary education have positive correlation with bone mineral density (BMD) where low body weight, shorter height and primary education have increase risk of osteopenia and. No correlation noted between age, age at menopause, duration of menses or parity with BMD. Smoking and exercise had no association with BMD. The result of the study comparable to urban midlife population of Malaysia.

Conclusions : With high prevalence of osteopenia and osteoporosis in the population, the problem of fracture will be major health issues to the society and nation.

KEY WORDS : Malaysia; Osteoporosis; Osteopenia; Prevalence; Menopause

Dr. Mohd Iskandar Mohd. Amin : Supervisor
Prof. Zulmi Wan : Co. Supervisor

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**THE EFFECT OF AUTOLOGOUS NON-
VASCULARISED PETRIOSTEUM WRAPPED CORAL
ON NEW BONE FORMATION**

Dr. Eskandar @ Zulkarnain Hassan
MMed Orthopaedics

**Department of Orthopaedics,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.**

Introduction : The study was designed to evaluate the use of coral as space filler. The coral was augmented with the free autologous non vascularized periosteum wrapped around it. This was an animal experiment. It was a descriptive in nature and carried out at Universiti Sains Malaysia School of Medical Sciences, Kubang Kerian, Kelantan.

Material & Methods : A total of 12 matured male New Zealand White rabbit were used in this study. The rabbits were divided into 2 groups of 8 and 12 week. The control study was designed to be in vivo. All rabbits were operated on and a 2.5cm length of right tibia was resected and replaced with the equal length of coral; partially covered with the free autologous non vascularized periosteum harvested from contralateral tibia. The coral was transfixed with 'Kirchner wire' and leg was immobilized with plaster of paris. At the end of 8th and 12th week, all the rabbits were assessed clinically, radiologically and sacrificed for histology evaluation. Bony union achieved in 3 out of 5 rabbits at 8th week while 3 out of 4 at 12th week as shown by plain radiographs and CT scans. 3 rabbits died during the experiment. Histological examination showed healing at coral-cortical junction by callus formation with simultaneous osteoblasts invasion into the coral at 8th week and later coral disintegration and calcification of newly formed bony matrix with marrow fat formation at 12 week.

Results : In conclusion, the autologous non vascularized periosteum plays role in protecting the underlying coral from early disintegration.

The coral provides an excellent scaffold for osteoconduction.

Prof. Zulmi Wan : Supervisor

Prof. Hasnan Jaafar : Co-Supervisor

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A RANDOMISED CONTROLLED TRIAL ON ENDOTRACHEAL TUBE (EYF)-PROSEAL LARYNGEAL MASK (PLMA) EXCHANGE AND AWAKE EXTUBATION WITH LIDOCAINE DURING EMERGENCE OF ANAESTHESIA IN CONTROLLED HYPERTENSIVE PATIENTS UNDERGOING ELECTIVE SURGERY IN HOSPITAL UNIVERSITI SAINS MALAYSIA

Dr. Foong Kit Weng
MMed Anesthesiology

**Department of Anesthesiology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Objectives: The aim of this study was to compare the use of ETT-PLMA exchange and awake extubation with lidocaine in the attenuation of the cardiovascular response and respiratory complications among hypertensive patients. A substudy of the effects of beta blocker antihypertensive therapy on the haemodynamic changes of both groups will also be explored.

Methodology: A total of 62 controlled hypertensive patients were recruited. Standard anaesthetic management was provided during the preoperative and intraoperative period. Thirty one patients were placed in group 1 where awake extubation was performed after a 2 minutes prior dose of 1 Lidocaine 1 mg.kg while the other 31 patients were placed in group 2 where a PLMA was inserted in deep plane of anaesthesia replacing EU before emergence of anaesthesia. Neostigmine and glycopyrrolate were chosen as the choice of reversal. Haemodynamic changes consisting of systolic, diastolic and mean arterial blood pressure, heart rate and rate pressure product were charted on arrival to the operation theatre (baseline), at removal of EU or PLMA, at 1, 2, 3, 5 and 10 minutes after airway removal. Incidence of respiratory complications was noted. Haemodynamic variables were analysed by repeated measures ANOVA followed by paired and independent t-test while respiratory complication data by Chi-square (χ^2) test. Subset of patients with beta blocker therapy were analysed to assess its haemodynamic effects.

Results: Demographic data were comparable in all groups. There was no difference in the baseline haemodynamic parameters. Group 1 subjects demonstrated an immediate and significant increase in SBP, DBP, MAP, HR and RPP while Group 2 subjects haemodynamic variables showed an initial slight insignificant rise. There was a significant difference in the haemodynamic parameters between group 1 and 2. Presence of beta blocker therapy reduced slightly the baseline haemodynamics and blood pressure changes over the 10 minutes measurement. A significant difference persisted in the BP measurements between group 1 and 2 treated with beta blocker. Measured heart rates were lower and stable resulting in a lower and favourable RPP index. Smooth emergence with minimal minor respiratory complications was noted in 93.5% of EIT-PLMA group subjects as compared to 87.1% in lidocaine group. No major respiratory complication was noted.

Conclusion: EIT-PLMA exchange is a safe and easy procedure that provides a bridge to smoother emergence with a secure airway. It is superior in attenuating the haemodynamic response to emergence of anaesthesia with least haemodynamic variability compared to lidocaine 1mg.kg⁻¹ in hypertensive patients. Treatment with long term beta blocker offer little additional blood pressure lowering effect in the presence of IV Lidocaine and usage of ETT-PLMA for emergence but was able to ensure a lower and stable heart rate resulting in a lower RPP index (<12,000) especially in the IV Lidocaine group.

Dr. Mahamorowi Omar : Supervisor

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THE ANALYSIS OF ROUTINELY PERFORMED HISTOPATHOLOGICAL EXAMINATION IN TONSILLECTOMIES INDICATED BY CHRONIC TONSILLITIS

Dr. Irfan Mohamad
MMed ORL-HNS

**Department of ORL-HNS,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Objective: The objective of this study was to see the outcome of sending routine specimen for histopathological examination in term of final diagnosis and incidental findings.

Method: This was an observational prospective study whereby 197 patients who had undergone tonsillectomy between August 2005 to January 2007 were recruited. Malignant suspicion cases were excluded. All of the operations were performed with conventional dissection method at Hospital Universiti Sains Malaysia. All specimens were sent for histopathological examination as routinely performed.

Result: All of the studied specimens showed reactive lymphoid hyperplasia changes. No specimen noted to be malignant. Actinomyces colonies were common incidental findings.

Conclusion: This study concluded that the clinical diagnosis was different with the histopathological result. The examination should not be performed as a routine procedure unless if there was any malignant suspicion or for medicolegal purposes.

Assoc. Prof. Dr. Shahid Hassan : Supervisor

Dr. Rosdan Salim : Co Supervisor

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COMPUTED-TOMOGRAPHY STUDY OF THORACIC PEDICLE MORPHOMETRY OF THE GROWING SPINE IN HUSM

Dr. Irwan Arifin
MMed Orthopaedics

**Department of Orthopaedics,
School of Medical Sciences, University Sains Malaysia,
Health Campus, Kelantan, Malaysia.**

Introduction : The posterior spinal instrumentation using pedicle screws has become one of the most practiced spine surgeries due to its sound biomechanical properties. Majority of the patients who benefits from pedicle screw fixation are the adults and adolescents. This is because extensive work has been published on the pedicle morphology of the adult and adolescent. Less is known about the pedicle morphology of children.

Objectives : To investigate the pediatric pedicle morphology in the thoracic spine (T1 to T12) and to determine the feasibility of pedicle screw instrumentation in local pediatric population. To compare quantitative difference on pedicle morphology at different phase of growth i.e. juvenile, early adolescent and late adolescent phase. To investigate sexual dimorphism of the thoracic pedicle of the growing spine.

Patients & Methods : A cross sectional study was conducted in Hospital Universiti Sains Malaysia (HUSM). The pedicle of the thoracic vertebra from T2 to T12 were studied from a total of 25 patients ages 4 to 17 (12 males and 13 females) who had undergone computed tomography studies of the lungs in Radiology Department, HUSM from 2004 to 2006. The patients were grouped to age: Group 1 (4 to 9

years old), Group 2 (10 to 14 years) and Group 3 (15 to 18 years old). All the images were reformatted and the multiplanar reconstructions were used to attain images of thoracic pedicle on axial, sagittal and coronal planes. The 5 measured parameters were pedicle chord length, transverse pedicle width, sagittal pedicle width, transverse pedicle angle and sagittal pedicle angle.

Results : The mean smallest pedicle chord length were 26.0 mm in Group 1, 29.9 mm in Group 2 and 29.3 mm in Group 3 which was the T1 pedicle. The average smallest pedicle width was at T5 in all groups (0.9 mm in Group 1, 1.2 mm in Group 2 and 1.3 mm in Group 3). The largest pedicle width were observed at T12 in all the groups. The largest pedicular angulation (transverse and sagittal pedicle angle) was observed at the first 3 thoracic vertebra. There were significant difference in majority of the linear measurement (pedicle chord length, transverse and sagittal width) in between the 3 groups. Chord length was significantly differs except at T2, T3 and T7. Transverse pedicle width did not show any significant difference at T1, T3, T4, T5 and T6 whereas sagittal pedicle width showed significant differences among the groups. Angular measurement (transverse and sagittal pedicle angle) did not show significant differences between the 3 groups. Comparison between male and female did not demonstrate significant difference in all parameters.

Conclusions : The transverse width of thoracic pedicle in Group 1 could not accommodate the 4.5 mm screw (the smallest pedicle screw in most systems) at any levels. The pedicle at the lowest 3 thoracic vertebra for Group 2 and 3 might accommodate this screw size but preoperative CT scan is highly recommended. There was significant difference in the dimension of pedicle among the age groups suggesting significant growth still exist in some parts of the spine and pedicle screw size could be judged based on the age of the pediatric patient. There was no sexual dimorphism in the thoracic pedicle of the growing spine.

Dr. Abdul Halim Yusof : Supervisor
Dr. Mohd. Ezane Aziz : Co Supervisor

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PROGNOSTIC FACTORS OF OUTCOME IN SEVERE TRAUMATIC BRAIN INJURY (TBI) IN CHILDREN AGED 2 TO 16 YEARS IN KUALA LUMPUR HOSPITAL FROM 2001 TO 2006

Dr. Kan Choon Hong
MSurgery (Neurosurgery)

**Department of Neurosciences,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.**

Introduction : Maturing brain of children reacts to traumatic insult in a way different from matured brain and thus those predictors used for assessing outcome in adult TBI might not be accurate in predicting outcome in pediatric TBI. The evidence and impact of various prognostic factors for TBI such as hyperglycemia and coagulopathy have been limited yet controversial in pediatric population. Glasgow Coma Scale (GCS) have frequently been reported not reliable in predicting outcome of pediatric TBI.

Objectives : The objective of this study was to analyze the characteristics of severe TBI in the pediatric age group in a regional neurotrauma center and to evaluate the impact of various prognostic factors on the outcome.

Methods : A retrospective case study design was applied to investigate children aged between 2 to 16 years old presenting with severe TBI treated in Kuala Lumpur Hospital (HKL) from Jan 2001 till Dec 2006. Data regarding initial Coma score, pupillary reactivity, motor score, presence of hypotension (defined as less than 5th percentile according to age-appropriate systolic blood pressure (AASBP) and development of Diabetes Insipidus (DI) within 3 days were retrieved

from hospital notes. Laboratory results of serum glucose, PT and aPTT ratio, INR, platelet counts and total white blood cell (TWBC) counts on admission were recorded. Computerized Tomography (CT) scan graded according to Marshall classification, presence of brain swelling, traumatic subarachnoid hemorrhage and intraventricular hemorrhage were recorded. Peak intracranial pressure (ICP) and lowest cerebral perfusion pressure (CPP) were recorded for those patients who had undergone ICP-CPP targeted therapy. Outcomes at 6 months was assessed with Pediatric Cognitive and Performance Categories (PCPC) scale and categorized into good and poor outcome group. Data entry and analysis were done using Statistical Package for Social Sciences (SPSS) version 12.0. Means and standard deviations were calculated for continuous variables, and frequency and percentages for categorical variables. Independent t test, Chi square test and Fisher's Exact test were applied for univariate analysis whenever appropriate. The level of statistical significance was set at 0.05. Multiple logistic regression was applied to develop a model of poor prognostic factors of pediatric severe TBI. Independent variables were entered into the logistic regression model in a stepwise procedure with a significance cutoff of $p < 0.25$. p value of less than 0.05 was interpreted as significant at 95% Confidence Interval (CI). Hosmer-Lemeshow test was used to check the goodness-of-fit. The research protocol was approved by ethics committee of Universiti Sains Malaysia in 2006.

Results : One hundred and forty-six patients fulfilled the inclusion criteria during the period of the study. The median age was 13 years with the mean of 11.8 years and standard deviation of 4.2mm. Male children were preponderant (84.2%) and majority of them were Malays (73.3%) patients. Eighty-nine cases (61%) of our patients had a good outcome. There were 35 cases of death (24%). Most of the cases were referred from other centres (83.6%), with only 24 cases (16.4%) being direct admission. The commonest mechanism of injury was road traffic accidents (RTA), 118 (80.8%) patients; followed by fall from height 14 (9.6%) patients; contact sport 2 (1.4%) patients; assault 2 (1.4%) patients. The mechanism of injury was unknown in 5.5%. Analysis of outcome with univariate method showed statistically significant difference in AASBP ($p=0.006$), Coma score on admission ($p=0.038$), motor response ($p=0.007$), pupillary reactivity in those with equal and not dilated pupil ($p=0.001$), presence of DI ($p<0.001$), serum glucose level ($p=0.001$), TWBC counts ($p=0.043$), aPTT ratio ($p=0.03$), PT ratio ($p<0.001$), INR ($p=0.009$), peak ICP value ($p=0.028$), minimum CPP value ($p=0.001$), Marshall CT grading ($p=0.025$), presence of brain swelling ($p=0.009$) and presence of IVH ($p=0.042$). ICP monitoring and ICP-CPP directed therapy were only available in 58 (39%) patients of severe TBI in children aged 2-16 years old during that periods of study and thus was not included in logistic model. Multiple logistic regression model with forward LR (Likelihood ratio) method concluded that Coma score on admission (odds ratio [2.88; 95% confidence interval [1.04-7.92), presence of DI (OR, 7.16; 95% CI; 1.74-29.50, PT ratio (OR, 23.17; 95% CI; 2.99-179.50), serum glucose level (OR, 1.19; 95% CI; 1.00-1.42) and TWBC counts (OR, 1.08; 95% CI; 1.01-1.61) on admission were poor prognostic factors in outcome of pediatric severe TBI.

Conclusion : Our series represent one of the largest series of severe TBI in children in this region and represents the urban Malaysian population. It is concluded that low coma score on admission, development of DI within 3 days post TBI and the presence of hyperglycemia, leucocytosis and prolonged PT ratio were independent predictors of poor outcome in children.

Prof. Jafri Malin Abdullah : Supervisor
Dr. Mohd Saffari Mohd Haspani : Co-Supervisor

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EFFECT OF P-GLYCOPROTEIN INHIBITORS ON CHLOROQUINE RESISTANT PLASMODIA IN VITRO AND IN VIVO: TOWARDS IDENTIFYING CHEMOSENSITIZERS FOR MALARIA

Khairul Mohd. Fadzli bin Mustafa
MSc Pharmacology

Department of Pharmacology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

Introduction : Chloroquine resistant (CQR) malaria parasites show a strong decrease in chloroquine (CQ) accumulation in comparison with CQ sensitive (CQS) parasites. The concrete role of mutated *Pfmdr1* gene in chloroquine resistance parasite is still not clear. *Pfmdr1* is a member of the superfamily of ATP-binding cassette (ABC) transporters which is encoded P-glycoprotein homologue one (Pgh1). *Pfmdr1* has been proposed to efflux the CQ in the chloroquine resistant plasmodium. Pgh1 is a homologue of P-glycoprotein (PgP) of mammalian system, which is mostly associated with drug resistance in cancer. PgP inhibitor such as Verapamil (VPL) is known to inhibit FgP in cancer cell. Similarly, the PgP inhibitors are proposed to increase the accumulation of CO into food vacuole of the plasmodia by inhibiting the Pgh1 protein. Therefore, the use of PgP inhibitor is a good strategy to slow the spread of CO resistance and reversing the CQ resistance in malaria.

Objectives : Hence, the objective of this study is to find the effective PgP inhibitors in-combination with CO, towards reversing CQR in vitro and *in vivo* using malaria model system. Molecular studies on CQR *P. falciparum* Dd2 strain showed that there was a mutation at codon N86P in *Pfmdr1* gene. Meanwhile in *Pfcr1* gene, there was non-synonymous mutation at codon K76T compared with 3D7 in the CQ sensitive strain, which this mutation is known to have a major role in conferring CQ-resistance.

Material & Methods : In this *in vitro* study, *P. falciparum* Dd2 strain culture was established and the interaction of eight selected PgP inhibitors; Roxithromycin (ROM), Fluoxetine (FLX), Itraconazole (ITR), Glibenclamide (GLB), Ciprofloxacin (CIPRO), Simvastation (SIM), Clarithromycin (CLR) and Albendazole (ABZ) in-combination with CQ was studied. The strain was synchronized and inhibition assayed was done with various concentrations of CQ individually and in combination with various concentrations of inhibitors and ³H-hypoxanthine in a microtiter plate. The incorporation of ³H-hypoxanthine in each well was determined by using a liquid scintillation-counting detector (b counter) and the median inhibitory concentration (IC₅₀) values of CQ, inhibitors and combinations of CQ with various inhibitors were derived by probit analysis using SPSS software ver 11.5. An isobologram was drawn to investigate the effects of each combination by determining the mean fractional IC₅₀ (mean FIC₅₀) index.

Results : From the eight PgP inhibitors tested, FLX and ROM showed synergistic effects towards CO (mean FIC₅₀ index 0.55 and 0.70 respectively) on Dd2 strain, when compared to with 3D7 sensitive strain (mean FIC₅₀ index 1.17 and 1.34 respectively). GLB and ABZ gave a mild synergy effect (mean FIC₅₀ 0.88 and 0.98 respectively), meanwhile CIPRO, CLR, ITR and SIM gave an antagonistic effect (mean FIC index 1.18, 1.15, 1.19 and 1.94 respectively). Therefore the potential PgP inhibition, namely FLX and ROM which gave synergistic effects in vitro were further evaluated in vivo study by using Swiss Albino mice infected intraperitoneally with CQR *P. berghei* NK65 infected erythrocytes. The infected mice were grouped and were treated for 4 days either with CQ, FLX or ROM alone or in-combination of CQ-FLX or CQ-ROM. Results showed a progressively increasing parasitemia in non-treated group, FLX and ROM alone leading to mouse death, meanwhile for CO group, 10 mg/kg/day of CQ alone produced an effective dose (ED₅₀) against the infection compared to 2.5, 5.0, 10, 20 and 30 mg/kg/day. Therefore 10 mg/kg/day of CQ was chosen to be administered with the various concentration of FLX and ROM. Ten mg/kg/day of CQ administered with FLX or ROM effectively eliminated asexual stages, delayed the recrudescence period (day 14 versus day 7 in control group) and increased the survival rate (FLX, 87% and ROM, 100%) when compared to the control group (10 mg/kg/day alone).

Conclusions : This finding showed that CQ-FLX or CQ ROM combinations were effective and well tolerated in the treatment by delaying the recrudescence and prolonged the survival time. Therefore, we conclude that FLX and ROM are potential drugs to reverse CQ-resistance and should be evaluated further before it can be used for clinical purposes.

Assoc. Prof. Dr. S. Sivachandran : Supervisor
Assoc. Prof. Dr. M. Ravichandra Raju : Co. Supervisor
Prof. Norazmi Mohd Nor. : Co. Supervisor

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ANORECTAL MALFORMATION (ERM): THE HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM) EXPERIENCE FROM 1999 TO 2006

Dr. Kirubakaran a/l Malapan
MMed (General Surgery)

Department of Surgery,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

Introduction : Anorectal malformations (ARM) are a complex group of malformations diagnosed at the time of birth because of absence or an atopic of anus. The usual reported incidence in between 1 per 1500 and 1 per 5000 live births and they are more often seen in boys than in girls. The incidence of associated organ anomalies with ARM is variously reported from 20% -70% some being minor anomalies but others being life threatening. Further management depends on the sex of the patient, type of malformation either high or low and the associated anomalies. All operative procedures for the correction of ARM aim at providing portal for the discharge of feces from the perineum and establishing a working relationship between the bowel and sphincter.

Objectives : The aim of study is to review the patients presenting with anorectal malformations (ARM) to Hospital Universiti Sains Malaysia (HUSM) and describe the demographics and outcome in relation to the type of ARM.

Patients and Methods : The study was a retrospective case review which was carried out in the Paediatric Surgery Unit, Department of Surgery, Hospital Universiti Sains Malaysia (HUSM) between January 1999 and January 2006. The case notes and operative notes were screened for epidemiological data and data relevant to the study. Patients diagnosed with ARM but did not undergo surgery, and patients whose case notes could not be traced or incomplete were excluded from the study. All the data entry and analysis were carried out using the social science and statistical packaged (SPSS) version 12 licensed to USM. A p value of less than 0.05 was considered statistically significant.

Results : Ninety eight patients were included into the study after fulfilling the inclusion criteria. The male to female ratio was 2 to 1 and 97% of the patients were Malays. The birth weight of the patients in this study ranged from 1.3kg to 4.5kg. Forty two point eight percent of the patients presented to HUSM within the first day of life. The most common chromosomal anomalies (17.3%). Fifty two patients (53%) underwent surgical repair for low ARM which were mini PSARP (69.2%) followed by anoplasty (25%) and anal shift (5.8%). Fifty six patients (46.9%) underwent surgery for high ARM of which only 2% underwent single stage PSARP repair. Forty four patients (73.3%) who had colostomy formed were later diagnosed with high type of ARM. The remaining 16 patients who had colostomy formed were diagnosed with low ARM (26.7%). Post operative complications were similar to those reported in earlier studies. In this study, there were 46 patients (46.9%) with high type of ARM and 52 patients (53.1%) with low type of ARM. Only 44 patients were able to be contacted and interviewed to assess their functional outcomes. Anal stricture was a significant complication in patients who were not compliant with the anal dilatation protocol (p = 0.007). Patients with low ARM were noted to have more adequate weight gain as compared to high ARM patients

($p=0.002$). The incidence of constipation was higher among patients with low ARM and this was highly significant ($p=0.000$). However, the incidence of soiling and incontinence was higher among patients with high ARM ($p=0.000$). Seven patients achieved full continence at follow up and they were all males ($p=0.048$). Only 7 patients in our study achieved “good” outcome following surgery, 54 patients achieved “fair” outcome and 16 patients had “poor” outcome. The mortality rate after definitive surgery in this study was 4%.

Conclusions : The demographic finding in the study is quite similar to those published in the literature from other parts of the world. The clinical diagnosis of type of ARM was accurate in 76.8% of the patients and it was more difficult in making a diagnosis of high ARM clinically, compared to low ARM. The high incidence of associated anomalies in our study makes careful clinical examination and evaluation during the neonatal and early infantile period mandatory in all cases of ARM. Anal dilations are vital part of the postoperative management to avoid stricture at the anoplasty site. The low number of patients with good outcome in our study suggest that more attempts must be made to keep these patients on follow up, with the development of a proper bowel management program and an integrated team approach to achieve better outcomes.

Dr. Mohd. Ridzuan Abdul Samad : Supervisor
Dr. Vimal K. Vasudeavan : Co-Supervisor

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THE ROLE OF PROSTANOID RECEPTOR GENE (PTGR) POLYMORPHISM AND ITS ASSOCIATION WITH ANTERIOR SEGMENT BIOMETRY IN PRIMARY

Dr. Kodisvary R. Maharaja
MMed Ophthalmology

Department of Ophthalmology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia

Introduction : Ocular biometric parameter and its role in the pathogenesis of primary angle closure/acute angle closure (PAC/AAC) have been well documented. The occurrence of an acute attack of PAC has not been clearly understood and the possibility of other factors such as genetics predisposition that may influence the biometry of the eyes has not been explored.

Objectives : To identify the presence of prostanoid receptor gene (PTGFR) polymorphisms in PAC/AAC patients and its role predisposing these susceptible eyes to PAX/AAC, the demographic and ocular risk factors were also studied.

Material & Methods : A comparative cross sectional was conducted on PAC/AAC patients and age and sex match controls. Ocular biometric assessments consisting of anterior chamber depth, lens thickness, axial length measurements and anterior chamber angle grading were performed by application of Redman Smith method, handheld ultrasound A-scan, Van Herick’s grading of the ACD and Shaffer’s grading of anterior chamber angles respectively. 3cc of venous blood was obtained for genetic study and DNA extraction. PTGFR polymorphisms at two regions (IVS3.-97A>T and EX4 1209A>G) of the PTGFR gene were identified among the PAC/AAC patients and the controls using denaturing High Performance Chromatography (dHPLC). The genotype and phenotype analysis was then performed.

Results : A total of participants (27 PAC/AAC and 30 controls) were recruited in this study. The allele frequency of the IVS3-97A>T polymorphism among PAC/AAC patients, were Adenosine (A) (0.74), Thiamine (T) (0.6) and among controls it was (A) (0.73) and (T) (0.27). The allele frequency of the EX4 1209A>G polymorphism in PAC/AAC was (A) (0.80) and Guanine (G) (0.20) and in controls it was (A) (0.77) and (G) (0.23). There were no significant associations between the allele frequency of these polymorphisms in PAC/AAC and controls. However, the genotype frequency of the IVS3-97A>T polymorphism

was statistically significant among AAC patients compared to PAC patients within the study group ($p=0.03$), this mainly consisted of the A/T genotype of the IVS3-97A>T polymorphism. The ocular biometric parameters between PAC/AAC and control showed significant differences. The mean ACD by handheld ultrasound A-scan was 2.39mm in PAC/AAC patients as compared to controls (3.04 mm) ($p=0.01$). Mean central ACD by Redman Smith method was 2.44mm in PAC/AAC and 3.08mm in controls ($p=0.01$). Van Herick’s grading of the peripheral ACD between PAC/AAC and controls was significant ($p=0.00$). Mean lens thickness in PAC/AAC was 4.54mm and in controls it was 3.29 nmi ($p=0.01$). The mean axial length in PAC/AAC was 21.26mm and it was 23.10mm in controls ($p=0.01$). There was no association found between the ocular biometric parameters in PAC/AAC and the identified polymorphisms.

Conclusions : Ocular biometric parameters are important risk factors for the development of PAC/AAC. The IVS3-97A>T polymorphism may have a role in increasing the susceptibility of PAC patients to develop acute attack. The mechanism through which this is not known. Future research on this gene is needed to determine its role in PAC/AAC.

Dr. Liza Sharmini : Supervisor
Assoc. Prof. Dr.Wan Hazabah Wan Hitam : Co-Supervisor

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MATERNAL OBESITY AND PREGNANCY OUTCOME

Dr. Kumar Ramasamy
MMed (Obstetric & Gynaecology)

Department of Obstetric & Gynaecology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia

Introduction : Overweight and obesity are associated with serious social and psychological consequences in addition to the physical health implications. Across the globe obesity has reached an epidemic proportions with almost 1 billion people are either overweight or obese. The incidence of obesity among women in the reproductive age group has increased in concordance with the prevalence in the general population with the reported incidence of obesity during pregnancy varying between 6% and 28%. This has critical consequences for fetal and maternal health in the antenatal, intrapartum and postpartum periods.

Objectives : The aim of the study was to determine the fetal/maternal outcomes in obese pregnant women (antenatally, intrapartum and postpartum) and to compare the adverse outcome between obese and normal weight pregnant women.

Methodology : This was a prospective cohort study carried out in the Obstetrics and Gynecology Department, Hospital Ipoh from October 2005 to October 2006. All pregnant women who booked their pregnancy in Hospital Ipoh and surrounding health clinics before or by 16 weeks of pregnancy were included into this study once they fulfill the inclusion criteria. Once enrolled the progress of the pregnancy was followed up until delivery and six weeks into the postpartum period. The Body Mass Index (BMI), calculated with the help of the weight and height taken between 12 to 16 weeks of pregnancy was taken as the measurement of obesity. The study group were divided into two arms, obese (BMI = 27.5 kg/m²) and the control group of normal weight mothers (BMI 18.5 — 22.9 kg/m²) Once the subjects recruited into the study, they undergo routine antenatal care and managed accordingly. The various maternal and fetal outcomes were compiled with the help of a questionnaire. All the data entry and analysis were carried out using the social science and statistical packaged (SPSS) version 12. A p value of less than 0.05 was considered statistically significant.

Results : Number of patients enrolled in this study was 1200 with obese mothers represent 50% of the study sample. There was no significant difference ($p < 0.05$) in the mean age between the two study groups. The bulk of the studied population were Malays (59.3%) but

when analysed individually the highest prevalence of obesity (59.9%) was noted among the Indian mothers. Majority of the study population in the obese category were multiparas (66.7%) where else the normal weight category consist of almost equal number of primi (49.5%) and multigravida 's (46.3%). This difference was found to be statistically sign cant (<0.001). There is an higher incidence of Diabetic Mellitus (30.8%) among the family members of the obese mothers as compared to mothers in the normal weight category (17.2%) which is significant ($p < 0.001$). Using a multivariate analysis even after adjusted for the possible confounders the following conditions were significantly associated with maternal obesity [quoted as adjusted odds ratio (OR) and 95% confidence interval (CI)] . incidence of abortion (OR 1.09 ; 95% CI . 0.81-1.48), incidence of Gestational Hypertension and Pre-eclampsia (OR 6.93 , 95% CI. 4.60- 10.44), incidence of Gestational Diabetic Mellitus (OR 3.48 , 95% CI 2.43-4.9 7), incidence of Caesarean deliveries (OR . 2.65; 95% CI: 1.91-3.69), rate of augmentation of labour (OR : 2.20; 95% CI: 1.56-3.12) and incidence of delivering macrosomic baby (OR : 3.52; 95% CI: 2.15-5.76). No sign differences were noted between the two groups in terms of non spontaneous rupture of membrane, postdatism, labour induction, instrumental delivery, third or fourth degree perineal tear, postpartum haemorrhage, thromboembolism and perinatal complications such as prematurity, shoulder dystocia, low Apgar scores, neonatal intensive care unit admission, meconium aspiration and perinatal mortality. There was also an increasing trends of adverse fetal/maternal outcomes in relation to the severity of the degree of obesity.

Conclusions : Maternal obesity in early pregnancy is an independent risk factor for a number of adverse obstetric outcomes and is sign associated with an increased incidence of macrosomic baby.

Assoc. Prof. Dr. Nik Mohd Zaki Nik Mahmood : Supervisor
Dr. Japaraj Robert Peter : Co Supervisor

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EVALUATION OF CHOLERA VACCINE CANDIDATES VCUSM2 (0139), VCUSM4 (EL TOR) AND ITS BIVALENT VACCINE FORMULATION

Kurunathan Sinniah
MSc Microbiology

Department of Microbiology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, Kelantan, Malaysia.

Introduction : Cholera has been implicated in many parts of the worlds and two serogroup identified for causing epidemic cholera are the *V. cholerae* O1 and *V. cholerae* 0139. Sharp increase of cholera cases and deaths in 2006 showed potential of *V. cholerae* to cause more severe damages and must not taken lightly. Better understanding of *V. cholerae* as non-invasive organism and oral route vaccination can optimally induce intestinal immune response has led to the preference of oral cholera vaccine over parenteral cholera vaccine. Vast majority of vaccine created were directed against O1 serogroup only. Since cross protection cannot be established between O1 and O139 serogroup there is need for bivalent vaccine for cholera.

Objectives : In this study we attempted to formulate a bivalent vaccine capable of protecting against *V cholerae* O1 and *V cholerae* O139.

Material & Methods : A bivalent vaccine composed of auxotrophic VCUSM2 and VCUSM4 previously developed was evaluated for immunogenicity, reactogenicity, safety and protective ability as well as their characteristic similarities to their respective parent strain. VCUSM2 and VCUSM4 were created by *hemA* mutation making them dependent on amino levulinic acid (ALA) for survival.

Results : When supplemented with optimal ALA VCUSM vaccine strains characteristically similar to parent strains but not in absence of ALA. In the absence of ALA, VCUSM vaccine strains showed

weakened characteristics. Auxotrophic strains development focused on retaining characteristic features of wild types but attenuated in term of survival abilities. VCUSM2 and VCUSM4 had limited survival capabilities in various environmental waters. VCUSM2 and VCUSM4 did not cause diarrhea when tested in rabbit models when compared with virulent wild type *V cholerae*. Bivalent vaccine elicited immune response against both serogroups. Protection studies using high dose of virulent of either wild types showed complete protection in rabbits vaccinated with bivalent vaccine.

Conclusions : Bivalent vaccine showed promising result in term of safety, immunogenicity, side effects and protective capabilities and can be used against both O1 and O139 serogroups of *V. cholerae*.

Assoc. Prof. M. Ravichandran : Supervisor
Prof. Zainul F Zainuddin : Co Supervisor

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A STUDY OF 5-YEAR SURVIVAL AND PROGNOSTIC FACTORS IN BREAST CANCER TREATMENT IN HUSM FROM 1987 TO 2000L A RETROSPECTIVE RECORDS REVIEW

Dr. Lew Voon Meng
MMed General Surgery

Department of Surgery,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

Introduction : Breast cancer is the most common cancer diagnosed in women globally. Both the incidence and mortality rates varied significantly between geographical locations, in which Asian countries had the lowest incidence and mortality rates compared with the US white women. Nevertheless, amongst the Asian countries, the incidence of breast cancer is on the rise, including Malaysia. The only published breast cancer data available in Malaysia was from the Penang Cancer Registry. In Universiti Sains Malaysia Hospital, Kelantan. east coast of Malaysia, from the clinical practice the trend of breast cancer presentation and mortality rate was noted to be surprisingly late and high respectively. Hence, a study needed to be done to confirm and understand these observations in order to creat measures to treat the problem.

Objectives : The objectives of this are to determine the 5-year survival rate of breast cancer women treated in HUSM from 1987 to 2000 and identify the prognostic factors which influence the breast cancer survival.

Methodology : This is a study of retrospective records review of 185 patients with breast cancer. Recruitment phase of the study subjects were from 1/1/1987 to 3 1/12/2000. All patients were followed up until 31 / 12/2001. The sample size was calculated using the Power and Sample Size (PS) calculation software (PS Software, 1997). The study sample was recruited from the hospital record unit. The studied parameters were all collected using a data collection sheet. All deaths (end point of study) were confirmed by documentation in the patient medical records, from the National Registry Department of Kelantan or death certificates during house visits. All data entered and analysed using SPSS software version 12.0. The studied parameters were analysed using frequency and percentage, Kaplan Meier, univariate and multivariate cox regression. The significance of the model was checked by using the Likelihood Ratio test (LR test). The Proportional Hazards assumption was checked by using Log-Minus-Log plot (LML plot).

Results : Breast cancer most commonly affected middle age women. A total of 97 (5 2.4%) of 185 patients who presented with breast cancer were aged between 3 6-49 years. Malay women being the most affected by this cancer as Kelantan are densely populated by the Malay community. The number was 147 (79.5%) of 185 patients. Most of the patients presented at premenopausaj, state with 115 (62.2%) out of

185 women. The commonest stage of presentation of breast cancer was at stage IV with a total amount of 49 (26.5%) of 185 women. Out of 185 patients, 49 (26.5%) of them had distant metastasis upon presentation. Most of the patients who had been diagnosed with breast cancer already had more than one site of met High percentage of patients appeared at the worst tumour stage which was tumour ulceration or chest wall involvement with the highest number of 78 (42.2%). 127 (68.6%) breast cancer patients had axillary lymph node involvement. Almost all Patients were diagnosed with invasive ductal carcinoma. The total number was 162 (87.6%). Grade III tumours had the highest number of patients with 61(33.0%) out of 117 breast cancer women (68 missing values). Overall, there were a very small number of patients presented with carcinoma in situ. The figure was 7(3.8%) out of 185. Only 42 out of 185 patients had their receptors status reported in the HPE report. From that, 17 (9.2%) were ER positive and 25 (13.5%) were ER negative. Compared to ER receptor status, PR receptor status was even less reported 2 (1.1%) out of 10 patients were PR positive. Meanwhile 8 (4.3%) were PR negative. Only a total of 59 out of 185 patients had their status of lymphatic and vascular invasion reported in the HPE report. A total of 28 (15.1%) breast cancer woman had lymphatic invasion. The most performed surgery were simple mastectomy with a total number of 108 (58.4%). More patients had axillary dissection with a total number of 63 (34.1%) and 40 (21.6%) breast cancer women underwent axillary node clearance and sampling respectively. There were also many patients subjected to chemotherapy with 114 (61.6%) and 22 (11.9%) patients had adjuvant and neoadjuvant chemotherapy respectively. Most of the breast cancer patients received cyclophosphamide, methotrexate and 5-fluorouracil (CMF) regime. The number of patients received the regime were 47 (25.4%). The second most used regime was cyclophosphamide, adriamycin and 5-fluorouracil (CAF) in 38 (20.5%) patients. There were 70 (37.8%) breast cancer women given adjuvant radiotherapy However, 66 (35.7%) women did not receive radiotherapy A total of 144 (77.8%) patients received tamoxifen More women had post treatment metastasis with the figure showing 68 (36.8%) women The most frequent site of metastasis after treatment was actually more than 1 site which was seen in a 32 (17.3%) breast cancer women Local recurrence occurred in 42 (22.7%) breast cancer patients, whereas there was no local recurrence in 88 (47.6%) patients. From a total of 185 studied breast cancer patients, 127 (68.6%) died and 58 (31.4%) were alive! Censored. There were 94 (50.8%) patients completed the treatment and 91 (49.2%) patients did not. A total of 113 (61.1%) patients were willing to receive breast cancer treatment while 72 (38.9%) were reluctant. The most significant prognostic factors from 5-year survival probability. Kaplan Meier analysis were race, TNM staging, distant metastasis, tumour size, axillary lymph node involvement, breast surgery, axillary surgery, radiotherapy, post treatment metastasis, local recurrence, completion of treatment and patient willingness for treatment. The univariately significant prognostic factors were similar to those in Kaplan Meier analysis but also include histological type and histological grade The significant factors by multivariate analysis were axillary lymph node involvement, post metastasis and local recurrence.

Conclusion : In conclusion, the 5-year survival rate of breast cancer patients in HUSM treated from 87 to 2000 was 25.84%, with the mean of 72 and median survival time of 30 months. The significant independent prognostic factors that influenced the 5 year survival were axillary lymph node involvement, post treatment metastasis and local recurrence.

Dr. Zainal Mahmood : Supervisor
Prof. Syed Hatim Noor : Co. Supervisor

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FUNCTIONAL OUTCOME OF TOTAL KNEE REPLACEMENT (6 MONTHS FLOW UP)

Dr. Mohd. Farid bin Saidin
MMed Orthopaedic

**Department of Orthopaedic,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.**

Introduction : Osteoarthritis of the knee is a common degenerative disease of the old age which is really disabling because of the pain and reduce range of movement of the knee. Total knee replacement (TKR) is a reliable and widely used surgical procedure to treat these problems. In general knee flexion of 90° is needed for activities of daily living.

Objectives : This is an interventional study of pre and post total knee replacement for 1 year period from January 2005 to December 2005 at Hospital Alor Setar.

Patients & Methods : Forty seven patients with primary osteoarthritis of the knee involved in this study from. All total knee replacement done by a single qualified orthopaedic surgeon using only one system. Oxford Knee 12-items questionnaires, standard goniometer and Visual Analogue Scale were used as assessment tools. The measurement and the score taken before the operation and 6 months after the total knee replacement were taken for data analysis.

Results : The mean age of the patients is 61.62 with 40 female and 7 male. The visual analogue score (VAS) and Oxford Knee score were significantly reduced. The mean VAS is markedly reduce, pre operatively 7.7 to 2.06 post operatively. The mean Oxford Knee Score reduce from 40.96 pre operatively to 23.32 post operatively. Range of movement was improved both in flexion and extension of the knee. The mean flexion before TKR is 106.06° and post TKR is 111.17°. The mean post TKR extension is 0.74° compare with 7.87° before operation.

Conclusions : In general, total knee replacement improved the range of movement, functional score and significant pain relieved in patients with primary knee osteoarthritis even in short term duration.

Dr. Mohd. Iskandar Mohd Amin : Supervisor
Dato Dr. Suresh Chopra : Co-Supervisor

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A RELATIONSHIP OF VASCULAR PEDICLE WIDTH AND CENTRAL VENOUS PRESSURE WITH VENTILATOR PARAMETERS IN VENTILATED PATIENTS

Dr. Mohd. Fahmi bin Lukman
MMed Anaesthesiology

**Department of Anaesthesiology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Objectives : The objective of this study is to determine relationship of Vascular Pedicle Width (VPW), Central Venous Pressure (CVP), Positive End Expiratory Pressure (PEEP) and Peak Inspiratory Pressure (PIP) in adult ventilated patients using single supine chest radiograph.

Patients & Methods : This was a prospective, randomized study and had been approved by the Research and Ethics Committee, School Of Medical Sciences, Universiti Sains Malaysia. One-hundred and forty adult ventilated patients in Intensive Care Unit (ICU) and Neuroscience Intensive Care Unit of Hospital Universiti Sains Malaysia (HUSM) involved, from May 2006 until December 2006. CVP, PEEP and PIP was taken within 1 hour after chest radiograph taken. VPW was measured on digitalized chest radiograph by Radiology Researcher at separate occasion without clinical data related to patient's condition.

Results : There was a significant linear relationship between CVP and VPW ($p < 0.001$, CI 0.48 — 0.97 mmHg), with those who had CVP of 10 mmHg will have VPW wider for 7.3mm. There was also significant linear relationship between PEEP and VPW ($p < 0.05$, CI 0.00 — 0.97 cmH2O) with those who had PEEP of 10 cm H2O have VPW wider for 4.9mm. However, there was no significant linear

relationship between PIP and VPW. There was no interaction between independent variables.

Conclusions : From these three variables, CVP has a strongest correlation with VPW, which indicate it's usefulness in ICU. PEEP and PIP, served as ventilator parameters, have weaker relationship with VPW which makes implementation of VPW in ventilated patient regardless of ventilator setting become valuable.

Dr. Rhendra : Supervisor
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EFFECT S OF 50% ETHANOLIC EXTRACT OF ANDROGRAPHIS PANICULATA (BURM. F.) NEES ON MALE REPRODUCTIVE FUNCTIONS IN RATS

Dr. Mohd. Dasuki Bin Sul'ain
PhD Pharmacology

**Department of Pharmacology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Introduction : Herbal medication is still a controversial issue especially regarding its safety. This also includes the use of *Andrographis paniculata* (AP) extract. AP has been claimed as anti-viral, anti-inflammatory, anti-cancer and also as anti-diabetic. Earlier studies suggested that the standardized 50% ethanolic extract of this herb (APE) be developed as an anti- diabetic. However, the adverse effect of AP on male reproductive function is still not known.

Objectives : The present study aims to look at the effects of 50% AP ethanolic extract on the male Sprague Dawley rats' reproductive functions and to see whether it has anti fertility effects or other forms of toxicity. Four important endpoints of male reproductive functions were observed i.e. male reproductive performance (MRP), male sexual behavior (MSB), male specific endpoints and hormonal level assessment.

Material & Methods : Sixty adult male rats were used in this study and they were randomly divided into six groups. Five groups were administered with APE at doses of 0.5, 1.0, 10, 100 and 1000 mg/kg for not less than 77 days by oral gavage. In MRP study, each male mated with three female rats for a maximum duration of two weeks. 50% of the female rats were sacrificed on day 21 of gestation whilst the rest were sacrificed on day 21 post partum. MSB study took place 30 minutes and their sexual behavior was recorded. Blood was collected from male rats for hormonal assays.

Results : Results showed that there were no significant differences between treated and control male rats with regards to their reproductive performances, sexual behavior, body, reproductive organs and other internal organs weights. MRP indices remained unaffected and there were no toxic effects observed from pregnancy outcomes. The treatment of APE of up to 1000 mg/kg neither induce any significant changes in sexual behavioral parameters nor changes of body, reproductive organs and other internal organs weights. Sperm evaluations and histopathology evaluation also failed to show any differences between the controlled and treated male rats. These results suggested that there were no disturbances in spermatogenesis within the testis of APE treated groups and that they were able to produce sperms like the control rats. However, hormones level in rats treated with APE 1, APE 10 and APE 100 showed a significant increase in plasma testosterone level. Follicle stimulating hormone (FSH) and luteinizing hormone (LH) however remained unaffected between the treated groups. These results taken together refuted with the statement that APE has anti-fertility effects or toxic effects.

Conclusion : As a conclusion, APE seems, therefore, to be safe for rats and further research are needed using non-rodent species in order to confirm this finding before it can be considered as safe for human consumption.

Prof. Syed Mohsin Syed Sahil Jamalullail : Supervisor

Assoc. Prof. Hasnan Jaafar : Co-Supervisor
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MOLECULAR GENETICS STUDY OF PROSTAGLANDIN F_{2α} RECEPTOR GENE IN GLAUCOMATOUS PATIENTS IN MALAYSIA

Mohd. Nizam bin Zahary
MSc Human Genetics

Human Genome Center, University Sains Malaysia, Health Campus, Kelantan, Malaysia.

Introduction : The adverse reaction that arises from topical antiglaucoma drug namely, Latanoprost, has already been reported. The effectiveness of the drug may vary according to individual. We hypothesize that any changes in the human prostanoid (FP) receptor, the receptor to which the drug acts, could be responsible for the variation in the effectiveness of the drug as well as the adverse reaction.

Objectives : The objective of this study was to identify the types and frequencies of prostaglandin F receptor gene polymorphisms among the Malaysian population and its implication to the glaucoma patients.

Material & Methods : Polymerase Chain Reaction (PCR) was used to amplify all the four exons of prostaglandin F receptor gene. The polymorphisms of prostaglandin F_{2α} receptor gene was screened by using denaturing High Performance Liquid Chromatography (dHPLC). Any mutations detected by dHPLC were then confirmed by DNA sequencing. Intraocular pressure (IOP) and any side effects for each of the patients were monitored within three months post initiation of tatanoprost treatment.

Results : Out of the twelve regions that amplified from the four exons of prostaglandin F_{2α} receptor gene, two SNPs were found. A novel SNP IVS3-97 A>T was found in 34 patients and 32 controls after 160 glaucoma patients and controls were screened. Another SNP, EX4 1209 A>G was identified in 23 patients and 27 controls among the study subjects. However, both of these SNPs which were found within the prostaglandin F receptor gene did not show any statistically significant association either with glaucoma susceptibility or IOP lowering effect in glaucoma patients who received topical latanoprost.

Conclusions : We believe that a larger coverage of the gene has to be screened, with a larger sample size, multicenter and longer period of study is perhaps needed to confirm the possible association between polymorphisms of prostaglandin F receptor gene and the variation of responsiveness of patients to the latanoprost.

Assoc. Prof. Dr. Zilfalil bin Alwi : Supervisor
Dr. Liza Sharmini Ahmad Tajudin : Co Supervisor
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DONOR SITE MORBIDITY FOLLOWING RESECTION OF VASCULARIZED FREE FIBULAR GRAFT FOR SKELETAL RECONSTRUCTION

Dr. Mohd. Ruzaimi bin Abd. Razak
MMed Orthopaedic

**Department of Orthopaedic,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.**

Introduction : Fibular graft is a useful technique to restore skeletal integrity of bony defects. Despite the benefit of this procedure, there are some reported problems associated with donor site particularly with regards to ankle joint.

Objective : The purpose of this study is to objectively measure the morbidity to the ankle joint after fibular graft harvest and to study the

significant radiological changes in the ankle joint. Also to know the minimal residual distal length of the fibula that should be maintain to minimize the donor site morbidity.

Methodology : A cross-section study was performed on patients who had undergone autogenous vascularized fibular graft harvest. Twenty patients who had undergone unilateral fibula harvest with normal contralateral ankle were identified. Patients were evaluated within 15 to 96 months post operation with average of 45.25 month. Mazur's ankle score was used to analyze the subjective symptom and sign. Radiological assessments to both ankle which include mortice views on non weight bearing and weight bearing were performed. The distance of the tips of lateral melleolus and the tips of medial melleolus were calculated and the tilting angle of the residual distal fibula were measured.

Result : Mazur's ankle score revealed 15(75%) patients has excellent outcome (scoring mark 90 and above) and 5(15%) patients had good outcome (scoring mark from 79 to 89), none of them had fair or poor results. In weight bearing mortise view of ankle x-ray, there is significant proximal migration of residual distal fibula with average 7.45 mm. The analysis for correlation between Mazur's ankle score and residual distal length of fibula shows a significant positive linear correlation with a good correlation.

Conclusion : Mazur's ankle score is good objective scoring system for subjective assessment of donor site following vascularized fibular grafting. Limitation of functional activity to the ipsilateral ankle following fibular harvest is not considered significant enough to discourage transplantation of large segment of fibula. There is significant radiological changes in mortise view of ankle x-ray post fibular harvest especially proximal migration of residual distal fibula on weight bearing. The significant linear correlation between Mazur's ankle score with residual distal length of fibula was observed. The minimum of 7 cm residual distal fibular correlate with Mazur's ankle score more than 90%.

Assoc. Prof. Dr. Mohd. Imran Yusof : Supervisor
Prof. Dr. Abdul Sukari Halim : Co-Supervisor

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COMPARING THE HEARING THRESHOLDS BETWEEN MASTER (MULTIPEL AUDIOMETRY STEADY-STATE RESPONSE) AND PTA (PURE TONE AUDIOMETRY) IN NORMAL HEARING AND IMPAIRED HEARING INDIVIDUALS

Dr. Nik Adilah binti Nik Othman
MMed ORL-HNS

Department of ORL-HNS,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

Introduction : Hearing impairment in adults and children need to be identified early and accurately. This is important for the proper implementation of intervention and rehabilitation. The Auditory Steady-State Response (ASSR) has been established as a frequency-specific, objective audiometric procedure, which can provide reliable thresholds to within 5-20 dB of the pure tone behavioural thresholds. And since, its measurements are not influenced by age, it is appropriate to use ASSR for the hearing assessment in children.

Objectives : The aim of the study is to obtain the norms for the population and to compare hearing thresholds obtained by Pure Tone Audiometry (PTA) and by Multiple Auditory Steady-State Response (MASTER) in order to determine the accuracy of MASTER in estimating hearing thresholds for normal hearing and hearing-impaired individuals.

Methodology : A cross-sectional study was conducted in the Audiology Unit, Department of Otorhinolaryngology, HUSM from

January to July 2007. A total of forty adults and thirty-four children were involved in the study. They are further divided into normal hearing and hearing- impaired groups. Each subject underwent PTA and MASTER on the same day.

Results : The mean threshold difference between PTA and MASTER was 18 dB HL (standard deviation= 8.5) in normal hearing adults and 14 dB HL (SD=6) in normal hearing children. However these values were smaller in the hearing-impaired subjects. The mean threshold difference was 13 dB HL (SD=8.5) in adults and 11 dB HL (SD=6) in children. The PTA and MASTER were highly correlated ($r=0.73$) and when analysed according to the frequencies, the correlation coefficients of 0.57, 0.52, 0.77 and 0.70 for 0.5, 1.0, 2.0 and 4.0 kHz, respectively, shows good correlation.

Conclusions : This study confirmed that MASTER is an accurate predictor of the PTA thresholds in normal hearing and hearing-impaired subjects.

Assoc. Prof. Dr. Din Suhaimi : Supervisor
Dr. Rosdan Salim : Co. Supervisor

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IMMUNOLOGICAL STUDIES OF DNA (PJWVACII) AND SURFACE DISPLAY (R-STVACII) VACCINE CANDIDATES EXPRESSING A SYNTHETIC MULTIEPITOPE GENE OF MYCOBACTERIUM TUBERCULOSIS IN A PRIME BOOST STRATEGY USING A MOUSE MODEL

Norhanani Bt. Mohd. Redzwan
MSc Immunology

Department of Immunology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

Introduction : Tuberculosis (TB) in humans is caused by the bacterial pathogen *Mycobacterium tuberculosis* and is still a major health problem worldwide. The only TB vaccine currently available is an attenuated strain of *M. bovis*; Bacille Calmette Guerin (BCG). BCG demonstrated variable protective efficacies ranging from 0 to 80% in different field trials. BCG is effective at preventing childhood manifestation of TB but it does not prevent the most prevalent disease which is pulmonary TB in adults. DNA vaccination is an important new approach to the control of infectious agents and induces both humoral and cellular immune responses.

Objectives : Two previously constructed vaccine candidates, pJWVaccII and r-STVaccII were used in this study employing a prime-boost strategy.

Material & Methods : The naked DNA vaccine, pJWVaccII was given intramuscularly to mice whilst the surface display vaccine, r-STVaccII was given orally. Splenocytes from the vaccinated mice were tested for various immunological tests.

Results : The results showed that splenocytes from immunized mice were found to proliferate more aggressively when stimulated with the antigen (Inak-nVaccII). Flow cytometric intracellular cytokine analysis of splenocytes from vaccinated mice also showed that both CD4+ and CDS+ T cells produce /L-2 and IFN- γ following stimulation with the antigens. In the prime-boost approach, the study showed that mice primed with the DNA vaccine, pJWVaccII and boosted with the surface display vaccine, r-STVaccII is the best strategy to stimulate immune response in mice.

Conclusion : As a conclusion, the data obtained from this study suggest that DNA vaccination in combination with surface display vaccination using prime-boost approach provides a new strategy for developing a candidate vaccine against TB.

Assoc. Prof. Mustaffa Musa : Supervisor
Prof. Zainul F. Zainuddin : Co-Supervisor

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INTRACRANIAL PRESSURE, CEREBRAL PERFUSION PRESSURE AND CEREBRAL COMPLIANCE MONITORING AND THEIR RELATIONSHIP AMONG ADULT SEVERE HEAD INJURY

Dr. Nufaimin Udin
MSurgery (Neurosurgery)

Department of Neurosciences,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia

Introduction : The study is to observe the correlation between intracranial physiological parameters namely intracranial pressure (ICP), cerebral perfusion pressure (CPP) and cerebral compliance in adult severe head injured patients. In addition the relationship of the above parameters with post operative computed tomography scan and other potential clinical, non clinical factors and outcome were also analyzed.

Research methodology : This is a prospective cohort study on severe head injured patients with Glasgow Coma Score of eight and below. The patients were admitted into Neuroscience Intensive Care Unit for monitoring of intracranial and extracranial physiological parameters after evacuation of mass lesion. We excluded patients with bilateral fixed and dilated pupil, those who suffered from severe injury not expected to live longer than 24 hours, those with bleeding diathesis, those whose follow up was not possible or those with significant brain stem involvement. All patients were treated with standard protocols and guidelines in the management of severe head injury. These patients were monitored continuously until the parameters were normal and stabilized or death. Post operative computed tomography was obtained within 48 hours after surgical evacuation of mass lesion or earlier if intracranial hypertension was refractory. Outcomes of the patients at first and sixth month after the injury were assessed using Glasgow Outcome Scale.

Results : The study included 30 patients with 24 males and 6 females, between 13 and 65 years of age who were admitted with severe head injury. We demonstrated higher CPP and compliance values were obtained whenever the ICP was maintained at 20 mmHg or lower, while reduced CPP and compliance value once the ICP was elevated above 20 mmHg following surgery to remove the mass lesion in severe head injured patients, p value = 0.001 and 0.030 respectively. The similar findings were demonstrated when cerebral compliance was measured using PVJ, p value < 0.001. There was a statistically significant correlation between CPP and compliance as well as CPP and PVI at ICP above 20 mmHg, p value < 0.001. Our study also revealed higher ICP and lower compliance and PYT when the CPP was below 60 mmHg. The ICP reduced (p value < 0.001) and both compliance (p value = 0.002) as well as PVI (p value < 0.001) improved when the CPP was preserved above 60 mmHg. Post operatively, our study revealed significant relationship between ICP and C PP with states of basal cistern (p value = 0.001 and 0.022) as well as ICP with Marshall Classification (p value < 0.001). However we failed to demonstrate significant relation between compliance with post operative CT scan findings even though higher compliance value was observed when the basal cistern was opened, less midline shift and Marshall I or H. We also found an association between preoperative GCS with ICP and type of operation with compliance value which may help in the management plan of severe head injured patients, p value = 0.006 and 0.033 respectively. Age, preoperative GCS, pupil equality and reactivity, basal cistern, post operative CT scan edema and ICP were associated with the outcome of the patients at one month after severe head injury, p value < 0.050, although we only found pupil equality and reactivity (p value = 0.025) and barely ICP (p value 0.057) as independent outcome predictors. Larger sample size is required to demonstrate the validity of other parameters as an independent predictor. Lastly the

invasive procedure such as insertion of ICP monitoring is not without catastrophic complication.

Conclusion : There were correlation between ICP, CPP and cerebral compliance as long as the cerebral autoregulation remained intact. However no significant relation was observed between these intracranial parameters with the patient's outcome. Other than that, the findings of post operative CT scan obtained after evacuation of mass lesion may help in predicting the intracranial pressure.

Prof. Jafri Malin Abdullah : Supervisor
Dr. Zamzuri Idris : Co-Supervisor

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DETERMINATION OF PROGNOSTIC MARKERS IN CERVICAL CANCER

Rahmatul Wahida Bt. Ahmad
MSc (Pathology)

Department of Pathology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia

Introduction : Biomolecular factors could possibly improve the prediction of prognosis and diagnosis in cancer. Understanding specific molecular pathways could possibly shed some light in improving therapeutic modalities so that the treatment plan can be modified to suit individual cases. Various markers including factor VIII related antigen (MVD), Cyclooxygenase-2 (COX-2), E-cadherin, human telomerase reverse transcriptase (hTERT) and insulin like growth factor receptor (IGF-R) have been shown to play important roles in carcinogenesis and in predicting the prognosis of cervical cancer. Proliferation of tumor cells is uncontrolled, excessive and requires less growth factor since tumor cells have aberrant expression of IGF-R. However, tumor cells cannot grow more than 1-10mm unless it is vascularised through angiogenesis by the formation of microvessels. Furthermore high expression of COX-2 suppress apoptosis, promote angiogenesis and tumor invasion. Malignant tumor cells have high metastatic potential because the cells are less adherent to each other as a result of decreased expression of E-cadherin. Cancer cells also do not undergo replicative senescence during each cell division because the hTERT enzyme synthesizes new telomerase and prevent apoptosis.

Material & Methods : This retrospective study was done among normal cervix, cervical intraepithelial neoplasia (CIN) and squamous cell carcinoma (SCC) of cervix which have been histopathologically diagnosed from year 1998 to 2003 in HUSM. All samples were subjected to immunohistochemistry approach to quantify the microvessel density (MVD) and to estimate the percentage of the expression of COX-2, E-cadherin, hTERT and IGF-R.

Results : Our results revealed that there were significantly increased expression of MVD, COX-2, hTERT and IGF-R as the disease become more cancerous ($p < 0.001$). However, decreased expression of E-cadherin were seen in SCC samples compared to normal and CIN samples ($p < 0.001$). MVD expression has been shown to be the most related with all clinical and clinicopathological parameters including lymph node metastasis ($p = 0.005$), parametrial involvement ($p = 0.003$), vascular space involvement ($p = 0.004$), deep stromal invasion ($p = 0.003$) and tumor differentiation ($p = 0.002$). While COX-2 protein expression showed a significant correlation with lymph node metastasis ($p = 0.006$), parametrial involvement ($p = 0.004$) and tumor differentiation status ($p = 0.001$). E-cadherin, hTERT and IGF-R protein expression showed significant correlation only with h node metastasis and tumor differentiation ($p < 0.05$). For overall survival, our result showed that MVD, tumor differentiation, lymph node status and deep invasion were significant prognostic markers ($p < 0.05$). For disease free survival we found that COX-2 protein expression, deep stromal invasion, vascular space involvement and parametrial involvement was a good prognostic markers.

Conclusions : It is concluded that factor VIII related antigen (MVD), Cyclooxygenase-2 (COX-2), E-cadherin, human telomerase reverse transcriptase (hTERT) and insulin like growth factor receptor (IGF-R) are expressed in different histological stages of cancer and may have potential values used as diagnostic or prognostic marker in cervical cancer.

Prof. Dr. Nor Hayati Othman : Supervisor
Assoc. Prof. Dr. M. Madhavan : Co Supervisor

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THE EFFECT OF PRE-INDUCTION DEXMEDETOMIDINE ON INTRAOPERATIVE SEVOFLURANE REQUIREMENT

Dr. Samantha Rampal A/P Hardyal Rampal
MMed (Anaesthesiology)

Department of Anaesthesiology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, Kelantan, Malaysia.

Introduction: Dexmedetomidine is a highly selective α_2 agonist with potent sedative, anaesthetic-sparing and analgesic effects. Due to these effects, it has currently become an important adjuvant to current anaesthetic practices.

Objectives : The aim of this study is to evaluate if there is a reduction in the amount of expired fraction of intraoperative sevoflurane used with dexmedetomidine given as a single intravenous (i.v.) dose of 1 mg/kg, 10 minutes before anaesthetic induction.

Patients & Methods : A prospective, randomized double-blinded clinical trial was conducted on 60 patients planned for minor orthopaedic procedures less than 3 hours of duration. This was done in a time frame of twelve (12) months, between August 2006 and August 2007 at the operation theater of Hospital Universiti Sains Malaysia (HUSM). Sixty patients were randomized to receive either dexmedetomidine (n=30) or normal saline (n=30). Sedation score was evaluated using Ramsey sedation scale during and after drug administration, till patients were induced with fentanyl, sodium thiopentone and rocuronium. Anaesthesia continuation was maintained with 30%: 70% oxygen: nitrous oxide. Amount of sevoflurane administered was adjusted to maintain the bispectral index scale between 40 and 60. The expired fraction of sevoflurane, haemodynamic parameters and analgesia requirement were recorded at 5 minute intervals throughout the intraoperative period. The extubation time, which is the duration taken from the cessation of sevoflurane administration to the time patient is extubated was noted. The postoperative pain score (VAS) was documented at the recovery.

Results : Results show that there was a 27.8% reduction in the expired fraction of sevoflurane and a 25% drop in the thiopentone requirement in the dexmedetomidine group. The mean heart rate was also significantly lower in the dexmedetomidine compared to normal saline group (mean (CI); 69.20 (64.03, 74.37) versus 82.00 (72.12, 91.87) per minute, $p = 0.005$). Patients, who received dexmedetomidine, were observed to be more sedated just before induction when compared to patients who received normal saline. The postoperative pain score (VAS) was significantly lower in the dexmedetomidine compared to normal saline group (SD) 1.507 (0.275) versus 2.209 (0.403), $p = 0.0051$. There were no significant differences observed in the demographic characteristics, the mean systolic and diastolic blood pressure measurements and the extubation time between the two groups.

Conclusion : In conclusion, preoperative administration of a single dose intravenous dexmedetomidine, decreased the expired fraction of sevoflurane by 27.8% in minor orthopaedic surgeries and has proven to be a good anaesthetic adjuvant as it not only blunts the haemodynamic response to intubation but also reduces the postoperative opioid requirement. Patients were noted to be more comfortable, alert and

complained of less pain during the postoperative period.

Assoc. Prof. Dr. Nik Abdullah Nik Mohamad : Supervisor
Dr. Mahamarowl Omar : Co Supervisor

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STUDIES ON DIABETIC AND PREDIABETIC VASCULAR DISEASE AND THE EFFECT OF SELECTED THERAPEUTIC MODALITIES ON ASSOCIATED VASCULOPATHY

Sayeeda Rahman
PhD

Department of Orthopaedics,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

Introduction : Type 2 diabetes (T2DM) now accounts for 90% of all diabetes and 80% of deaths in this group are cardiovascular related. The risk of cardiovascular mortality is also substantially higher in individuals with impaired glucose tolerance (IGT) than in those with normal glucose levels and the pathological changes in vascular function begin many years before the diagnosis of overt T2DM.

Aim of studies : The aims of this thesis are (i) to investigate clinical epidemiology of pre-clinical vasculopathy in newly-diagnosed, untreated T2DM and IGT patients and their normoglycaemic offspring (Study I), and (ii) to examine whether pharmacological interventions with thiazolidinedione and angiotensin converting enzyme (ACE) inhibitors can reverse pre-clinical vasculopathy in newly diagnosed diabetic and IGT individuals (Study 2).

Methodology : Initial screening of 1620 subjects was conducted of which 644 met study criteria. They had oral glucose tolerance test (OGTT) — 70 (10.87%) were T2DM and 66 (10.25%) IGT individuals. For Study I (Part I), the first 30 T2DM and 30 IGT patients were recruited and compared with age- and sex-matched 30 normoglycaemic controls. Haemodynamic variables, pulse wave velocity (PWV) and augmentation index (AI) were measured. Study-I (Part-2) involved 30 healthy normoglycaemic offspring of T2DM and 30 healthy normoglycaemic offspring of IGT patients, compared with 30 age- and sex-matched healthy offspring of normoglycaemic parents. Haemodynamic variables, PWV and AI were measured. For Study-2, age- and sex-matched 33 T2DM and 33 IGT patients were enrolled, comparing one-year treatment with rosiglitazone, ramipril and placebo. Haemodynamic variables were measured at three treatment phases (1st, 7th and 12 month) and PWV and AI were measured throughout the treatment period (1st (week 1, week 2, week 4), 3rd, 5th, 7th, 11th, and 12th month).

Result : In Study (Part-I), PWV was significantly higher in T2DM patients (10.37 ± 2.64 vs. 8.70 ± 1.29 m/s; $p = 0.035$) and was of borderline significant in IGT subjects (9.54 ± 1.56 vs. 8.70 ± 1.29 m/s, $p = 0.078$) compared to normoglycaemic individuals. Augmentation index was higher of borderline significant in T2DM (134.53 ± 17.32 vs. 129.17 ± 11.18 %, $p = 0.055$) and IGT patients (132.02 ± 16.11 vs. 129.17 ± 11.18 %, $p = 0.059$) compared to normoglycaemic individuals. In Study I (Part-2), offspring of T2DM and IGT patients demonstrated significantly higher AI compared to controls (105.62 ± 14.2 vs. 96.42 ± 7.7 , $p = 0.01$; 104.98 ± 11.1 vs. 96.42 ± 7.7 %, $p = 0.004$ respectively). Significantly higher PWV was noted in offspring of T2DM compared to offspring of normoglycaemic parents (6.94 ± 0.9 vs. 6.33 ± 0.7 m/s, $p = 0.010$) It was also found to be significantly higher in the offspring of T2DM compared to that of IGT (6.94 ± 0.9 vs. 6.43 ± 1.1 , $p = 0.021$). In Study-2, rosiglitazone showed a significant reduction in PWV ($p = 0.039$) and AI ($p = 0.31$) and ramipril demonstrated a significant reduction of AI ($p = 0.025$) in IGT patients in comparison to placebo on the 12 month of treatment. With rosiglitazone and ramipril, no significant difference was observed in PWV ($p = 0.962$ and $p = 0.000$ respectively) and AI ($p = 0.897$ and $p = 0.677$ respectively) in T2DM patients in comparison

to placebo during overall treatment period.

Conclusion : Newly diagnosed untreated T2DM patients demonstrated early preclinical manifestations of macrovascular diseases as shown by significantly increased PWV. Normoglycaemic healthy offspring of T2DM patients had demonstrable pre-clinical vasculopathy as assessed by significantly increased PWV and AI. Normoglycaemic healthy offspring of KiT individuals had also large artery abnormalities as shown by significantly increased AI. Rosiglitazone significantly reverses pre-clinical vasculopathy in IGT patients as evident by significant decrease in PWV and AI after one-year treatment. After one-year of ramipril treatment, reduction of large artery stiffness was also observed among IGT patients as shown by significant decrease in AI.

Prof. Abdul Rashid Abdul Rahman : Supervisor Assoc. Prof. Aziz Al-Shafi Al-Ismail. : Co. Supervisor

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THE EFFECT OF VITAMIN E ON BASIC FIBROBLAST GROWTH FACTOR LEVEL IN HUMAN FIBROBLAST CELL CULTURE

*Dr. Shawaltul Akhma Bt Harun Nor Rashid
MSurg (Plastic Surgery)*

**Reconstructive Sciences Unit,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.**

Introduction : Cosmetic products that contain vitamin B have not been proven effective in the treatment of scars. Since vitamin E is a major lipid soluble antioxidant in skin, it has been thought that it can speed healing and improve the cosmetic outcome of wounds. Tocotrienol is a class of vitamin E analogs. Although the absorption mechanisms are essentially the same for all vitamin E analogs, tocotrienols are degraded to a greater extent than tocopherols. Basic fibroblast growth factor (bFGF) is angiogenic and effective in down-regulating excess collagen production suggesting a potential role in collagen remodeling during wound healing. It is possible to alter the growth factor profile of a wound either by adding or by blocking the actions of growth factors. Aberrant wound healing may arise from a local overproduction or insufficiency of certain growth factors. Here we may be able to manipulate the process of wound healing.

Objectives : The purpose of this study is to evaluate the effectiveness of Tocotrienol Rich Fraction (TRF) in altering the level of basic fibroblast growth factor in human fibroblasts. We also undertake to determine the difference of bFGF level production according to time and various concentration of TRF in this study.

Material & Methods : In this *in vitro* model, normal human fibroblasts were propagated in one percent bovine serum and treated with 0, 30, 60, 100, 120, 180, 200 and 240 mg/ml Tocotrienol Rich Fraction for 3, 24, 48 and 72 hours. Cells were used from 5th — to 8th passage and seeded on 24-well plate trays at a concentration of 6 x 10⁴ cells per milliliter. Levels of bFGF in the supernatants were determined by Enzyme-Linked Immunosorbant Assay (ELISA).

Results : This study has demonstrated that TRF stimulated bFGF production by fibroblast. The maximum effect was evident in the first 24 hours of culture. Cells treated with higher concentrations of TRF produced higher levels of bFGF but the rise of bFGF level between the different concentrations of TRF was not statistically significant. However, the viability of fibroblast was reduced when higher concentrations of TRF were used.

Conclusion : In conclusion, bFGF production by fibroblasts can be stimulated by different concentrations of TRF. The effect of TRF on cell viability is dose-dependent ; higher concentration can induce cell death. Methods that increase bFGF may decrease aberrant scar formation by inhibiting excess collagen deposition as well as by increasing collagen degradation.

**Prof. Ahmad Sukari Halim : Supervisor
Dr. Ananda Aravazhi Dorai : Co-Supervisor**

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A RANDOMISED CONTROLLED TRIAL ON ENDOTRACHEAL TUBE (EYF)-PROSEAL LARYNGEAL MASK (PLMA) EXCHANGE AND AWAKE A STUDY ON OPTIC DISC PARAMETERS AMONG MALAY STUDENTS IN HEALTH CAMPUS, UNIVERSITI SAINS MALAYSIA BY HEIDELBERG RETINAL TOMOGRAPH II

*Dr. Shawarinin binti Jusoh
MMed Ophthalmology*

**Department of Ophthalmology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Introduction : Assessment of optic disc is an important aspect to diagnose or to detect progression of any optic neuropathies. The Heidelberg Retinal Tomograph II (HRT II), a current technology of confocal laser scanning ophthalmoscope provides quantitative, objective, three dimensions of evaluation of optic disc topography. Many studies conducted previously found that optic disc parameters were affected by race, gender, refractive error and size of disc area. Therefore a normative database of optic disc parameters differentiate between normal or abnormal optic disc is highly important.

Objective : To study the optic disc parameters among Malay students in the Health Campus, Universiti Sains Malaysia To compare optic disc parameters between gender and between ametropic and emmetropic group among Malay student To determine the correlation between the optic disc parameters with age, refractive error and size of disc area.

Methods : Across sectional study of optic disc parameters was done among Malay Students at the School of Medical Sciences, Health Campus, Universiti Sains Malaysia. The optic disc topographic analysis of 200 eyes of healthy Malay students in the Health Campus, Universiti Sains Malaysia aged 20 to 37 years was performed using confocal scanning laser ophthalmoscope, the Heidelberg Retinal Tomograph II. A total of 12 optic disc parameters were calculated by HRT II for each subject. The comparison of optic disc parameters between emmetropic and ametropic group among Malay students were done. Optic disc parameters in between gender were also compared. The correlation disc parameters with age, refractive error and disc area were determined. Statical analysis was performed using SSPS version 12 programme.

Results : A total of 200 subjects (106 women and 94 men) were included in the study. There was twelve of optic disc parameters in Malay Students in the Schools of Medical Sciences, Health Campus, USM had been evaluated by HRT II. The mean of disc area was 2.237 mm² (SD: 0.523) and other mean optic disc parameters of Malay students obtained. Only mean RNFL thickness was statistically significant difference in myopia group compared to the emmetropia (p=0.004). There were five parameters (disc area, cup area, cup volume, cup to disc ratio and mean RNFL thickness) that statistically significant difference between males and females. Age was detected to have statistically significant correlation in rim area. Only rim area was statistically significant correlated but weak with the degree of myopia in myopic group (p=0.019, r=0.227). All of the parameters were significantly correlated (p <0.05) with the size of optic disc except the cup shape measure (p= 0.082). However, only the cup area was strongly correlation with the size of optic disc.

Conclusion : We present data of optic disc parameters among the Malay young adults aged between 20 to 40 years old. Age, gender, refractive error and disc area were affected significantly with one or more optic disc parameters measured by the Heidelberg Retinal tomography II. Age, gender, refractive error and disc area are the factors which be considered during the evaluation of optic disc.

Dr. Bakiah Shaharuddin : Supervisor
Assoc. Prof. Dr. Wan Hazabah Wan Hitam : Co-Supervisor

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A STUDY OF SENSITIVITY AND SPECIFICITY OF SKIN PRICK TEST AND SERUM SPECIFIC IGE FOR ALLERGIC RHINITIS

Dr. Suhaimi Yusof
MMed Otorhinolaryngology

**Department of Otorhinolaryngology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Introduction : Allergic rhinitis (AR) is a symptomatic disorder of the nose induced by an IgE mediated inflammation after allergen exposure of the membranes of the nose, characterized by one or more of the following symptoms including nasal itchiness, nasal blockage, running nose and sneezing. Skin prick test is a known conventional method and is widely used to diagnose AR. However with the emerging of new technology method, it may help further in diagnosis and management of AR. In this study, we were comparing the serum specific IgE (in vitro study) with skin prick test as the gold standard.

Objectives : To evaluate the findings of serum specific IgE method in comparison with standard skin prick test, and to determine the sensitivity and specificity of serum specific IgE in diagnosing AR.

Methodology : A cross-Sectional study was carried out in Otorhinolaryngology Clinic HUSM from January 2007 till September 2007. Ninety patients with history suggestive of AR were included in this study. The patients' particulars and history takings were recorded and compiled. Selected patients were examined by using nasal speculum for anterior rhinoscopy and findings were recorded. Patients then undergone skin prick test and blood taken for serum specific IgE. The allergen included in this study was cat (*Felis Domesticus*), wheat flour, house dust mite (*Dermatophagoides pteronyssinus*), mucor mucedo, peanut, egg yolk, egg white and chicken meat.

Results : The highest prevalence of positive skin prick test among studied patients was house dust mite (63.3%) and the lowest prevalence was chicken meat (3.3%). The highest prevalence of positive serum specific IgE among studied patient was also house dust mite (74.4%) and the lowest prevalence was white egg (35.6%). The highest sensitivity for serum specific IgE was mucor mucedo (100%) followed by cat (90.5%) and house dust mite (86%). The lowest sensitivity was chicken meat (33.3%). The highest specificity for serum specific IgE was egg white (68.7%) followed by egg yolk (60.2%) and mucor mucedo (59.8%). The lowest specificity was cat (44.9%). For house dust mite, mucor mucedo, egg yolk and egg white; it showed that there was good correlation between diameter of wheal and flare of skin prick test and serum specific IgE result. While cat, wheat flour, peanut and chicken meat showed fair correlation between both tests.

Conclusion : Skin prick test is sensitive, rapid and a useful method in diagnosing AR. However, with the advancement of the new technology, the combination of both skin prick test and serum specific IgE will improve the management of AR.

Dr. Rosdan Salim : Supervisor
Dr. Che Maraina Che Hussin : Co Supervisor
Dr. Shamim Ahmed Khan : Co Supervisor

A STUDY ON MALAYSIAN CHILDREN WITH RETINOBLASTOMA : CLINICAL PRESENTATION AND POCKET B EIA DOMAIN MUTATION OF RB1 GENE

Dr. Sit Raihan Bt. ishak
MMed Orthopaedics

**Department of Orthopaedics,
School of Medical Sciences, University Sains Malaysia,
Health Campus, Kelantan, Malaysia.**

Introduction : The data on retinoblastoma genetic isolation of the patients around the globe mainly represents the Caucasian community. Genetic study on RB in Asian countries particularly in Southeast Asian is less highlighted and was never been studied in Malaysia.

Objectives : To determine the presence of exon 20 to 22 (pocket B El A Domain) mutations of RB1 gene and their clinical presentation in Malaysian children with retinoblastoma.

Methodology: Children with retinoblastoma from two main tertiary centers in Malaysia, Hospital Universiti Sains Malaysia and Hospital Kuala Lumpur who fulfilled the inclusion criteria were enrolled in this study. Their clinical presentation were analyzed according to the age, sex, laterality, stage of presentation (ICRB,RE and TNM), defaulted rate and outcome of disease. Three millilitres of peripheral blood were taken for the genetic analysis. RB I gene mutation of exon 20 to 22 (pocket B El A domain) identification was done using denaturing High Performance Chromatography (dHPLC) followed by DNA sequence.

Results : A total number of 69 eyes from fifty retinoblastoma children were recruited in this study. The most common presentation of patient in this study was leukocoria (65%) followed by other features, strabismus (9%), proptosis (7%), orbital inflammation (10%), vitreous haemorrhage (3%) and secondary glaucoma (3%). Majority presented at advanced stage (77 % Stage E ICRB). There was three mutations found including two novel mutations at exon 22. The novel mutations were identified as transversion of 162108A-) and insertion of 162106_162107insC. Another mutation was identified at the flanking region of intron 19, substitution AG . In the mutation of exon 22, the whole frame is shifted.

Conclusion : As reported in most of the studies elsewhere, leukocoria is also the main clinical presentation in this study. Although proptosis and orbital inflammation accounts about 17% of the patients, it cannot be considered as rare presentation. This study also managed to identify three mutations including two novel mutations, namely the insertion of C and substitution of A T in exon 22 and another one mutation at flanking region of intron 19 (substitution A G).With these findings, we can conclude that further detailed study on the complete RB1 gene mutation has to be done in future.

Dr. Liza Sharmini Ahmad Tajudin : Supervisor
Assoc. Prof. Dr. Wan Hazabbah Wan Hitam : Co Supervisor

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ASSESSMENT OF THE OUTCOME IN PATIENTS ADMITTED DUE TO COMMUNITY- ACQUIRED PNEUMONIA IN HUSM

Dr. Shaharudin Abdullah
MMed Medicine

**Department of Medicine,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.**

Background : Community-acquired pneumonia (CAP) remains an important cause of hospital admission. Studies have shown that the mortality of patients admitted with community-acquired pneumonia is high. The outcomes have been shown to be influenced by various clinical variables at presentation. Applications of these variables as predictor of severity have been shown to improve patients management outcome. The outcome of patients admitted due to CAP has not been studied in Hospital University Science Malaysia (HUSM). The main purpose of this study was to evaluate outcome in patients who required admission due to community acquired pneumonia in HUSM and to determine factors that influenced their poor outcome.

Methodology : This was a retrospective cohort study between

January 2004 to December 2004. Records of patients with community-acquired pneumonia admitted to HUSM were screened. This study included all patients aged more than 12 years old who met the inclusion criteria. The following information; demographic data, initial clinical findings, laboratory investigations and type of antibiotics regime given were recorded into customized data collection sheet. Variables obtained were examined for association with mortality. Severity prediction criteria were formulated from identified variables that showed significant association with mortality.

Results : Records of 155 patients' that met the inclusion criteria were evaluated. The mean age at presentation was 62 ± 17 years. The mortality rate was 19.4%. Variables that significantly influenced the mortality on multivariate analysis at presentation were presence of important co-morbid illnesses (OR 11.13; p = 0.001), confusion (OR 18.72; p = 0.001) and hypoxaemia (OR 10.62; p = 0.002). Other factors identified were low diastolic blood pressure and random blood sugar greater than 13 mmol/l with odds ratio of 1.08 (p=0.002) and 6.37 (p=0.007) respectively. The presence of any three of following variables on admission; presence of co-morbid illness, confusion, low diastolic blood pressure of 60 mmHg, low oxygen saturation and random blood sugar equal or greater than 13 mmol/l was associated with a 46.3 fold increase in death. The suggested predictive severity rule identified 21 of the 27 patients who died as having severe community acquired pneumonia. The sensitivity of the suggested severity model for predicting death was 0.70 and specificity of 0.95. The rule had a negative predictive value of 0.93.

Conclusion : The mortality from community-acquired pneumonia requiring hospitalization in our centre is high compared to previous studies. We found that certain factors that influenced the outcome of our patients were almost similar with other previous studies. We found that the presences of three of the five variables (co-morbid illness, confusion, low diastolic blood pressure, hypoxaemia and hyperglycaemia) would allow us to detect patients who at risk of poor outcome.

Assoc. Prof. Dr. Zainal Darus : Supervisor
Dr. Che Wan Aminud-din Hashim : Co-Supervisor
Dr. Than Winn : Co-Supervisor

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INCIDENCE AND GRADINGS OF TUBERCLE OF ZUCKERKANDL OF THYROID GLAND AND ITS IMPLICATIONS IN THYROID SURGERY

Dr. Usha Devi A/P Arunasalam
MMed ORL-HNS

Department of ORL-HNS,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

The tubercle of Zuckerkandl is an important anatomical landmark which aids in the Identification of recurrent laryngeal nerve during thyroid surgeries. The TZ is a lateral or posterior projection from the lateral thyroid lobe, which indicates the point of embryonic fusion of the ultimobranchial body and the principal median thyroid process. The tubercle of Zuckerkandl is located at the postero-lateral edge of the thyroid gland and can only be encountered after full mobilization of the respective lobes. Although various methods of localizing the RLN have been described, surgeons should be aware of the variations and have a thorough knowledge of normal anatomy in order to achieve a high standard of care. This will ensure the integrity and safety of the RLN in thyroid surgery. The anatomical variation may be minor in degree, but is of great importance as it may affect the outcome of the surgery and the patient's quality of life.

Objectives : This study evaluates the Incidence and grades of a recognizable TZ in surgical patients undergoing thyroid surgery in HUSM , and also to confirm the relationship of tubercle of

Zuckerkandl with recurrent laryngeal nerve and inferior thyroid artery.

Methodology : In the period of study, from December 2006 to October 2007, the thyroid glands of patients who underwent unilateral or bilateral thyroid surgeries were observed intraoperatively and documented. All the patients were selected from the Otolaryngology clinic, HUSM.

Results : Thyroid diseases was common among female patients which accounts for 80% (24 cases) and male 20% (6 cases). Bilaterally present tubercle of Zuckerkandi was not in 36.7% of patients (11/30) and (56.7%) present unilaterally (17/30). Out of 60 lobes that has been analyzed, we found grades 0 in 10%, grade 1 in 6.7%, grade 2 in 33.3% and grade 3 in 50%. 26 patients out of 30 studied, the recurrent laryngeal nerve passes posterior to the tubercle of Zuckerkandi, accounting to 86.7% out of total sample and passes laterally in 2 patients (6.7%) in 25 patients (83.3%) the nerve was found to cross the inferior thyroid artery posteriorly.

Conclusion : The outcome of this study proves that TZ of thyroid gland is a practical and useful landmark, which should be routinely looked for in thyroid operation. Hence it is crucial to recognized the TZ so as to ensure safe dissection, minimize complication rates and preservation of important adjacent structure.

Assoc. Prof. Shahid Hassan : Supervisor
Dr. Baharuddin : Co. Supervisor
Prof. Din Suhaimi : Co. Supervisor

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KNOWLEDGE, ATTITUDE AND PRACTICE OF HUSBANDS TOWARDS MODERN FAMILY PLANNING IN MUKALLA, YEMEN

Yahya Khamis Ahmed Almuallm
MSc Family Health

Department of Family Health,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

Objectives : The aim of this study is to assess the knowledge, attitude and practice of modern family planning among husbands in Mukalla, Yemen. This study was a cross-sectional study involving 400 husbands living in Alamol and Almustaubal quarters in Mukalla. These husbands were selected from households randomly selected from the two quarters. Husbands who do not meet pre-determined criteria were replaced with those from the nearest house. The selected husbands were interviewed using a structured questionnaire.

Results : The prevalence of family planning practice among the husbands were 39.0% and 44.3% among their wives. Only 44 (11.0%) of the husbands and 83(20.8%) of the wives were currently practicing modern family planning. There were only 77 couples (19.3%) where both husbands and wives have practiced family planning, 79(19.8%) of couples where husbands practice but their wives do not, 100(25.0%) of couples where husbands do not practice but wives do and 144 (36.0%) where both husbands and wives do not practice any family planning. Among users, the condom was the most common method used by the husbands (88.6%), while the pill was the most common method used by wives (54.2%) followed closely by intra-uterine devices (43.4%). More than 90% of husbands knew about pills, intra-uterine devices and condoms. Most of the husbands (89.3%) have positive attitudes towards family planning and agreed that modern methods are more effective than traditional methods. The majority of husbands (51.3%) agree that husbands should also practice family planning. However, 172 husbands (43.0%) felt that family planning should be practiced only by the wife. About 282 husbands (70.5%) believed that the decision regarding practice of family planning should be decided by husbands and 225 (56.3%) felt the wife only should decide on practicing family planning. The results indicate ambivalence by some husbands on the main decision maker for family planning practice.

Nearly all husbands (>90%) were aware of the common types of family planning except for male sterilization (51.0%). Male sterilization is uncommon in this study compared to female sterilization, which may explain the lower level of awareness. Very few husbands (20%) had poor attitude scores towards family planning. Among the positive attitude husbands, 132 (33.0%) had moderate scores while 247 (61.8%) had good scores and only 13 (3.3%) of the husbands had very good scores indicating that the husbands generally have positive attitudes towards family planning. Multiple regression analysis of the total knowledge score revealed significant association with years completed education of husband, years completed education of wife and the number of living children. For the attitude score, multiple linear regression analysis revealed a significant association with years completed education of husbands, the number of living children and monthly income of the wives.

Conclusion: Family planning programs in Yemen should also focus on Yemeni husbands to participate as joint decision makers in modern family planning practice. This can be achieved through targeted family planning education and promotion programs to Yemeni husbands. Religious leaders must be involved in clarifying religious issues regarding family planning.

Prof. Dr. Zulkifli Bin Ahmad : Supervisor
Dr. Nors'adah Bachok : Co-Supervisor

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ANALYSIS OF P27 AND CYCLIN DL GENES IN GLIOMAS AND MENINGIOMAS USING MOLECULAR GENETIC, IMMUNOHISTOCHEMICAL AND IMMUNOGOLD ELECTRON MICROSCOPIC TECHNIQUES

Farizan Binti Ahmad
MSc Neurosciences

**Department of Neurosciences,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Introduction : Meningiomas and gliomas are two most commonly reported brain tumor cases worldwide. These types of tumors might occur due to the disruption of the normal cell cycle which is highly controlled by p27 and cyclin D1 genes.

Objectives : This study was performed to determine the mutational status of p27 and cyclin D1, level of both protein expression and the localization of both proteins at ultrastructural level via analyses of molecular genetic, immunohistochemistry and immunogold electron microscopy respectively.

Results : The molecular genetic analysis revealed mutations in exon 4 of cyclin D1 gene but none was detected in other studied regions of exon 5 of cyclin D1 gene and exon 1 and 2 of p27 gene. Five different mutations were detected in 2 glioma (8.0%) and 3 meningioma (11.5%) samples. DNA sequencing for the two glioma samples revealed the presence of non-sense mutation which resulted to the change of C to T nucleotide at codon 223 (Lys223Lys). In the first glioma sample, we also detected a G base deletion at codon 214 which caused a frameshift mutation (Pro214Arg). In addition to that, we also found two other missense mutations in the second glioma sample. T to C nucleotide changes were detected at codon 215 and codon 217 which caused aspartic acid to Glycine changes in two different loci. Screening of mutations in meningiomas cases revealed 3 cases of non-sense mutations and 3 cases of missense mutations in a total of 3 samples. In all 3 samples, we found 3 cases of C to T nucleotide change which resulted to non-sense mutations at codon 223 (Lys223Lys). In the second and third meningioma samples, we found an additional of T to C nucleotide changes at codon 215 which caused missense mutations (Asp215Gly). Another missense mutation was found at codon 217 which showed T to C nucleotide change in the third meningioma sample. Immunohistochemistry analysis of the same group of samples revealed p27 protein overexpression in all

cases including meningiomas (82.6%), low grades gliomas (80.0%) and high grades gliomas (84.6%). We subsequently found high level of cyclin D1 expression in meningiomas (70.8%), equal expression of cyclin D1 in low grades of gliomas (50% are low expressors and 50% are high expressors), and downregulation of the protein in higher grades of gliomas (76.9% were low expressors). Immunogold electron microscopy analysis of cyclin D1 and p27 proteins showed that both proteins were found to be localized at cytoplasm and nucleus of the cells.

Conclusion : Our statistical analysis gave no significant correlation between the presence of cyclin D1 mutations with the downregulation of the protein in both meningiomas ($p=0.616$) and gliomas ($p=0.905$).

Prof. Dr. Jafri Malin Abdullah : Supervisor
Assoc. Prof. Dr. Hasnan Jaafar : Co-Supervisor

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PHYSIOLOGICAL DEMANDS AND TIME MOTION ANALYSIS OF SINGLES' BADMINTON PLAY FOLLOWING IMPLEMENTATION OF 21 POINT SCORING SYSTEM

Chee Lee Ming
MSc Sport Sciences.

**Sport Sciences unit,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Objectives : The purpose of this study was to investigate and compare the physiological responses, time motion analysis and notational analysis during 21 point singles' badminton play and the old scoring system (15 points for males and 11 for females).

Patients & Methods : Sixteen (8 males and 8 females) state-level badminton players with a mean age of 15.7 ± 1.2 years participated in this study. They were initially tested using incremental treadmill test following Bruce protocol to obtain individual heart rate- $\dot{V}O_2$ relationship. $\dot{V}O_{2max}$ of the male and female participants were 47.1 ± 5.2 ml kg^{-1} min^{-1} and 39.8 ± 6.2 ml kg^{-1} min^{-1} respectively. On a separate day, they played a simulated badminton match using 21 points (Trial 1) and 15 / 11 points (Trial 2) scoring system. During the trials, heart rate (HR) and predicted $\dot{V}O_{2max}$ were measured. Additionally, blood was withdrawn before and immediately after their match for the analysis of plasma lactate and plasma ammonia. Furthermore, a video camera was used for time-motion and notational analysis throughout the match.

Results : The statistical analysis showed that total number of shots and rallies in a match were the only parameters which were significantly higher in the 15 points compared to 21 points in men's singles match play 331.2 ± 51.6 vs 463.5 ± 24.7 (total shots) and 70.2 ± 1.2 vs 97 ± 6.6 (total rallies) respectively].

Discussion : Even though female players had a greater point difference (10 points) in the new scoring system compared to the male counterparts, there were no significant differences in all parameters measured. The patterns of play which were analysed through notational analysis were also not different in both scoring systems. Since the physiological parameters measured (mean HR, mean $\dot{V}O_2$, post plasma lactate and ammonia) were not different between trials in both male and female participants, it can be concluded that the physiological demands of the badminton game did not change following the implementation of the new scoring system. However, some differences in the physiological parameters, time motion and notational analysis were found between genders suggesting that there should be different training regimens for men and women in their respective disciplines due to greater intensity, speed of play and the longer rally lengths in men's singles.

Conclusion : It is recommended that players should place more emphasis in the development and improvement of the skills/techniques rather than making any drastic changes to the training programme to

develop their physical fitness to meet the demands of the match with the 21 point scoring system.

Dr. Chen Chee Keong : Supervisor
Assoc. Prof. Dr. Asok Kumar Ghosh : Co Supervisor

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EFFECT OF ISOKINETIC RESISTANCE TRAINING PROGRAMME AT DIFFERENT ANGULAR VELOCITIES FOR REHABILITATION OF KNEE OSTEOARTHRITIS

Mohd. Asn Ariffin
MSc Sport Sciences.

Sport Sciences unit,
School of Medical Sciences, University Sains Malaysia,
Health Campus, Kelantan, Malaysia.

Objectives : The purpose of this study is to determine if 12 weeks of isokinetic training programme, two times per week at two different angular velocities ($60^{\circ}.\text{sec}^{-1}$ and $120^{\circ}.\text{sec}^{-1}$) would improve the peak torque, pain score, thigh circumference and functional abilities of patients with knee osteoarthritis.

Patients & Methods : The first intervention group ($60^{\circ}.\text{sec}^{-1}$ trained group) age 52 ± 6 yrs participated in the prescribed training programme along with existing conventional physiotherapy. The second intervention group ($120^{\circ}.\text{sec}^{-1}$ trained group) aged 54 ± 6 yrs also participated in the prescribed training along with existing conventional physiotherapy. The control group aged 54 ± 5 yrs continued with conventional physiotherapy only.

Results : There was significant improvement ($p < 0.05$) of peak torque in both intervention groups compared to the control group. There was no significant difference ($p > 0.05$) between the control and intervention groups in terms of pain score, however, there was a decrease in pain score post training in control and $120^{\circ}.\text{sec}^{-1}$ trained group although statistically not significant. There was a significant main effect of time different ($p < 0.05$) in thigh circumference at post training in $120^{\circ}.\text{sec}^{-1}$ trained group compared to other groups. In terms of physical function, there was a significant improvement ($p < 0.05$) in both intervention groups at mid and post test compared to control group.

Discussion : These data indicate that isokinetic resistance training was able to improve knee muscle strength and physical function of knee patients with knee OA. This study revealed that six weeks of isokinetic resistance training combined with existing conventional physiotherapy was sufficient to improve the thigh muscle strength (Quadriceps and Hamstring). The prescribed training programme was also able to help in muscle hypertrophy especially in the fast angular velocity trained group ($120^{\circ}.\text{sec}^{-1}$) However, in terms of pain reduction, only the ($120^{\circ}.\text{sec}^{-1}$) trained group showed slight reduction in pain score although statistically not significant.

Conclusion : Isokinetic resistance training programme, especially at ($120^{\circ}.\text{sec}^{-1}$) angular velocity, combined with existing conventional physiotherapy is beneficial as a rehabilitation prescription for patients with knee osteoarthritis.

Dr. Bal Kishan : Supervisor
Assoc. Prof. Dr. Asok Kumar Ghosh : Co Supervisor

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EFFECTS OF PROGRESSIVE COMBINED FLEXIBILITY, STRENGTH AND AEROBIC EXERCISES ON MIDDLE AGED WOMEN WITH EARLY STAGE PRIMARY KNEE OSTEOARTHRITIS

Nelly Binti Sungkit
MSc Sport Sciences.

Sport Sciences Unit,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

Objectives : Purpose of the present study was to investigate the effects of progressive combined flexibility, strength and aerobic exercises on quadriceps muscles strength, functional exercise capacity, pain symptoms and physical function in middle aged women patients with early stage primary knee Osteoarthritis (OA).

Patients & Methods : Sixteen middle aged — women aged 50 — 64 years of among the patients diagnosed to have OA of the knee were recruited for the study and were randomly selected to either intervention or to the control group. Subjects were tested before and after 8 weeks of progressive combined training programme, with three sessions a week frequency, in six minutes walking distance to measure the functional exercise capacity, WOMAC questionnaires to assess pain symptoms and patients' ability to perform daily activities and isokinetic testing with Biodex Isokinetic Dynamometer to assess patients' quadriceps muscle peak torque.

Results : Walking distance in intervention group has increased significantly by 14.3% ($p < 0.05$) whereas it reduced by 3.4% in control group at post intervention tests. However there was no significant difference in walking distance between control and experimental groups in the post test ($p > 0.05$). Pain scores were significantly reduced by 44.1% in intervention group ($p < 0.05$), whereas they were increased by 48.8% in control group ($p < 0.01$). The difference in pain score between control and experimental groups was statistically significant at the post test ($p < 0.001$). Physical function scores were significantly reduced by 55.0% in intervention group ($p < 0.001$) and increased by 30.5% in control group ($p < 0.01$). The difference in physical function score between groups was statistically significant ($p < 0.001$) in the post intervention testing. Right and left quadriceps muscles peak torque values at $120^{\circ}/\text{s}$ and $180^{\circ}/\text{s}$ angular velocities in intervention group at the post test have increased statistically significant. Peak torque value of right quadriceps muscle at $120^{\circ}/\text{s}$ and $180^{\circ}/\text{s}$ increased by 41.2% ($p < 0.01$) and 32.2% ($p < 0.05$) respectively. Peak torque of left quadriceps muscle at $120^{\circ}/\text{s}$ and $180^{\circ}/\text{s}$ increased by 103.7% ($p < 0.001$) and 30.8% ($p < 0.01$) respectively. There were statistically significant differences in peak torque values of right and left quadriceps muscles at both angular velocities between intervention and control groups after completion of the intervention programme with obvious and statistically significant improvement in the intervention group in comparison to the control group.

Conclusion : We concluded that the short-term training programme combining flexibility, strength and endurance activities of eight weeks with partially supervised exercises programme lead to significant improvements in six minutes walking test, pain and disability assessment and quadriceps muscles peak torque in middle aged women with early stage primary knee OA.

Dr. Oleksandr Krasilshchikov : Supervisor
Dr. Tg. Muzaffar Tg. Mohd. Shihabuddin : Co-Supervisor

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THE EFFECT OF CONTINUOUS AND INTERMITTENT EXERCISE TRAINING PROGRAMS ON THE PLATELET ACTIVATION AND FIBRINOLYTIC PROFILES OF HEALTHY MALES

Nur Hasanah Bt. Ruslan
MSc Sport Sciences.

Sport Sciences Unit,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia

Objectives : The purpose of this study was to investigate the effectiveness of the continuous and intermittent training programs on

platelet activation and fibrinolytic profiles. The endurance training programs were observed to have several favorable effects on blood haemostasis which can reduce the risks of cardiovascular disease secondary to atherosclerosis.

Patients & Methods : 24 healthy sedentary males with mean age of 21.75 ± 3.73 years old participated in this study. They were divided into three groups, like, control group (n=9), continuous training group (n=7) and intermittent training group (n=8). The intensities for both the continuous group and intermittent group had been kept low for the first 4 weeks as familiarization trial, but increased considerably for the next eight weeks. Platelet activation and fibrinolytic profiles were measured by detecting P-selectin and glycoprotein IIb/IIIa. Coagulation parameters were determined by measuring the Thrombin time (TT), Prothrombin time (PT) and Activated Partial Thromboplastin Time Test (APTT). Concentration of the tissue plasminogen activator (t-PA) and concentration of plasminogen activator inhibitor type-1 (PAI-1) antigen were measured as fibrinolytic profiles.

Results : This study shows that, both the exercise groups provide better changes. The intermittent type of training only showed the decline of the gated percentage of CD62p whereas the continuous group showed the decline in both CD62p and PAC-1 activation. For the coagulation parameters, the intermittent group showed the beneficial effects by reducing the TT, PT and APTT. However, continuous group showed the improvement only on the PT. Continuous types of training programs also showed a reduction of t-PA and PAU antigen after training programs. However, the changes were significantly difference.

Conclusion : Both types of training programs showed favorable effects on platelet activation, coagulation system and fibrinolytic profiles. Intermittent group provide better effects only on platelet activation and coagulation parameter whereas continuous group exhibits better changes on all three parameters which are platelet activation, coagulation system and fibrinolytic profile.

Dr. Adibah Alawiah Abd. Razak : Supervisor
Assoc. Prof. Dr. R. G. Sirisinghe : Co-Supervisor

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MAXIMAL ACCUMULATED OXYGEN DEFICIT (MAOD) OF PHYSICALLY ACTIVE FEMALES DURING MID- FOLLICULAR (MF) AND MID-LUTEAL (ML) PHASES OF OVARIAN CYCLE

Shazlin Shaharudin
MSc Sport Sciences.

Sport Sciences Unit,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia

Objectives : This intervention study was undertaken with an objective to evaluate the anaerobic capacity in repeated sprint cycling bouts during different phases of ovarian cycle.

Patients & Methods : Twelve physically active females aged 22.41 ± 1.68 years, weight 52.06 ± 7.28 kg, height 158.17 ± 4.17 cm, and VO_{2max} of 34.92 ± 4.85 ml kg⁻¹ min⁻¹ contributed in this study. The method of measuring maximal accumulated oxygen deficit (MAOD) was implemented from Medb al., (1988). Initially, the VO_{2max} of the participant were measured on cycle ergometer following a graded exercise protocol. Then, the participants did sub-maximal cycling exercise for 10 minutes at 50%, 60%, 70% and 80% of VO_{2max} on separate days. The linear regression determined from the VO₂ — power relationship was used to approximate supra maximal power output at 120% VO_{2max}. Next, the participants performed repeated sprint cycling at 120% of VO_{2max} intensity with 20 minutes rest between consecutive sprints during mid-follicular (MF) and mid-luteal (ML) phases. The menstrual phases were verified through daily basal body measurement and serum progesterone analysis.

Results : Results indicated there were no significant difference in

maximal accumulated oxygen deficit (MAOD) and sprint performance between mid-follicular (MF) and mid-luteal (ML) phases in repeated sprint cycling. There was also no significant difference in plasma lactate and plasma ammonia concentration between mid-follicular (MF) and mid-luteal (ML) phases in repeated sprint cycling.

Conclusion : The ovarian phases of women with regular menstrual cycle, have no significant effect on anaerobic capacity.

Dr. Ahmad Amir Ismail : Supervisor
Assoc. Prof. Dr. Asok Kumar Ghosh : Co Supervisor

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EFFECTS OF VARIOUS JUMPING EXERCISE ON VERTICAL FORCE DISTRIBUTION AND EMG PATTERN IN SCHOOL CHILDREN

Siti Musyriifah binti Ismail
MSc Sport Sciences.

Department of Orthopaedics,
School of Medical Sciences, University Sains Malaysia,
Health Campus, Kelantan, Malaysia.

Objectives : Purpose of the present study was to determine the effect of 9 weeks of training based on various jumping exercises on vertical force distribution and EMG pattern in school children.

Patients & Methods : Forty school children (12 male and 28 female) aged between 13 to 17 years participated in this study. Subjects were divided evenly into 3 experimental groups: Group 1 (training based on jumps). Group 2 (training based on hops). Group 3 (training based on box drills) and a control group - Group 4. Intervention programme had been administered on the experimental groups for 9 weeks. During the 1 three weeks, the subjects were exercising once a week, followed by 3 weeks of exercising twice a week with last 3 weeks exercising thrice a week. No intervention programme was administered to the control group. Subjects were evaluated before, after 3 weeks (mid-test 1), 6 weeks (mid-test 2) and 9 weeks (post-test) in counter movement jump (CMJ), continuous jump with bent legs (CJb) and drop jump (DJ) with registration of jumps' characteristics and EMG.

Results : All intervention groups showed significant improvement in jump height and power within group between tests (p<0.001). By CMJ test, hop training brought highest improvements in jump height (27.9%) (p<0.001) and power (9.70%) (p<0.001), whereas box drills training improved force (15.5%) from pre-test values. Meanwhile by CJb test, jumps training brought the highest improvement in jump height (23.7%) (p<0.01) and power (13.8%), whereas force was improved the most by box training (34.9%) from pre-test. By DJ test, the highest improvement in jump height and power was brought by box drills training (27.9% and 19.6% respectively). Force improved 18.8 % under the influence of jumps training.

Discussion : There were no significant differences in the EMG peak amplitude and mean power frequency at muscle gluteus maximus, biceps femoris, rectus femoris, vastus media/is, medial gastrocnemius, and tibialis anterior in all types of jumping exercises. Muscle activation patterns differed in eccentric and concentric phases of the testing jumps.

Conclusion : Suggested training programmes, can be used as a conditioning programmes for volleyball and basketball players, track and field athletes specialising in vertical and horizontal jumps, they brought in significant improvement in jump characteristics.

Dr. Oleksandr Krasilshchikov : Supervisor
Dr. Mohamed Saat Bt Ismail : Co Supervisor

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THE EFFECTIVENESS OF EXERCISE AND ESTROGEN THERAPY IN REDUCING CARDIOVASCULAR RISK FACTORS IN THREE

MONTH OLD OVARIECTOMIZED RATS

Wan Mohd Norsyam Wan Norman
MSc Sport Sciences.

Department of Medicine,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

Introduction : Menopause plays an important role in lipid distribution in women. These explain the apparent acceleration in cardiovascular diseases after menopause.

Objectives : The aim of this study is to investigate the effectiveness of combination of regular exercise and estrogen therapy in reducing cardiovascular risk factors in post- menopausal animal model.

Material & Methods : Forty-nine Sprague-Dawley female rats aged three months were used in the study and randomly divided into two main groups which were ovariectomy and sham operation groups. Later, four groups which were non-treatment, estrogen therapy, exercise and combination estrogen therapy and exercise derived from ovariectomy controlled group and non- treatment and exercise groups derived from sham controlled group. Each group consists of 7-9 rats. Bilateral ovariectomy was done for all experimental and ovariectomised controlled groups while no ovary removal was performed to sham controlled groups. Estrogen therapy and swimming exercise were given for consecutive eight weeks after 4 weeks of operation and body weight progress was measured weekly. Rats were sacrificed via decapitation after a period of 8 weeks intervention and blood was collected for lipid and glucose analysis. The body weight progression of the rats was analysed by using paired t-test and repeated measures ANOVA with Bonferroni post-hoc test. The difference in plasma lipid profile and glucose were analysed by using One-way ANOVA with LSD post- hoc test.

Results : There was a significant ($p<.05$) body weight increase in ovariectomised rats, 4 weeks after ovariectomy as compared with the animals that undergo sham operation. No significant difference ($p>.05$) was detected in body weight after 8 weeks intervention among all ovariectomised groups. Estrogen therapy and swimming exercise treatment lowered the total plasma cholesterol and low density lipoprotein (LDL) cholesterol levels significantly ($p<.05$) as compared with estrogen therapy only. A higher plasma high density lipoprotein (HDL) cholesterol and HDL:LDL ratio ($p<.05$) were observed in ovariectomised animals with exercise treatment only. There was no significant difference in plasma glucose was observed among groups.

Conclusion : Estrogen therapy with exercise or exercise treatment alone was beneficial on lipid and lipoprotein metabolism which led to an Increase in cardiovascular health.

Assoc. Prof. Dr. Asok Kumar Ghosh : Supervisor
Assoc. Prof. Dr. Sit Amrah Sulaiman : Co-Supervisor
Dr. Chen Chee Keong : Co-Supervisor

EFFECTS OF CAFFEINE AND GINSENG SUPPLEMENTATION ON ENDURANCE PERFORMANCE IN THE HEAT

Wong Chee Ping
MSc Sport Sciences.

Department of ORL-HNS,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

Introduction : Athletes in Malaysia need to perform in a hot and humid environment due to the climatic nature of the country. Alteration in endurance performance following acute and chronic supplementation of caffeine has been studied in different populations but concurrent research in the Malaysian context has not been

attempted before. Equivocal findings of the ergogenic properties of *Panax ginseng* in enhancing physical performance were reported. However, data on the effect of acute supplementation of *Panax ginseng* on physical performance among Malaysian population is still lacking. Furthermore, combination of caffeine and *Panax ginseng* has never been investigated before on endurance running performance in the heat.

Objectives : In the present study, we examined the effect of acute supplementation of 5 mg caffeine per kg of body weight (C), 200 mg *Panax ginseng* (PG), combination of 5 mg caffeine per kg of body weight and 200 mg *Panax ginseng* (CPG) or placebo (PL) consumed one hour prior to the endurance performance. Supplements and placebo were given in the form of capsules in a randomised double blind cross-over trial.

Patients & Methods : Nine heat acclimated recreational runners (aged 254 ± 69 years) as well as nonusers of caffeine (237 ± 12.6 mg per day) participated in this study. Subjects ran at 70% of their on VO_{2max} a motorised treadmill in a heat-controlled laboratory ($31^{\circ}C$, 70% relative humidity). Subjects drank 3 niL of cool water per kg of body weight every 20 minutes during the trials to avoid the possibility of dehydration. Heart rate, mean skin temperature (chest, arm, thigh and calf), rectal temperature and RPE were recorded at an interval of 10 minutes.

Results : Oxygen consumption, fluid sensory scale and blood samples were collected at intervals of 20 minutes. Running time to exhaustion was significantly longer ($p=0.04$) in C trial compared to P1 trial. However, the longer time to exhaustion in the CPG trial did not reach statistical significance ($P=0.07$). Exhaustion time in PG trial showed no significant difference ($P=0.75$) in comparison with P1 trial. Heart rate, rectal temperatures, mean skin temperature, oxygen uptake, plasma insulin, glucose, lactate in the C, CPG and PG were not significantly different from the P1 trial. Plasma free fatty acid in the C and CPG trial were significantly higher in comparison with P1 trials. RPE were lowest in C trial and followed by CPG, PG and PL trials. Heart rate, rectal temperature, mean skin temperature, oxygen uptake, plasma insulin, glucose, lactate and fatty acid increased significantly during exercise from their respective resting values in all trials. Gastrointestinal discomfort was not reported during endurance performance in all trials.

Conclusion : It could be concluded that ingestion of 5 mg of caffeine per kg of body weight has an ergogenic effect on the nonusers of caffeine and heat-acclimatised recreational runners in a hot and humid environment.

Dr. Amit Bandyopadhyay : Supervisor
Dr. Chen Chee Keong : Co. Supervisor

VALIDATION AND RELIABILITY OF THE ROCKPORT FITNESS WALKING TEST (RFWT) AMONG STUDENTS OF THE HEALTH CAMPUS, UNIVERSITI SAINS MALAYSIA (USM)

Yeo Nga Ping
MSc Sport Sciences.

Department of Family Health,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.

Introduction : Direct measurement of maximal oxygen uptake (VO has been well accepted as the most valid test for cardiorespiratory fitness. However, this method requires sophisticated and expensive laboratory equipment as well as trained personnel. It is also time consuming to test each participant individually and the participants themselves have to be physically exerted to obtain a true maximum for the results to be accurate. To overcome these practical problems, the RFWT, which is a less strenuous field test, has been used to estimate

the VO.

Objectives : The purpose of the present study was to test the validity and the reliability of the RFWT among the students of the Health Campus, Universiti Sains Malaysia (USM).

Patients & Methods : Fifty healthy males (21.3 ± 1.5 year) and 50 healthy females (21.3 ± 1.5 year) participated in this study. They performed a maximal graded exercise test (GXT) and two RFWT with the minimal of 4 days rest. The maximal GXT on a motorised treadmill was conducted in a laboratory to determine their measured VO₂max that was used as the criterion value. The estimated VO₂max was obtained from the RFWT in an open field testing environment. The generalised equation of the Kline et al. (1987) was used for the calculation.

Results : The results of the present study showed that the correlation coefficient between the measured and estimated VO values was r = 0.79 (p <0.05). In terms of reliability, the RFWT has a high test-retest reliability (r = 0.92, p <0.05). However, when the results were analysed separately according to gender, the correlation coefficient was 0.72 (p <0.05) for the male participants and 0.31 (p <0.05) for the female participants. The coefficient for the test-retest reliability was 0.91 (p < 0.05) and 0.77 (p < 0.05) for the male and female participants respectively. These results suggest that the RFWT is a valid and reliable field test for estimation of VO₂max among the male students of the Health Campus, USM. However, the REMIT has been shown to over- predict the actual VO₂max in the female students of Health Campus.

Conclusion : The use of the RFWT on the female students to estimate their VO₂max should be treated with caution. We suggest another regression equation for the calculation of the VO from the RFWT for the female students.

Dr. Mohd. Asnizam Asari : Supervisor

Dr. Chen Chee Keong : Co-Supervisor

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NEONATAL SCREENING OF DEVELOPMENTAL DYSPLASTIC OF HIP (DDH) IN BREECH DELIVERED BABIES

*Dr. Zakaria Yusof
MMed Otopaedic*

**Department of Otopaedic
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Introduction : Development dysplasia of the hip (DDH) is a disorder that represents abnormal development or dislocation of the hip secondary to capsular laxity and mechanical factors. It was reported that incidence of DDH in life born babies was very low in Malaysia. However there is no reported study on breech babies in Malaysia. Neonatal screening using Ortolani and Barlow is known to have poor sensitivity which will become better with the experience of examiner. In the current practice, this test is done by medical officer as part of other neonatal screen We conducted this study to determine the incidence of DDH in breech babies using Ortolani and Barlow test. We also compared the finding of examination result between dedicated examiner and routine examiner.

Method: This was a cross-sectional study, conducted from October 2005 to December 2006 at Hospital Raja Perempuan Zainab II, Kota Bharu, Kelantan and at Hospital Universiti Sains Malaysia. In the period of the study, 180 babies were examined by dedicated examiner and it is equivalent to 66.9 % of breech deliveries in both hospitals t of this, 30 babies were selected to be examined by routine examiner and dedicated examiner which later confirm with ultrasound examinations as the gold standard. The selection was made based on parents consent for ultrasound examination.

Result: Out of 180 breech babies, six babies (3.3 %) had positive Ortolani and Barlow test. All 6 babies were among 127 babies delivered

through Lower Segment Caesarean section. Four out of six babies were female and two are male. From 30 selected samples, dedicated examiner detected five babies with positive Ortolani and Barlow test. However routine examiner did not detect any positive Ortolani and Barlow test. Based on ultrasound as gold standard. the dedicated examiner has sensitivity of 0.67 and specificity of 0.97.

Conclusion: High incidence (3.3%) of positive Ortolani and Barlow test among breech babies support the need for special attention to this population of patients. A dedicated hip screener for neonatal examination has the ability to detect DDH better than the routine examiner.

Dr. Abdul Razak Sulaiman : Supervisor

Dr. Yaacob Abas : Co-Supervisor

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A STUDY ON THE EFFECT OF FIREARMS ON THE HEARING OF MILITARY PERSONNEL

*Dr. Mohd Zambri bin Ibrahim
MMed Otorhinolaryngology*

**Department of Otorhinolaryngology
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Objectives : The aim of this study was to establish the prevalence of hearing impairment and transient effect of ear pathology among the army personnel who underwent firearm training without wearing hearing protection.

Material & Methods : A prospective cross-sectional study was carried out in RMAF 16 Melayu Infantry unit of Desa Pahlawan camp, Kelantan and from infantry unit of 301 camp, Tanah Merah, Kelantan from July 2007 till October 2007. The population was taken from an army personnel who involved in firearm training. The subject's particulars and history takings were recorded and compiled. The subject's were examined by using otoscope, tympanometry, portable audiometry and otoacoustic emission (DPOAE) and findings were recorded. Evaluation and examination was performed in three stage, pre shooting, post shooting less than 48 hours and post shooting more than 2 weeks. Hearing threshold above 30 db at any frequencies was considered hearing impairment. A total number of 210 army personnel were involved in this study. All were males. The age ranged was from 21 years to 47 years old.

Results : The prevalence for post shooting of the right middle ear effusion was 21.1% and for left 20%. Majority of the hearing impairment occurred at frequency of 6 kHz for both ears, 50.5% for right ear and 67% at left ear. The prevalence of temporary threshold shift was 26% for right ear and 21.4% for left ear. For permanent threshold shift, the prevalence for right and left ear was 11% and 8.1%. Those who were right handed shooter gave a significant p value < 0.05, caused hearing impairment to the left ear. There was strong relation between age, duration of work and frequency of firearm training causing hearing impairment, with p value < 0.05.

Conclusion : Results from this study indicate that there is an urgent need from the Ministry of Defense to develop appropriate intervention or hearing conservation program in order to prevent army personnel from developing the noise induced hearing loss.

Prof. Dr. Din Suhaimi Sidek : Supervisor

Assoc. Prof. Dr. Shahid Hassan : Co Supervisor

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EARLY DETECTION OF HEARING LOSS IN TUBERCULOSIS PATIENTS USING STREPTOMYCIN BY HIGH FREQUENCY DISTORTION PRODUCT OTOACOUSTIC EMISSIONS (DPOAE) AND PURE TONE AUDIOMETRY

Dr. Ali bin Haron
MMed Otorhinolaryngology

**Department of Otorhinolaryngology
School of Medical Sciences, University Sains Malaysia,
Health Campus, Kelantan, Malaysia.**

Objectives : Tuberculosis cases in Malaysia are on the rise. Combination of Streptomycin, Isoniazid, Rifampicin and Pyrazinamide (SHRZ) are treatment of choice for tuberculosis treatment during active phase. Streptomycin is known to cause ototoxicity, nephrotoxicity and neurotoxicity. The predictive value of pure tone audiometry in early detection of ototoxicity has been questioned. Distortion product otoacoustic emission is thought to be more sensitive and reliable for early detection of ototoxicity compare to pure tone audiometry. The aim of this study was to compare these two methods in newly diagnosed tuberculosis patients on streptomycin for early detection of ototoxicity.

Patients & Methods : A prospective cross sectional study was carried out at Otorhinolaryngology Clinic, Hospital University Science Malaysia and Hospital Raja Perempuan Zai nab 11, Kelantan from May 2006 till November 2007. Ninety six newly diagnosed tuberculosis patients on streptomycin were screened and 50 patients finally included in this study. High frequency Distortion Product Otoacoustic Emission (8,9,10 kHz) and Pure Tone Audiometry (0.25 were performed at 0,1 week ,2 weeks,4 weeks and 8 weeks of treatment.

Results : The incidence of ototoxicity in this study after completion two months of IM Streptomycin (15 mg/kg daily) is 29.2% (14 patients) using PTA (0.25 -8kHz). While using high frequency DPOAE detected ototoxicity in 77.1 % (37 patients). There was an association between ototoxicity with sex (P=0.011) and age (p=0.003). There was no association between ototoxicity with other medications taken (P0.621), pre treatment illness (P0.140) and urea level (P=1.0).

Conclusion : High Frequency Distortion Product Otoacoustic Emission (DPOAE) is a good monitoring tool for early detection of ototoxicity in tuberculosis patient on streptomycin compare to pure tone audiometry (PTA).

Dr. Mohd Khairi Md Daud : Supervisor
Dr. Hazama Mohamad : Co Supervisor

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**THE EFFECT OF BOVINE BONE SCAFFOLD ON
THE MICROSCOPIC BIOLOGICAL RESPONSE OF
HUMAN CHONDROCYTES**

Dr. Abdul Halim Shibghatullah
MMed Otorhinolaryngology

**Department of Otorhinolaryngology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia.**

Introduction : In the production of cartilaginous tissue, the choice of appropriate scaffold remains as a great challenge. The currently available scaffold, either natural or synthetic still does not meet the requirement of a scaffold for cartilage tissue engineering. An ideal scaffold has to provide a mechanical stability to the individual cell as a construct or transitional framework before synthesis of new extra cellular matrix.

Objective : The aim of this study was to evaluate bovine bone as a tissue engineering construct for cartilage reconstruction and to investigate the biological effects of bovine bone on human chondrocyte *in vitro*.

Method : Human chondrocytes were cultured and seeded onto bovine bone scaffold with seeding density of 1×10^6 cells per 100 μ l/ scaffold and incubated for 1 day, 2 days, 5 days and 7 days. Proliferation and viability of the cells were measured by mitochondrial

dehydrogenase activity (MU assay), adhesion study was analyzed using Scanning Electron Microscopy (SEM) and differentiation study was analyzed by Immunofluorescent staining using Confocal Laser Scanning Electron Microscopy (CLSM).

Result : The data showed the presence of proliferation and viability of the cells on the scaffolds by MIT method within 24 hours to 7 days observed. SEM pictures revealed presence of chondrocytes located on the scaffolds, showed increasing number of cell within the days and that cells readily grew on the surface and into the open pores of the scaffold. Immunofluorescent staining detected collagen type II on the scaffolds which was increasing within the days.

Conclusion : The results showed the potential of bovine bone as three dimensional scaffold for cartilage tissue engineering because of the good cells proliferation, attachment, maturity, non toxic, safe, easily resourced and relatively cheap.

Dr. Baharudin Abdullah : Supervisor
Prof. Rani Samsudin : Co-Supervisor

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**TEN YEARS REVIEW OF HEPATOCELLULAR
CARCINOMA IN HOSPITAL UNIVERSITI SAINS
MALAYSIA (1996-2005).**

Dr. Amen bin Ab. Latif
MMed Surgery

**Department of Surgery
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Introduction : Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver and one of the most common causes of death from cancer. Local literature on HCC are rather scare and hence the need for a study of this nature.

Patients & Methods : One hundred eight (108) patients were diagnosed of HCC in a period often years from 1996 to 2005 at Hospital Universiti Sains Malaysia were studied to determine the pattern of the disease and to highlight the clinical presentation, common risk factors, mode of investigation, stage at presentation, modalities offered for treatment and the survival rate.

Result : The mean age of occurrence was 57.9 \pm 11.5 years. Male to female ratio was 3:1 and predominantly affecting the Malays (83.3%). Hepatitis B was the main risk factor for HCC in 68(63%), where as Hepatitis C was positive in 9(8.3%). The clinical presentations included abdominal discomfort in 98(90.7%), abdominal pain in 55(50.9%), abdominal distension in 68(62.7%), loss of weight in 62(57.4%), stigmata of chronic liver disease in 51(47.2%) and jaundice in 52(48.1%) patients. Solitary type of lesion in 30(27.2%) and multiple type in 78(72.2%) patients. The largest diameter varied from <5cm in 33(30.5%), 5-10cm in 66(61.1%) to >10cm in 9(8.3%) patients. Portal vein thrombosis presented in 59(54.6%) and 27(25%) already with distant metastases. Severity of liver impairment as assessed by Child Pugh Classification, 39(36.1%) presented with Child's A, 40(37%) with Child's B and 29(26.9%) with Child's C. Tumor grading by TNM staging showed patients presented with unresectable tumor due to locally advanced stage were 66(61.1%) and advanced stage 32(29.6%). Where as 10(9.3%) of patients at resectable stage of tumor. Most patients 77(71.3%) given supportive treatment. Anti tumour agent only given to 4(3.7%) patients and 1(0.9%) patient underwent emergency surgical resection. Death mainly related to 11CC, account for 82.4% (89). Overall mean survival was 5.2 months. Statistically that sex, location of tumour, Child Pugh Classification, Okuda staging and mode of treatment were related with the survival in this study.

Conclusion : Most hepatocellular carcinoma cases admitted to HUSM presented in advanced stage put them unsuitable for surgical resection or anti tumour treatments modalities. More effort should be taken to detect early stage of 11CC so that curative treatment can be aimed to prolong the survival rate.

Dr. Mohd Nor Gohar Rahman : Supervisor

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A PROSPECTIVE STUDY ASSESSING THE USE OF UMBILICAL ARTERY DOPPLER AND BIOPHYSICAL PROFILE IN DETERMINING THE PERINATAL OUTCOME IN FOETUS WITH GROWTH RESTRICTION IN HOSPITAL UNIVERSITI SAINS MALAYSIA

*Dr. Himla Devi Veerasamy
MMed Obstetrics & Gynecology*

**Department of Obstetrics & Gynecology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Introduction : Since the introduction of Doppler in the field of Obstetrics and Gynaecology by Fitzgerald and Drumm in 1977 for in-utero assessment of foetus with growth restriction, in high risk pregnancy and post date pregnancy with oligohydramnios, many studies was conducted in the hope to assess the specificity and sensitivity as an antenatal monitoring tool. In Hospital Universiti Sains Malaysia, Doppler study was used on a daily basis in management of high risk pregnancy.

Objectives : To assess the use of Doppler study and biophysical profile score in assessment of foetus with growth restriction in terms of perinatal outcome. This was a prospective descriptive study.

Results : This study as conducted in Hospital Universiti Sains Malaysia from March 2006 to Jiiiy 2007 Hundred and seven patients were enrolled in the study after satisfying the inclusion criteria Hundred and one (94%) patients were malays and 6(6%) patients were Chinese The average age was 31.7+1/-6.40 years The mean weight, height and body mass index was 57 kilograms, 153 centimeters and 24 kg/m² respectively Fourtysix (43%) patients had hypertension and 7(6 5%) patients had diabetes Eightyfive patients had normal Doppler findings, 8 patients had suspicious. Doppler and 14 patients had pathological Doppler. The mean PI, RI and S/D for normal. Doppler was 0.644- 0.12, 0.57+1-0.09 and 2.494-0.33 respectively. For suspicious Doppler the mean PI, RI and SID was 1.29+/-0.12, 0.724-0.042 and 3.65+/- 0.58 respectively and for pathological Doppler was 1.394-0.11, 0.79+1-0.03 and 3.82+1-0.76 respectively. The mean gestational age at delivery was 37 +/- 2.7 weeks. Out of the 85 patients with normal Doppler findings, 27 patients underwent emergency lower segment caesarean section, 4 neonates had adverse perinatal outcome, 82 neonates had APGAR score of 7 and above and 12 neonates had pH of less than 7.4. Out of 8 patients with suspicious Doppler, 6 patients underwent emergency lower segment caesarean section, 7 neonates had APGAR score of 7 and above and 3 neonates had a cord blood pH of less than 7.4. Out of 14 patients with pathological Doppler findings, 11 patients underwent emergency lower segment caesarean section, 6 neonates had adverse perinatal outcome with 1 perinatal death, 13 neonates had APGAR score of 7 and above and 7 neonates had pH less than 7.4. In relation to biophysical profile score, only 1 patients had a score of less than 6. The patient underwent emergency lower segment caesarean section due to moderate meconium stained liquor. The neonate was intubated and admitted for more than 7 days to NICU and at birth the cord blood pH was less than 7.4.

Conclusion: In this study, Doppler study in assessment of foetus with growth restriction had a sensitivity of (81/85) 95.3%, a specificity of (8/22) 3 6.4%, positive predictive value (6/14) 42.9% and negative predictive value of (4/85) 4.7%. Biophysical profile score on the other hand had a sensitivity of 99.1% but poor specificity, positive predictive value and negative predictive value. The 2 method used in combination had a better diagnostic and monitoring value. Base on the cord blood pH recorded in this study, the conclusion that intervention to deliver early was decided much before the foetus suffered any form of acidosis. It will be fair to claim that the caesarean section rate can be reduce further, by supporting the decision to deliver early base on

combinationof the Doppler finding and biophysical profile score as well as the clinical assessment.

Dr. Che Anuar Che Yaacob : Supervisor

Assoc. Prof. Dr. Nik Mohamed Zaki Nik Mahmood : Co Supervisor

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THE EFFECTIVENESS OF EXERCISE AND ESTROGEN THERAPY IN REDUCING CARDIOVASCULAR RISK FACTORS IN THREE MONTH OLD OVARIECTOMIZED RATS

*Dr. Wan Mohd, Norsham Wan Norman
MSc Sport Sciences*

**Sport Sciences Unit,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Introduction : Menopause plays an important role in lipid distribution in women. These explain the apparent acceleration in cardiovascular diseases after menopause. The aim of this study is to investigate the effectiveness of combination of regular exercise and estrogen therapy in reducing cardiovascular risk factors in post-menopausal animal model.

Material & Methods : Fourty-nine Sprague-Dawley female rats aged three months were used in the study and randomly divided into two main groups which were ovariectomy and sham operation groups. Later, four groups which were non-treatment, estrogen therapy, exercise and combination estrogen therapy and exercise derived from ovariectomy controlled group and non- treatment and exercise groups derived from sham controlled group. Each group consists of 7-9 rats. Bilateral ovariectomy was done for all experimental and ovariectomised controlled groups while no ovary removal was performed to sham controlled groups. Estrogen therapy and swimming exercise were given for consecutive eight weeks after 4 weeks of operation and body weight progress was measured weekly. Rats were sacrificed via decapitation after a period of 8 weeks intervention and blood was collected for lipid and glucose analysis. The body weight progression of the rats was analysed by using paired t-test and repeated measures ANOVA with Bonferroni post-hoc test. The difference in plasma lipid profile and glucose were analysed by using One-way ANOVA with LSD post- hoc test.

Results : The results showed that there was a significant (pcz.05) body weight increase in ovariectomised rats, 4 weeks after ovariectomy as compared with the animals that undergo sham operation. No significant difference (p>.05) was detected in body weight after 8 weeks intervention among all ovariectomised groups. Estrogen therapy and swimming exercise treatment lowered the total plasma cholesterol and low density lipoprotein (LDL) cholesterol levels significantly (p<.05) as compared with estrogen therapy only. A higher plasma high density lipoprotein (HDL) cholesterol and HDL:LDL ratio (p<.05) were observed in ovariectomised animals with exercise treatment only.

Conclusion : There was no significant difference in plasma glucose was observed among groups. In conclusion, estrogen therapy with exercise or exercise treatment alone was beneficial on lipid and lipoprotein metabolism which led to an Increase in cardiovascular health.

Assoc. Prof. Dr. Asok Kumar Ghosh : Supervisor

Assoc. Prof. Dr. Siti Amrah Sulaiman : Co Supervisor

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AN EXPERIMENTAL STUDY ON INTRASTROMAL INJECTION OF AMPHOTERICIN B IN FUSARIUM SOLANI KERATITIS IN RABBITS

Dr. Che M.ahiran binti Che Daud
MMed Otorhinolaryngology

**Department of Otorhinolaryngology,
School of Medical Sciences, University Sains Malaysia,
Health Campus, 16150 Kelantan, Malaysia**

Objective : To compare the effectiveness between intrastromal injection of amphotericin B 0.15% (1.5mg/ml) and intrastromal injection of amphotericin B 0.0005% (5 µg/ml) and the safety of intrastromal injection Amphotericin B 0.0005% in *Fusarium solani* keratitis in rabbits.

Methodology : Fungal keratitis was induced with a standardized inoculum of *Fusarium solani* placed on the debrided cornea into the right eye of 18 New Zealand white rabbits. Rabbits in Group A (n were treated with topical 0.15% amphotericin B every hourly for 12 hours daily (control), while rabbits in Group B (n=6) were treated with intrastromal injection 0.15% (1.5mg/ml) of amphotericin B and Group C rabbits (n=6) were treated with intrastromal injection 0.0005% (5µg/ ml) of amphotericin B. The intrastromal injection was given at day 3, 6, 9 and 11. Serial clinical examination was conducted at day 3, 6, 9, 11 and 14 to look at the changes in the size of the epithelial defect, the depth of the ulcer, stromal infiltration, hypopyon and the presence of satellite lesion. The infected eyes were enucleated on the day 14 and sent for histopathology evaluation.

Results : The intrastromal injection of amphotericin B 0.0005% injection (group C) was found to be effective compared to intrastromal injection amphotericin B 0.15% (p<0.001) in treating *Fusarium keratitis* in rabbits. There was statistical significant difference in the size of epithelial defect (p=0.02) and satellite lesion (p=0.02) for the rabbits treated with intrastromal injection of amphotericin B 0.0005% compared to the intrastromal injection of amphotericin B 0.15%. Histopathological examination also revealed absence of fungal load, the depth of ulcer limited to anterior two third, moderate inflammatory responses and mild granulation tissue in the group treated with intrastromal injection amphotericin B 0.0005%. These histopathological findings were consistent with serial clinical observation. There was no evidence of corneal decompensation, severe punctate keratopathy and or cornea! melting in the group treated with intrastromal injection amphotericin B 0.0005%.

Conclusion : Intrastromal injection of amphotericin B 0.0005% (5µg/ ml) was found to be effective and safe in treating *Fusarium solani* keratitis. Thus, after undergoing clinical trial it can be applied to the patient whose refractory to conventional therapy and can reduce the cost and shorten the hospital stay.

**Dr. Liza Sharmini Ahmad Tajudin : Supervisor
Assoc. Prof. Dr. Mohtar Ibrahim : Co Supervisor**

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