1 DEVELOPMENT OF A PLLA-BASED BIORESORBABLE STENT FOR USE IN CONGENITAL HEART DISEASE

Ni J1, Seger C2, Alexy R1, Wu B2, Levi D1. 1UCLA, Los Angeles, CA and 2UCLA, Los Angeles, CA.

Purpose of Study: Stents used in the treatment of congenital heart disease (CHD) only need to serve as temporary scaffolding due to growing cardiovascular structures. Thus, biodegradable stents are promising alternative. In order to facilitate better open chest surgery in the treatment of CHD, such as coarctation of the aorta. Biodegradable stents, in contrast with traditional metallic stents, are completely absorbed by the body after the necessary support. This project aims to design a biodegradable stent for the treatment of congenital heart lesions in neonates and infants.

Methods Used: Poly-L-lactic acid (PLLA) and PLLA-blend tubes were fabricated using sputter deposition on a custom-built robot and tested for radial strength. Tubes laser-cut into stent geometry were crimped down on a balloon catheter for stent delivery. Due to crimping fractures, FEM stress analysis (Autodesk Inventor 2014) was conducted on the initial stent geometry to locate regions of concentrated stress and guide development of revised geometry.

Summary of Results: A sputter deposition based protocol for fabricating PLLA-based biodegradable stents for the treatment of congenital heart disease was developed and refined. Tubes of PLLA and PLLA blends were successfully laser-cut into stents and tested for radial strength and ability to be crimped and deployed. Using FEM stress analysis, the stent geometry was modified with curve and row intersection optimizations for better stress distribution, reducing risk of fracture when crimped.

Conclusions: We have made progress in the development of a novel PLLA-based biodegradable stent through fabrication and geometry optimization. Future steps involve refining polymer blends, crimping and heat-setting, and degradation profile.
WHOLE EXOME NEXT-GENERATION SEQUENCING IDENTIFIES NOVEL DISEASE GENES IN PRIMARY VASCULAR ANEURYSMS

D’souza RS, Gowen K, Sraw S, Jones K, Taylor M. University of Colorado, Aurora, CO.

Purpose of Study: Non-atherosclerotic arterial aneurysm is a highly morbid condition and its biological basis remains unclear outside the spectrum of an identifiable heritable connective tissue condition (e.g. Marfan or Ehlers-Danlos Syndromes). We identified a cohort of unrelated patients lacking a heritable connective tissue diagnosis in spite of manifesting multiple aneurysms and/or pseudoaneurysms in medium-sized arteries. We termed the condition multiple aneurysmal-pseudoaneurysmal syndrome (MAPS) and hypothesized that MAPS may be due to a novel disease gene. We utilized exome sequencing and bioinformatics analysis to identify potential disease genes which contribute to risk for MAPS.

Methods Used: Next-generation exome sequencing was performed for 15 MAPS patients and one family with multi-generational arterial aneurysms. Bioinformatics filtering of identified putative ‘mutations’ followed by Ingenuity Pathway Analysis of suspicious genes was performed.

Summary of Results: The familial MAPS phenotype was first targeted by exome sequencing to identify candidate MAPS genes. For sporadic MAPS cases, Ingenuity Pathway Analysis (IPA) software was used to search literature describing biochemical pathways between known vascular disease genes and bioinformatics-filtered candidate genes. Analysis of familial MAPS yielded 15 candidate genes, of which the PCDH12 gene was the most promising candidate due to its respective mutation being located in an extremely conserved gene region with a high bioinformatics score for predictive phenotypic damage. Analysis of sporadic MAPS using IPA software identified 6 candidate genes including BAG6, PRKCD, CTNNA1, JAG1, FNI, and MMP13.

Conclusions: Exome sequencing with bioinformatics filtering in the novel aneurysmal-pseudoaneurysmal syndrome identified several promising aneurysm candidate genes. Knock-out/knock-in animal models are being developed to further explore the relationship between candidate genes and phenotypic expression.

PREVALENCE OF RIGHT-TO-LEFT SHUNTING IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

Dasgupta N, Georgyran R, Tobis J. UCLA, Los Angeles, CA.

Purpose of Study: Right-to-left shunting (RLS), most commonly through a patent foramen ovale (PFO), has been associated with several medical conditions such as cryptogenic stroke, decompression illness, platypnea-orthodeoxia, and migraine headache with aura. PFO occurs in approximately 20-25% of the general population. However, recent studies indicate that PFO is present in over 65% of people with obstructive sleep apnea (OSA), and that the shunting of blood may be cause for increased severity of OSA symptoms in these patients. There are also observational reports of improvement in OSA symptoms following PFO closure. This study aims to determine the prevalence of RLS in patients with OSA and evaluate the association of RLS with the severity of disease.

Methods Used: Patients with OSA who presented to the UCLA Santa Monica Sleep Clinic from August 2011 to July 2013 were enrolled in the study. All patients underwent a Transcranial Doppler (TCD) study with agitation to determine the presence of RLS. The Spencer Logarithmic scale was used to grade the shunt level. Severity of OSA was evaluated with the apnea-hypoxia index (AHI), baseline SaO2 in wakefulness, and nadir of SaO2 during sleep. A control population consisted of patients who presented to the UCLA Cardiac Catheterization lab.

Summary of Results: A total of 80 patients were enrolled with a mean age of 54±14. RLS was documented in 42.5% of the patients with OSA versus 18% in the control group (p < .0001). Comparisons between OSA patients with RLS and those without revealed no statistically significant differences in the degree of desaturation or AHI.

Conclusions: The prevalence of RLS in patients with diagnosed OSA is higher than that of the general population. However, the presence of RLS does not contribute to the clinical severity of the disease.
PREVALENCE OF CORONARY ARTERY DISEASE ASSESSED BY DUAL SOURCE CT ANGIOGRAPHY IN WOMEN WITH MAMMOGRAPHICALLY DETECTED BREAST ARTERIAL CALCIFICATIONS

Gibson A, Ruehm S. DGSOM, Los Angeles, CA.

Purpose of Study: To assess the correlation between breast arterial calcifications (BAC) on digital mammography and the extent of coronary artery disease (CAD) as determined by dual source coronary CTA in a population of women both symptomatic and asymptomatic for coronary artery disease.

Methods Used: Sixty-six women (aged 38-79 years) who underwent both coronary CTA and digital mammography were included in the study. Health records were reviewed to determine the presence of cardiovascular risk factors such as hypertension, hyperlipidemia, diabetes mellitus, and smoking. Digital mammograms were reviewed for the presence and degree of BAC, graded by severity and extent. Coronary CTA was reviewed for CAD, graded by the extent of calcified and non-calcified plaque, and the degree of major vessel stenosis. A four point grading scale was used for both coronary CTA and mammography.

Summary of Results: All women with moderate or advanced BAC on mammography (n=11) demonstrated moderate to severe CAD as determined by coronary CTA. Three women with no BAC did have advanced CAD. For all women, the positive predictive value of BAC for CAD was 1 (11 of 11 patients) and the negative predictive value was 0.73 (40 of 55 patients).

Conclusions: The presence of BAC on mammography appears strongly correlated with CAD as determined by coronary CTA.

Role of Adipose Tissue Hypoxia in Insulin Resistance

Bredbeck B1, Lawler H1, Erickson C1, Rasouli N1-2, 1 University of Colorado, Aurora, CO and 2 Denver VA, Denver, CO.

Purpose of Study: We hypothesized that improved angiogenesis in expanding fat results in decreased adipose tissue hypoxia and protection from insulin resistance. Adipose tissue oxygenation (AT pO2) and markers of angiogenesis and inflammation were investigated in obese insulin sensitive (OBIS) compared to obese insulin resistant (OBIR) and lean subjects.

Methods Used: Non-diabetic, sedentary subjects were enrolled in this study. OBIS subjects were characterized by BMI 30-40 kg/m2, absence of metabolic syndrome criteria and insulin sensitivity (SI) values above 2.7x10^-4 min^-1.l μmol^-1. SI was calculated using insulin modified frequently sampled intravenous glucose tolerance test. Total body fat was quantified by dual energy X-ray absorptiometry. Partial pressure of oxygen in abdominal subcutaneous adipose tissue (SAT) was measured in vivo. Plasma angiogenesis factors were measured using ELISA. The expression of candidate genes involved in angiogenesis and inflammation were measured in SAT using SYBR qPCR.

Summary of Results: Obese group (n=12) had a BMI of 34.1±1.3 while lean group (n=4) had a BMI of 22.9±1.0 (p<0.001 v. obese). OBIS (n=6) and OBIR groups were similar in age, BMI and body fat but different in SI. The mean SI was 4.4±0.8, 3.5±0.3, and 1.8±0.2 in the lean, OBIS, and OBIR groups, respectively (p<0.001, OBIS v. OBIR). ATpO2 was increased in lean as compared to obese subjects (53±1.9 v. 37.7±2.9 mmHg; p<0.001). Obese subjects had increased gene expression of CD68 and decreased VEGF-A by 31% and -192% respectively (p<0.05 vs lean); but mRNA levels of HIF1a, FGF2, HGF, ANGPTL2 and endothelin were similar among groups. However, OBIS subjects had increased plasma levels of ANGPTL2 (335.0±40.7 v. 159.5±33.5 pg/ml, p=0.008 v. OBIR), and HGF (37.2±3.87 v. 25.7±1.2 pg/ml, p=0.05 v. lean). Plasma VEGF-A and FGF2 levels were similar among groups and EGF and endothelin were undetectable in circulation. ATpO2 correlated with mRNA levels of VEGF-A and negatively with BMI (r=0.7, -0.8 respectively, p<0.05) but it did not correlate with SI.

Conclusions: We confirmed that obesity was associated with adipose tissue hypoxia and inflammation; yet there was no distinction in ATpO2 between the OBIS and OBIR groups. Our data suggest that adipose tissue hypoxia is simply a consequence of fat expansion and not related to insulin resistance.

Estrogen Receptor Alpha-Mediated Repression of Inflammation in Macrophages and Its Relevance in Type 2 Diabetes

Sokolski E, Saijo K. UCSD School of Medicine, San Diego, CA.

Purpose of Study: 17β-estradiol (E2) has been used in hormone replacement therapy (HRT) since the 1940s, when the FDA approved estrogen replacement to treat the symptoms of menopause. In 2003 the Women’s Health Initiative (WHI) showed that there is an increased risk of type 2 diabetes in post-menopausal women taking HRT. Type 2 diabetes is associated with chronic inflammation and macrophage recruitment to adipose tissue. The purpose of this study is to identify endogenous ligands for estrogen receptor alpha (ERα) that repress inflammation in macrophages, elucidate the molecular mechanism by which they act, and determine their ability to prevent the development of type 2 diabetes in a murine model.

Methods Used: Screening of endogenous steroid ligands was done in both the RAW macrophage cell line and murine bone marrow derived macrophages (BMDM) cells. Biochemistry experiments were done in BMDM cells via co-immunoprecipitation followed by western blotting. Genome-wide RNA-sequencing studies were done in BMDM cells and results were analyzed using Homer software. Animal studies were done in male C57BL/6 mice fed on a high fat diet (HFD) and treated with either 16-epiestriol (16-EpiE3) or E2OH vehicle control. Progression to type 2 diabetes was evaluated by measuring weekly weight gain and by a glucose tolerance test (GTT) at the end of the study.

Summary of Results: Several steroid ligands were able to repress inflammatory cytokine production in macrophages. Ligand-bound ERα was found to act by binding to p65 at NFκB sites to repress transcription. On a genome-wide level, RNA-sequencing studies provided detailed information on the differential mRNA expression of steroid-treated cells. Animal studies provided evidence that 16-EpiE3, one of the anti-inflammatory steroidal ligands, is effective at preventing type 2 diabetes development in a murine model. HFD mice treated with 16-EpiE3 gained an average of 10g less than control and did not develop glucose intolerance.

Conclusions: While E2 is a poor agent for type 2 diabetes prevention, this study shows that other endogenous ERα ligands may provide novel therapies. There is still much that is unknown about the molecular mechanisms through which these steroids act, and future biochemistry and genome-wide studies will add greatly to the current model.

A Novel Target for Combating Insulin Resistance

Ma G, Lopez-Sanchez I, Ghosh P. UCSD School of Medicine, San Diego, CA.

Purpose of Study: Insulin Resistance (IR) is a hallmark of type II Diabetes (T2DM) and is an independent risk factor for atherosclerosis, heart
failure, and stroke. IR results from dysregulation(s) in the signaling network downstream of the insulin receptor (InsR). Effective therapeutic strategies to restore insulin sensitivity require the identification of key players that can modulate the activation of InsR, its major downstream intermediate, IRS1, and the trimeric G protein, Gi. It also requires identification of novel substrates of PKCθ, a kinase activated by fatty acids during IR. GIV, a newly identified multi-modular signal transducer and a guanine exchange factor (GEF) for trimeric Gi, fulfills all these criteria. This study dissects the mechanisms by which GIV maintains insulin sensitivity and how its inhibition confers IR.

**Methods Used:** Insulin response was investigated by analyzing key signaling cascades downstream of the InsR, the profile of adaptor proteins that bind activated InsR, GLUT4 translocation to the PM, and measuring glucose uptake as readouts of insulin response in Hepa and L6 myotubes expressing wild-type and GIV-deficient mice. The potential of GIV-GEF to serve as a therapeutic target in the treatment of IR was explored using cell-permeable, Tat-fused GIV peptides to manipulate insulin sensitivity directly in a dose-dependent manner.

**Summary of Results:** Depletion of GIV, expression of GEF-deficient (F1685A) or phosphomimicking (S1689D) substrates for PKCθ mutants dramatically inhibited PI3K-Akt activation, efficient GLUT4 translocation to the PM and glucose uptake, demonstrating that GIV enhances insulin response via its GEF function and that its phosphoinhibition by PKCθ triggers IR. GIV directly binds and colocalizes with ligand-activated InsR at the PM, and enhances recruitment and activation of IRS1 and PI3K. GIV associates with GLUT4-containing vesicles via exocyst complexes, and modulates activation of RabGAPs that regulate GLUT4 exocytosis. The percentage of beta-cells positive for nuclear CHOP increased 3.6 fold in UCHL1+/-, hIAPP-Tg mice revealed a 1.6 fold increase in the number of autophagosomes (p<0.001 vs hIAPP-Tg mice) and for p62, a ubiquitin-binding protein. The percentage of beta-cells positive for nuclear C/EBP homologous protein was evaluated by confocal microscopy. The potential of GIV-GEF to serve as a therapeutic target in the treatment of IR was explored using cell-permeable, Tat-fused GIV peptides to manipulate insulin sensitivity directly in a dose-dependent manner.

**Summary of Results:** Depletion of GIV, expression of GEF-deficient (F1685A) or phosphomimicking (S1689D) substrates for PKCθ mutants dramatically inhibited PI3K-Akt activation, efficient GLUT4 translocation to the PM and glucose uptake, demonstrating that GIV enhances insulin response via its GEF function and that its phosphoinhibition by PKCθ triggers IR. GIV directly binds and colocalizes with ligand-activated InsR at the PM, and enhances recruitment and activation of IRS1 and PI3K. GIV associates with GLUT4-containing vesicles via exocyst complexes, and modulates activation of RabGAPs that regulate GLUT4 exocytosis.

**Conclusions:** We conclude that GIV is a critical regulator of insulin sensitivity and its inhibition by PKCθ as a major trigger for IR. GIV’s phosphomodifications could serve as a marker for IR and its GEF motif could serve as a therapeutic target to combat IR.

12

**UCHL1 IS REQUIRED FOR PANCREATIC BETA-CELL SURVIVAL UNDER STRESS CONDITIONS ASSOCIATED WITH PROTEOTOXICITY**

Johansen DO, Costes S, Garlo T, Rivera J, Butler P. UCLA DGSOM, Los Angeles, CA.

**Purpose of Study:** Type 2 diabetes is characterized by a deficit in beta-cell mass due to beta-cell apoptosis induced, in part, by toxic forms of misfolded islet amyloid polypeptide (IAPP). We recently reported that increased expression of human-IAPP disrupts the ubiquitin/proteasome system in beta-cells of individuals with diabetes, as demonstrated by the accumulation of polyubiquitinated proteins due to the deactivation of adaptor proteins that bind activators of autophagy degradation. This study reveals a previously unrecognized role of UCHL1 in the regulation of autophagy and ER quality control in beta-cells exposed to misfolded hIAPP.

**Methods Used:** Mouse genetics to elucidate the synergistic effect of UCHL1 deficiency with excess hIAPP in diabetes exacerbates ER stress and autophagy defects in this model.

**Summary of Results:** Depletion of autophagosome number, and for p62, a ubiquitin-binding protein. The percentage of beta-cells positive for nuclear CHOP increased 3.6 fold in UCHL1+/-, hIAPP-Tg mice revealed a 1.6 fold increase in the number of autophagosomes (p<0.001 vs hIAPP-Tg mice) and for p62, a ubiquitin-binding protein. The percentage of beta-cells positive for nuclear C/EBP homologous protein was evaluated by confocal microscopy. The potential of GIV-GEF to serve as a therapeutic target in the treatment of IR was explored using cell-permeable, Tat-fused GIV peptides to manipulate insulin sensitivity directly in a dose-dependent manner.

**Conclusions:** UCHL1 deficiency exacerbated hIAPP-induced beta-cell death caused, in part, by an increase in ER stress and an amplified alteration of autophagy degradation. This study reveals a previously unrecognized role for UCHL1 in the regulation of autophagy and ER quality control in beta-cells exposed to misfolded hIAPP.

13

**ANGIOTENSIN-(1-7) PROMOTES GLUCOSE-STIMULATED INSULIN SECRETION IN MOUSE ISLETS**

Griesbach R, Barrow B, Znika S. University of Washington School of Medicine, Seattle, WA.

**Purpose of Study:** Angiotensin-(1-7) (Ang(1-7)), a product of the renin-angiotensin system, increases first-phase insulin secretion in diabetic rats. Ang(1-7) is cleared into Ang(1-4) by nephrilysin, a widely expressed peptidase present in islets. However, it remains unknown whether Ang(1-7) per se or its cleaved product(s) contributes to this beneficial effect on beta-cell function. Thus, we sought to determine how the peptidase activity of nephrilysin on Ang(1-7) affects the ability of Ang(1-7) to promote glucose-stimulated insulin secretion (GSIS) in mouse islets.

**Methods Used:** C57BL/6.NEP⁺/⁻ and C57BL/6.NEP⁻/⁻ (nephrilysin deficient) mouse islets (n=6/group) were cultured for 48 hours in Ang(1-7) (10⁻⁹ M, 10⁻⁷ M, or 10⁻⁵ M) or control (no Ang(1-7)). Then, insulin secretion in response to 2.8 mM (basal) and 20 mM (GSIS) glucose, and insulin content were measured.

**Summary of Results:** Ang(1-7) did not alter basal insulin secretion from islets of either genotype, but in C57BL/6.NEP⁺/⁻ islets it increased GSIS compared to control (Table; p<0.05 by Kruskal-Wallis test). In contrast, in C57BL/6. NEP⁻/⁻ islets, GSIS decreased with increasing doses of Ang(1-7) (p<0.05). Insulin content did not differ between Ang(1-7)-treated and control islets for both genotypes, indicating no effect of Ang(1-7) on insulin production. Conclusions: Ang(1-7) impairs GSIS in the absence of nephrilysin while promoting it when nephrilysin is present. Thus, we conclude that a cleavage product of nephrilysin rather than Ang(1-7) per se is responsible for Ang(1-7)’s beneficial effect on beta-cell secretory function.

14

**IMPAIRED MITOCHONDRIAL DYNAMICS IN DIABETIC VASCULATURE**

Geary K¹,², Keller A¹,², Knaub L¹,², Reusch J¹,². University of Colorado, Aurora, CO and Denver VA Medical Center, Denver, CO.

**Purpose of Study:** Mitochondrial dysfunction in diabetes (DM) may contribute to accelerated atherosclerosis by increasing smooth muscle cell (SMC) proliferation and impairing vasoreactivity. As vital organelles for optimal cellular functioning, mitochondria necessitate a tightly regulated interplay of fission and fusion. We hypothesized that DM causes disequilibrium of mitochondrial fission and fusion leading to dysfunctional mitochondria. We postulated that the abnormal balance of fission and fusion is driven by mitochondrial membrane potential (Ψm) hyperpolarization and impaired transition pore (MTP) opening.

Griesbach R, Barrow B, Znika S. University of Washington School of Medicine, Seattle, WA.

**Purpose of Study:** Angiotensin-(1-7) (Ang(1-7)), a product of the renin-angiotensin system, increases first-phase insulin secretion in diabetic rats. Ang(1-7) is cleared into Ang(1-4) by nephrilysin, a widely expressed peptidase present in islets. However, it remains unknown whether Ang(1-7) per se or its cleaved product(s) contributes to this beneficial effect on beta-cell function. Thus, we sought to determine how the peptidase activity of nephrilysin on Ang(1-7) affects the ability of Ang(1-7) to promote glucose-stimulated insulin secretion (GSIS) in mouse islets.

**Methods Used:** C57BL/6.NEP⁺/⁻ and C57BL/6.NEP⁻/⁻ (nephrilysin deficient) mouse islets (n=6/group) were cultured for 48 hours in Ang(1-7) (10⁻⁹ M, 10⁻⁷ M, or 10⁻⁵ M) or control (no Ang(1-7)). Then, insulin secretion in response to 2.8 mM (basal) and 20 mM (GSIS) glucose, and insulin content were measured.

**Summary of Results:** Ang(1-7) did not alter basal insulin secretion from islets of either genotype, but in C57BL/6.NEP⁺/⁻ islets it increased GSIS compared to control (Table; p<0.05 by Kruskal-Wallis test). In contrast, in C57BL/6. NEP⁻/⁻ islets, GSIS decreased with increasing doses of Ang(1-7) (p<0.05). Insulin content did not differ between Ang(1-7)-treated and control islets for both genotypes, indicating no effect of Ang(1-7) on insulin production. Conclusions: Ang(1-7) impairs GSIS in the absence of nephrilysin while promoting it when nephrilysin is present. Thus, we conclude that a cleavage product of nephrilysin rather than Ang(1-7) per se is responsible for Ang(1-7)’s beneficial effect on beta-cell secretory function.

14

**IMPAIRED MITOCHONDRIAL DYNAMICS IN DIABETIC VASCULATURE**

Geary K¹,², Keller A¹,², Knaub L¹,², Reusch J¹,². University of Colorado, Aurora, CO and Denver VA Medical Center, Denver, CO.

**Purpose of Study:** Mitochondrial dysfunction in diabetes (DM) may contribute to accelerated atherosclerosis by increasing smooth muscle cell (SMC) proliferation and impairing vasoreactivity. As vital organelles for optimal cellular functioning, mitochondria necessitate a tightly regulated interplay of fission and fusion. We hypothesized that DM causes disequilibrium of mitochondrial fission and fusion leading to dysfunctional mitochondria. We postulated that the abnormal balance of fission and fusion is driven by mitochondrial membrane potential (Ψm) hyperpolarization and impaired transition pore (MTP) opening.
Methods Used: We subjected primary SMC from a rat model of DM (Goto Kakizaki-GK) and control (Wistar-W) to metabolic stress. SMC were incubated in 5 mM glucose and exposed to 25 mM glucose (high glucose-HG) for 1, 4, or 24 hours. Fission (Fis-1, Drp-1) and fusion (Opa-1, Mfn-1, Mfn-2) proteins were assessed by Western blot. Flow cytometry was used to assess mitochondrial content (mitoTracker) and ROS (mitoSox). We then measured \( \Psi m \) (JC-1) and MTP opening.

Summary of Results: Initial experiments indicated that primary GK SMC exhibit an abnormal vascular phenotype of decreased mitochondrial protein (Mito-complex) and respiration (OROBOROS O2K) with increased ROS production (Amplex Red). W SMC exposed to HG demonstrated an increase in Mfn-1 (62%) and DRP1 (40%) at 4 hours compared to baseline, suggesting a coupled fusion and fission response. GK SMC demonstrated discordant changes in fission and fusion with decreased Opa-1 (29%) and MFN1 (71%) but increased Fis-1 (30%) at 4 hrs. In addition, Fis-1 significantly decreased at 24 hours (p = 0.0087) suggesting a failed capacity to accen-tuated fission levels when metabolically stressed. In contrast to W SMC exhibiting depolarized \( \Psi m \) and enhanced MTP opening in the face of HG stress, GK mitochondria became hyperpolarized, precluding MTP opening.

Conclusions: GK SMC exhibit an abnormal mitochondrial phenotype of decreased respiration, increased ROS, and impaired dynamics. In response to HG stress, fusion and fission are enhanced in W but GK lack the capacity for sustained adaptation. Hyperpolarized \( \Psi m \) and impaired MTP opening pose a significant and plausible mechanism driving the abnormal fission and fusion processes in DM vasculature.

Health Care Research I: Measuring Health Outcomes
Concurrent Session
12:30 PM
Thursday, January 23, 2014
15
PRONTO TRAINING IMPROVES DELIVERY CARE IN RURAL GUATEMALA
Walton A1, Holme F2, Walker D2,3,1 University of Washington, Seattle, WA; 2University of Washington, Seattle, WA and 3University of Washington, Seattle, WA.

Purpose of Study: Guatemala has the second highest maternal mortality rate in Latin America (120 deaths per 100,000 live births), with women in rural and indigenous communities disproportionately affected. Meeting the United Nations’ Millennium Development Goals 4 and 5 to reduce child mortality and improve maternal health remains a distant hope. In 2012, 217 skilled birth attendants in 15 randomly selected intervention clinics (matched with 15 controls) were provided PRONTO training, a low-tech simulation-based program for effective management of obstetric and peri-natal emergencies. We aim to evaluate the impact of PRONTO training in improving delivery care.

Methods Used: Two investigators observed births in intervention and control sites, completing a standardized data collection form for each birth. The Guatemala Ministry of Health and UW IRB approved this study.

Summary of Results: We observed 25 births in 8 intervention clinics and 17 births in 6 control clinics, with no difference in mean patient age, gesta-tional age, or obstetric history.

Intervention sites employed undesirable practices, e.g., episiotomies (8%) and uterine pressure (28%), less than controls (29% and 38%, respec-tively). Intervention sites also utilized certain evidence-based birth practices more often: immediate contact between neonate and mother (Intervention: 96%, Control: 75%), drying off neonate immediately (Intervention: 88%, Control: 50%), and suprapubic countertraction (Intervention: 96%, Control: 69%).

Effective teamwork and communication strategies, including checkbacks (Intervention: 48%, Control: 13%), SBAR (Intervention: 83%, Control: 33%), and thinking out loud (Intervention: 84%, Control: 53%), were observed more often in intervention sites. Team leaders in control sites tended to be more authoritarian (Intervention: 13%, Control: 24%).

Conclusions: Preliminary evidence shows that PRONTO training increases teamwork, patient-centered care, and evidence-based practices. Further analysis is pending to determine statistical significance and will contribute to a larger intervention to decrease maternal and infant mortality in Guatemala.

16
THE EFFECTS OF PRIOR INJURY AND SURGERY ON RECRUITMENT OF NCAA DIVISION I ATHLETES: A SURVEY OF ATHLETIC DIRECTORS
Mehta PA, Hane SL. UCLA School of Medicine, Los Angeles, CA.

Purpose of Study: An ongoing study has shown that athletes who are recruited with prior injuries have an increased likelihood of further injury during their college career. The current study aims to better understand how prior injury history influences the recruiting process of intercollegiate athletes.

Methods Used: A questionnaire designed to ascertain recruitment data was developed using the online research-secure REDCap software. An invitation to participate was e-mailed to 436 Division I athletic directors.

Summary of Results: In total, 45 survey responses have been collected. Of the 45 respondents, 30 belong to institutions that require athletes to have health insurance to cover possible athletic injuries. Moreover, at 38 institutions all recruits undergo physical examination by a university physician; 4 institutions indicated that only athletes of certain sports are required to under-go physical exam during the recruitment process.
Conclusions: At the majority of institutions, injury history is collected and used as part of the evaluation process of incoming athletes. Considering the increased likelihood of injury recurrence, there is value in requiring that all recruits undergo a recruitment physical exam in addition to requiring that all athletes have health insurance.

HOSPITAL-BASED OCULAR EMERGENCIES: EPIDEMIOLOGY, TREATMENT, AND VISUAL OUTCOMES
Cheung C1, Rogers-Martel M2, Golas L3, Chepurny A2, Martel J2, Martel J2 1

Method Used: Records of 1,027 patients with ocular emergencies seen between July 2007 and November 2010 at three community hospitals emergency departments and two hospitals with level II trauma centers were retrospectively examined. Unpaired t-Test and Pearson Chi-square Test were used to determine statistical significance.

Summary of Results: The incidence of patients requiring ophthalmic intervention was 77.19 per 100,000 in the community hospitals and 208.94 per 100,000 in the trauma centers. Rates of ocular emergencies were higher in middle aged, Caucasian males. There were no statistically significant differences between the visual outcomes of those treated in community hospital emergency departments and trauma centers despite the severity of ocular cases treated in trauma centers. Orbital fractures were found in 86% of all orbital contusion cases in trauma centers. 66.7% of fall patients with open globe diagnoses resulted in legal blindness.

Conclusions: The middle-aged, Caucasian male demographic is more vulnerable to ocular injuries caused mainly by motor vehicle accidents. The ability of trauma centers to provide comparable increases in vision outcomes, despite treating more severe ocular emergencies, demonstrates the effectiveness of trauma centers. Patients diagnosed with orbital contusions or who are victims of fall injuries deserve careful evaluation, as they are more likely to suffer more severe sight-threatening injuries.

EFFECTS OF ENGAGEMENT SURVEY ON TYPE II DIABETES OUTCOMES
Solomon VE, Barnes E, Ochoa C. Western University-COMP, Pomona, CA.

Methods Used: 30 patients from the Western Diabetes Institute at Western University of Health Sciences were enrolled in this 3-arm randomized protocol. All patients received standard of care for TIDDM, a second arm also received basic ADA-type dietary advice, and a third arm received the same dietary advice and an 8-item engagement survey about knowledge of TIDDM, complications, risk behaviors, and available health resources. The primary endpoints of the study were: HbA1c, blood pressure, total cholesterol and BMI with follow-up at 3 months. Six and 9 month data are not yet available. The data were analyzed by repeated measures ANOVA and Kruskal-Wallis One Way ANOVA.

Summary of Results: The survey plus dietary advice(1), dietary advice alone(2), and control(3) groups had the following mean HbA1c/sd/N values at baseline: 9.5/0.86/9(1), 8.8/1.5/7(2), 10.0/1.6/8(3). Three-month HbA1c data were 9.1/1.2/9 (1), 8.6/2.7/7(2), 8.9/1.9/8(3). Baseline and 3 month systolic BP were 134.9/17.9/9(1), 130.6/21.3/9(2), 122.5/24.8/8(3) and 132.0/16.3/9(1), 128.4/19.4/8(2), 119.5/19.3/8(3). Baseline and 3 month cholesterol data were 155.0/11.3/2(1), 146.5/4.5/3(2), 155.0/4.3/3 and 171.0/25.2/3(1), 158.8/32.5/2(2), 185.9/35.6/7(3). Baseline and 3 month BMI data were 41.9/9/8(1), 37.7/9/8(2), 34.7/8/8(3) and 42.4/9.4/8 (1), 37.9/10.0/8(2), 34.6/8/8(3). No statistically significant differences were found with repeated measures ANOVA. Using K-W One Way ANOVA, Arm 3 had the highest ranks and Arm 1 the lowest with a P-value of 0.08.

Conclusions: There appears to be no evidence supporting a benefit to giving focused dietary information or a brief survey on improving TIDDM outcomes. In fact, a trend showed the control had the best TIDDM outcomes and the survey plus dietary advice had the least impact. However, our study was not powered to identify such changes. The study also had a small N, high attrition rate, and lack of complete lab panels in those patients remaining in the study.

ABERRANT BEHAVIORS AMONG PATIENTS ON CHRONIC OPIOID THERAPY ARE MOST COMMON AT HIGHER DOSES
Thompson EC, Rosenblatt R, Grande L. University of Washinton School of Medicine, Seattle, WA.

Purpose of Study: The Centers for Disease Control and Prevention has declared an epidemic in the United States of overdose deaths from opioid pain medications. Studies have shown that patients on high opioid doses
are at increased risk of overdose death, but it is unclear whether these patients exhibit more behaviors indicative of misuse or addiction that can be identified by provider monitoring. The purpose of this study is to determine whether patients on high opioid doses exhibit more aberrant behaviors than those on lower doses.

Methods Used: 234 patients in a mid-sized primary care community-based practice receiving six or more opioid prescriptions over a two-year period were studied. Dose information and instances of aberrant behaviors were extracted from an electronic medical record and entered into a de-identified database. The average dose of each patient was categorized as low (<40 morphine equivalent mg/day (MED)), medium (40-119 MED), or high (120 MED and above). An association between opioid dose level and frequency of aberrant behaviors was analyzed using a chi-square analysis.

Summary of Results: 50% of patients on high dose opioids (23/46) exhibited three or more aberrant behaviors vs. 34.5% of those on low dose opioids (49/142), (p<.0378). In contrast, only 11% vs. 28% of high and low dose patients, respectively, exhibited no aberrant behaviors. There was no statistical difference between the low- and medium-dose groups (p=.207), though there was an upward trend in aberrant behavior across dose level categories. The most common aberrant behaviors overall were missed appointments (47%), multiple early refill requests (46%), not taking as prescribed (31%), rude/angry behavior (21%), lost/stolen medicine (19%) and emergency room pain visits (19%).

Conclusions: In a mid-sized primary care community-based practice, patients on high opioid doses exhibited significantly higher rates of behaviors that may indicate misuse or addiction. This study provides evidence in support of current guidelines that recommend against prescription of opioid doses equivalent to 120 mg morphine or more. Downward tapering or discontinuation of current guidelines that recommend against prescription of opioid doses that may indicate misuse or addiction. This study provides evidence in support of current guidelines that recommend against prescription of opioid doses equivalent to 120 mg morphine or more. Downward tapering or discontinuation of opioids, at least for patients who show signs of misuse or addiction, could result in a reduction in overdose deaths.

Summary of Results: nNIF was isolated from cord blood of preterm and term neonates. The 29 amino acid peptide shares significant homology with the nNRP, CRISPP and both were synthesized and shown to inhibit NET formation by stimulated human PMNs in vitro (1 nM, 1 hour pre-incubation). A scrambled peptide control was used for all experiments. We also demonstrated that CRISPP binds and inactivates NE. Both CRISPP and the NE inhibitor Simvastatin (200 nM) inhibited NET formation equally.

Conclusions: nNIF is a NET-inhibitory peptide isolated from cord blood. The nNRP CRISPP inhibits NET formation through inhibition of NE activity in human PMNs. These results suggest potential efficacy of nNIF and CRISPP in ameliorating sequelae of dysregulated NET formation leading to inflammatory tissue damage.
**Conclusions:** Studies of iBALT have associated serum RA-related Abs, and these associations were with CCP2 (Table). RA-related Abs, and 15 of 39 had iBALT present. Prevalence of iBALT and GCs was associated with serum RA-related Abs, and the strongest association was with CCP2 (Table). Conclusions: iBALT is associated with serum RA-related Abs, and these findings, in combination with published data, suggest that specific immunologic changes in the lung leading to iBALT formation and active GCs may serve as a site of Ab generation in RA.

<table>
<thead>
<tr>
<th>iBALT present (Ne=23)</th>
<th>iBALT absent (Ne=16)</th>
<th>P-value</th>
<th>GC present (Ne=7)</th>
<th>GC absent (Ne=16)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCP2 7</td>
<td>0</td>
<td>&lt;0.01</td>
<td>4</td>
<td>6</td>
<td>0.03</td>
</tr>
<tr>
<td>CCP3.1 8</td>
<td>2</td>
<td>0.03</td>
<td>6</td>
<td>0.03</td>
<td>0.04</td>
</tr>
<tr>
<td>CCP2 and/or CCP3.1 9</td>
<td>2</td>
<td>0.07</td>
<td>5</td>
<td>6</td>
<td>0.01</td>
</tr>
<tr>
<td>RF-1gA 8</td>
<td>2</td>
<td>0.03</td>
<td>7</td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>RF-1gM 7</td>
<td>2</td>
<td>0.07</td>
<td>7</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>RF-1gG 7</td>
<td>5</td>
<td>0.51</td>
<td>9</td>
<td>0.34</td>
<td></td>
</tr>
<tr>
<td>Any RF 12</td>
<td>6</td>
<td>0.07</td>
<td>13</td>
<td>0.09</td>
<td></td>
</tr>
</tbody>
</table>

**OUTCOMES ASSOCIATED WITH SUSTAINED LOW AQUEOUS HUMOR PROTEIN LEVEL IN CHILDREN WITH CHRONIC ANTERIOR UVEITIS**

Danesh JN, Boeni C, Yu F, Holland GN. Ocular Inflammatory Disease Center, Jules Stein Eye Institute and the Department of Ophthalmology, David Geffen School of Medicine at UCLA, Los Angeles, CA.

**Purpose of Study:** An elevated aqueous humor protein (“flare”) level, as measured by laser flare photometry, is a known risk factor for vision-limiting complications in children with chronic anterior uveitis (CAU). A drop in flare during follow-up is protective against adverse events. We determined specific outcomes for children with CAU who present with no complications and have sustained low flare values.

**Methods Used:** We performed a retrospective chart review of 115 children (205 eyes) with CAU seen by one investigator (GNH) during the period 1993-2006. Demographics, disease characteristics and treatment details were collected. Low flare was defined as <20pu/msec.

**Summary of Results:** Among 35 eyes (25 children) with no complications at presentation and low flare throughout follow-up, 6 developed mild cataracts (none resulting in vision loss) and 16 had elevated intraocular pressure (IOP) at least once (none resulting in glaucoma). No eye developed any of 7 other complications seen in the entire CAU population. Nearly all eyes that developed complications among the low flare subgroup were receiving topical corticosteroid treatment, which can cause cataracts and increased IOP.

**Conclusions:** Children with CAU who present without complications and whose flare values stay low during follow-up are at low risk for severe complications, even when inflammatory cells are present. Overly aggressive corticosteroid use in this subpopulation may pose a greater risk to vision than the disease itself.
THYMIC STROMAL LYMPHOPOIETIN (TSLP) IS ELEVATED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS OR RHEUMATOID ARTHRITIS

Cabling MG1, Weldon A2, Benitez A2, Su R2, Sachdeva S1, Colburn K1, Moldovan I1,2, Payne K2, 1Loma Linda University Medical Center; Loma Linda, CA; 2Loma Linda University, Loma Linda, CA and 3Beaver Medical Group, Redlands, CA.

Purpose of Study: Thymic stromal lymphopoietin (TSLP) is an IL-7-like cytokine produced by epithelial and stromal cells that is important in T and B cell development. TSLP has been associated with the pathogenesis of airway diseases such as asthma and is thought to promote the progression of cancer. Recent studies suggest that TSLP plays a role in inflammatory arthritis by activating dendritic cells, leading to the activation and differentiation of naïve T-cells into Th help 2 (Th2) cells and the production of inflammatory cytokines such as TNF-α. The aim of this study is to evaluate plasma and synovial fluid (SF) levels of TSLP in patients with Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA). Information from these studies will provide insights into the role of TSLP in these inflammatory B-cell mediated diseases.

Methods Used: Peripheral blood and SF were collected from RA and SLE patients, as well as from patients with non-inflammatory osteoarthit, OA) as controls. All patients were receiving treatment during the study. All samples were collected through an IRB-approved protocol. The TSLP levels in plasma and SF from patient samples were measured by ELISA using the Human TSLP ELISA MAX kit (Bioslegend). TSLP levels between patient groups were compared using the Mann and Whitney one-tailed U test. A P value of less than 0.05 was considered significant.

Summary of Results: TSLP levels in plasma from SLE patients were elevated as compared to OA (p<0.0276) and RA (p<0.007) patients. A comparison of SF showed higher levels of TSLP in RA as compared to OA patients (p<0.0101).

Conclusions: When plasma was compared, TSLP levels in SLE patients were significantly higher than in RA patients or in OA patients, which served as controls. This is the first study to show elevated TSLP levels in SLE patients. When SF was compared, RA patients had higher levels of TSLP than OA controls, which is consistent with published reports. These data further implicate TSLP as a contributor to inflammation in B-cell mediated autoimmune diseases. Ongoing studies are focused on the role of TSLP in inflammation and correlation of TSLP with disease severity and treatment.
of how inflammatory stress mediates pro-inflammatory and vasoactive gene expression within the newborn lung may lead to novel therapies aimed to attenuate or prevent PPHN associated with chorioamnionitis.

31
HEPATOCYTE GROWTH FACTOR STIMULATES FETAL SHEEPALEVOLEAR TYPE II CELL AND ENDOTHELIAL CELL GROWTH AND IMPROVES LUNG STRUCTURE IN EXPERIMENTAL BRONCHOPULMONARY DYSPLASIA
Metoxen A1,2, Seedorf G2, Abman S2, 1University of Colorado School of Medicine, Aurora, CO and 2University of Colorado, Aurora, CO.
Purpose of Study: Decreased vascular endothelial growth factor (VEGF) signaling contributes to impaired lung structure in bronchopulmonary dysplasia (BPD). Although VEGF stimulates hepatocyte growth factor (HGF) production, the effects of HGF on the fetal lung are uncertain. To determine the potential role of HGF in BPD, we studied the direct effects of HGF on fetal lung alveolar type II cells (AT2C) and endothelial cells (EC), and whether HGF treatment could restore lung growth after VEGF inhibition in vivo.
Methods Used: AT2C and EC were harvested from late-gestation fetal sheep lungs and characterized by immunofluorescence and morphotype. Proliferation assays were performed in the presence or absence of HGF (25 ng/mL) over 4 days. Tube formation with or without HGF was studied in EC by standard methods over 18 hours. Newborn rat pups (<1 day old) were treated with a single subcutaneous injection of SU5416, a VEGF receptor inhibitor, or vehicle control. Lungs were harvested at 2 weeks and fixed with paraformaldehyde. Radial alveolar counts (RAC) were measured by standard methods.
Summary of Results: HGF enhanced AT2C growth by 50% (p<0.05), and also stimulated EC growth and tube formation by 40% (p<0.001) and 42% (p<0.01), respectively. These effects of HGF on ECs were inhibited by JNJ-38877605, a selective c-Met antagonist. SU5416 decreased RAC by 30% (p<0.05), which was attenuated by HGF treatment in vivo.
Conclusions: We found that HGF stimulates fetal AT2C and EC proliferation and EC tube formation. In addition, HGF treatment improved lung structure after VEGF inhibition in vivo. These data suggest that HGF treatment may improve lung structure in experimental BPD.

32
TRANSGENERATIONAL MOLECULAR AND PHENOTYPIC CHARACTERIZATION OF THE PERINATAL NICOTINE EXPOSURE-INDUCED EFFECT ON BONE MARROW-DERIVED MESENCHYMAL STEM
Liu J, Husain S, Sakurai R, Rehan V. LABIOMED, Torrance, CA.
Purpose of Study: We have recently shown that perinatal nicotine (NIC) exposure drives the differentiation of alveolar lipofibroblasts (LIFs) to myofibroblasts (MYFs). Under appropriate conditions, bone marrow-derived mesenchymal stem cells (BMMSCs) can differentiate into a wide variety of cell-types, and have been shown to be important for lung injury/repair. However, whether perinatal NIC exposure blocks offspring BMMSCs' lipogenic differentiation and whether it drives these cells towards a MYF phenotype are not known. Furthermore, whether these effects are limited only to the exposed offspring or these could be transmitted transgenerationally is not known. The objective of this study is the transgenerational molecular and phenotypic characterization of perinatally NIC exposed BMMSCs.
Methods Used: Time-mated Sprague Dawley rat dams received either placebo or NIC (1 mg/kg, sc) in 100 μl volumes once daily from e6 until term. Pups delivered spontaneously at term and breast fed ad libitum. Dams continued to get treatment according to their assigned groups up to 3 weeks after delivery; however, at delivery, pups were divided into two groups, one group received placebo and the other group received RGZ (3 mg/kg, ip) in 50 μl volumes once daily from PND1 to PND21. At PND21 pulmonary function (lung resistance, compliance, and tracheal contractility) and the expression of mesenchymal markers of airway contractility (α-SMA, Calponin, Fibronectin, Collagen I & III) were determined by immunoblotting and immunostaining for evidence of reversibility of perinatal NIC exposure-induced lung injury.
Summary of Results: Compared to controls, perinatal NIC exposure caused 1) a significant increase in airway resistance and a decrease in airway compliance following methacholine challenge; 2) a significant increase in acetylcholine-induced tracheal constriction; and 3) increased pulmonary and tracheal expression of the mesenchymal markers of contractility. Treatment with RGZ, starting on PND1, reversed all of the NIC-induced molecular and functional pulmonary effects, virtually, normalizing the pulmonary phenotype of the treated animals.
Conclusions: Functional and molecular alterations in upper and lower airways in a rodent model of perinatal nicotine exposure were reversed by administration of PPARγ agonist RGZ. We speculate that perinatal smoke exposure-induced asthma in offspring can be effectively reversed by PPARγ agonists. Disclosure: Supported by NIH HD51857, HD71731.

33
REVERSAL OF PERINATAL NICOTINE EXPOSURE-INDUCED ASTHMA IN RAT OFFSPRING
Liu J Rehan V. LABIOMED, Torrance, CA.
Purpose of Study: Background: We have previously suggested that down-regulation of homeostatic mesenchymal PPARγ signaling following perinatal nicotine (NIC) exposure might be a contributor to offspring asthma and that perinatal NIC exposure-induced asthma can be effectively prevented by concurrent administration of PPARγ agonist rosiglitazone (RGZ). However, whether perinatal NIC exposure-induced asthma can be reversed is not known.
Hypothesis: The effects of perinatal NIC exposure on offspring pulmonary function and mesenchymal markers of airway contractility will be reversed by PPARγ agonist RGZ.
Methods Used: Pair-fed pregnant rat dams received either placebo or NIC (1 mg/kg, sc) in 100 μl volumes once daily from e6 until term. Pups delivered spontaneously at term and breast fed ad libitum. Dams continued to get treatment according to their assigned groups up to 3 weeks after delivery; however, at delivery, pups were divided into two groups, one group received placebo and the other group received RGZ (3 mg/kg, ip) in 50 μl volumes once daily from PND1 to PND21. At PND21 pulmonary function (lung resistance, compliance, and tracheal contractility) will be reversed by PPARγ agonist RGZ.
Summary of Results: Compared to controls, perinatal NIC exposure caused 1) a significant increase in airway resistance and a decrease in airway compliance following methacholine challenge; 2) a significant increase in acetylcholine-induced tracheal constriction; and 3) increased pulmonary and tracheal expression of the mesenchymal markers of contractility. Treatment with RGZ, starting on PND1, reversed all of the NIC-induced molecular and functional pulmonary effects, virtually, normalizing the pulmonary phenotype of the treated animals.
Conclusions: Functional and molecular alterations in upper and lower airways in a rodent model of perinatal nicotine exposure were reversed by administration of PPARγ agonist RGZ. We speculate that perinatal smoke exposure-induced asthma in offspring can be effectively reversed by PPARγ agonists. Disclosure: Supported by NIH HD51857, HD71731.

34
miRNA-MEDIATED ADIPOGENIC DIFFERENTIATION OF BONE MARROW-DERIVED MESENCHYMAL STEM CELLS OBTAINED FOLLOWING NUTRITIONAL STRESS DURING PREGNANCY
Antony SF, Gong M, Sakurai R, Rehan V. LABIOMED, Torrance, CA.
Purpose of Study: Childhood obesity is a major health problem worldwide, resulting in huge health care costs, related to marked detrimental effects on the quality of life not only during childhood, but also during later life. The molecular mechanisms underlying childhood obesity remain incompletely understood, precluding any reliable predictive biomarkers. Since maternal food restriction (MFR) during pregnancy is known to be associated with later obesity and metabolic syndrome, we used this model to determine
mechanistic insights and novel predictive/therapeutic biomarkers of childhood obesity.

**Methods Used:** Rat dams, 10 days into pregnancy, received either ad lib feeds (controls) or only 50% of standardized laboratory diet (MFR group). After delivery, both groups were provided ad lib diets. At postnatal day 21, bone marrow-derived mesenchymal stem cells (BMDMSCs) were isolated and studied to determine their adiogenic and myogenic potentials using morphologic, molecular, and functional characteristics (Oil Red O staining, Western blotting, q-RT PCR, and miR profile).

**Summary of Results:** The adiogenic proteins PPARγ, C/EBPα, and lipoprotein lipase increased in the MFR compared to the control group (p < 0.05). The mRNA expression of these markers was also up-regulated, with PPARγ and its up-stream regulator Zfp423 showing 9-10-fold increases (p < 0.05). In contrast, Wnt signaling markers such as β-catenin and LEF1 were decreased at both mRNA and protein levels (p < 0.05). These changes were obvious under both basal and adiogenic/myogenic induction conditions. Screening for adipogenesis-related miRNAs confirmed their increased expression in the BMDMSCs from MFR group, with miR-30d, showing a 30-fold increase. Inhibition of the miR-30d blocked adipogenesis, while its over-expression stimulated adipogenesis by regulating its target RUNX2.

**Conclusions:** BMDMSCs isolated from rat offspring subjected to nutritional stress during pregnancy show markedly enhanced adiogenic molecular (high expression miR-30d, which targets the transcription factor RUNX2), and functional profiles, suggesting a likely link between intrauterine nutritional stress and later offspring obesity, providing novel predictive and therapeutic targets for childhood obesity. Supported by NIH HD51857, HD71731.

**Neonatology – General I**

**Concurrent Session**

12:30 PM

Thursday, January 23, 2014

**35 IMPACT OF A NOVEL DECISION SUPPORT TOOL ON ADHERENCE TO NEONATAL RESUSCITATION PROGRAM ALGORITHM**

Fuerch J1, Yamada NK1, Coelho P2, Vale B2, Halamek LP1. 1Lucile Packard Children’s Hospital at Stanford, Palo Alto, CA and 2MedicalCue Inc., Mountain View, CA.

**Purpose of Study:** Studies have shown that healthcare professionals have a 16-55% error rate in adherence to the Neonatal Resuscitation Program (NRP) algorithm. Errors in resuscitation are the largest cause of preventable neonatal death. We evaluated a novel decision support tool that provides auditory and visual cues to guide implementation of the NRP algorithm via a tablet mounted at the bedside during resuscitation.

**Objective:** Evaluate adherence to the NRP algorithm from memory (control) as compared to prompts from a decision support tool (intervention) during simulated neonatal resuscitation.

**Methods Used:** Sixty-five healthcare professionals (physicians, nurse practitioners, obstetrical/neonatal nurses) with a current NRP card were randomized to control or intervention group and performed 3 simulated neonatal resuscitations. Subject adherence to NRP algorithm guidelines regarding initiation/discontinuation of positive pressure ventilation (PPV) & chest compressions (CC) was scored and then analyzed using the Mann-Whitney U Test.

**Summary of Results:** PPV was performed correctly 57-79% of the time in the control group vs. 94-99% in the intervention group across all 3 scenarios (p < 0.001). CC were performed correctly 71-79% of the time in the control group vs. 92-95% in the intervention group in the 2 scenarios in which they were indicated (p < 0.001). PPV & CC were both performed correctly in 54-59% of the time in the control group vs. 86-94% in the intervention group (p < 0.001). (Figure 1)

**Conclusions:** Healthcare professionals demonstrated significantly improved adherence to the NRP algorithm when utilizing a decision support tool compared to use of memory alone.

**36 IMPROVING THERMOREGULATION FOR VERY LOW BIRTH WEIGHT INFANTS AT A LEVEL IV NEONATAL INTENSIVE CARE UNIT**

Thorton K, Voos K, McNellis E. Children’s Mercy Hospital and Clinics, University of Missouri-Kansas City School of Medicine, Kansas City, MO.

**Purpose of Study:** Thermoregulation (TR) is a cornerstone practice in neonatal care. Prevention of hypothermia improves survival of premature, very low birth weight (VLBW) infants. Providing adequate TR is a simple concept, in theory, but can become quite challenging for clinical practice. Unique barriers exist when caring for infants who undergo interfacility transport. The purpose of this project was to identify specific barriers to providing adequate TR for VLBW infants referred to a level IV neonatal intensive care unit (NICU).

**Methods Used:** A root cause analysis was performed to identify barriers to providing adequate TR by analyzing data on VLBW infants who were transported and admitted by Children’s Mercy Hospital (CMH) during a one year period; surveying the CMH transport medical providers, CMH neonatal nursing staff and referring hospital nursing staff; and comparing current TR practices at CMH with evidence-based literature.

**Summary of Results:** Of 78 VLBW infants transported to the CMH NICU from January to December 2010, 42% were hypothermic (<36.5°C) at the referring hospital and 60% were hypothermic on arrival to CMH. Further information was available for 53 infants and, of those, 19% had new or worsening hypothermia after admission. The nursing and transport staff identified a lack of emphasis placed on TR practices during transport and admission as a common barrier to current practice. Current TR practices were not always consistent with published guidelines. Also, infants were often hypothermic at the referring center before the CMH transport team assumed care.

**Conclusions:** Several barriers to adequate TR were identified throughout all aspects of an infant’s NICU hospitalization. With these findings, clinical care policies were modified to include TR practices during delivery, transport, admission, and throughout care until discharge. Education was provided for referring center staff as well as the CMH nursing, physician, and transport staff. A new practice for sterile draping during umbilical line placement was implemented to improve TR during procedures. Plans for continual assessment of TR practices by the CMH transport and NICU staff were implemented.

**37 COLLABORATIVE VS INDIVIDUAL QUALITY IMPROVEMENT FOR DELIVERY ROOM NEONATAL MANAGEMENT**

Lee HC1, Bennett M1, Powers R2, Sharke P3. 1Stanford University, Stanford, CA and 2Good Samaritan Hospital, San Jose, CA.

**Purpose of Study:** To study the optimal method of implementing evidence-based practices for delivery room management by comparing neonatal resuscitation practices and outcomes amongst 3 groups: 1) Collaborative
DH: - participants in an intensive multi-hospital project with regular meetings, expert panel, and data review, 2) NICU QI - single hospitals with access to materials participating in a local project, and 3) Control - hospitals not participating in either project.

Methods Used: The setting was the California Perinatal Quality Care Collaborative. Inclusion criteria: gestational age 22-29 weeks or birth weight < 1501 gms from June 2010-2011. The study period was divided into baseline (June 2011-May 2012), intervention (June 2012-May 2013), and post-intervention (June 2012-2013). The primary outcome was percent of patients with hypothermia (defined as first temperature before 1 hour of age < 36.5°C). Secondary outcomes included respiratory practices in the delivery room. Multivariate logistic regression models accounted for birth weight, sex, maternal age, race, multiple gestation, delivery mode, small for gestational age, and congenital anomalies.

Summary of Results: There were 9,808 infants among 79 NICUs. All 3 groups improved hypothermia rates from the baseline to post-intervention period. The Collaborative QI had the most significant change in hypothermia from 39% to 19%, compared to NICU QI 38% to 30%, and control 42% to 34%. After risk adjustment, the Collaborative QI had twice the decrease in percentage of newborns with hypothermia compared to the other 2 groups. The Collaborative QI had an increase in hypothermia (< 37.9°C) from 6% to 9%, which was not seen in the other groups. The Collaborative QI group had greater decrease in delivery room intubation (53% vs 39% vs NICU QI 43% to 37% vs control 42% to 39%) and surfactant administration (37% vs NICU QI 18% vs 12% vs control 17% to 17%). Infants receiving CPAP increased for all 3 groups: Collaborative QI 57% to 66%, NICU QI 44% to 61%, and control 38% to 49%.

Conclusions: Collaborative QI resulted in larger improvements in delivery room outcomes and processes than individual NICU QI and control. This has implications for planning broad quality improvement projects in the NICU.

38 DETERMINATION OF FETAL RHD STATUS USING FETAL NUCLEIC ACID IN THE MATERNAL CIRCULATION

Nagji SZ, Shower AL, Shariﬁf A, Rossol S, McConoughy S, Ohls RK. UNM School of Medicine, Albuquerque, NM.

Purpose of Study: The discovery of free fetal DNA in plasma of pregnant women has opened a new avenue for non-invasive prenatal diagnosis. In RhD negative women, the detection of the D gene by quantitative PCR in DNA derived from maternal plasma has been used to assist in prenatal management; however a negative result (no D gene detected) must still be evaluated for adequacy of fetal DNA sample. We hypothesized that signiﬁcant epsilon globin gene expression (a component of embryonic hemoglobin) could serve as a positive control for the presence of an adequate fetal sample, thus preventing the unnecessary use of Rhogam in mothers with Rh negative fetuses.

We previously identiﬁed abundant epsilon globin mRNA in fetal blood, liver and marrow. For this study we measured epsilon globin expression in maternal serum (17-34 weeks gestational age), and in serum from healthy, non-pregnant adults.

Methods Used: Total RNA was isolated from maternal serum samples (1734 weeks gestation). RNA isolation was performed using a commercial tri-reagent. Total RNA was measured spectrophotometrically. Quantitative polymerase chain reaction was performed on a 7500 Fast Real-Time PCR System using epsilon globin primers and probe. Quantitative expression of α-actin was used as an internal control to normalize starting quantities of sample RNA.

Summary of Results: Epsilon globin gene expression was identiﬁed in 25 maternal samples evaluated thus far. No signiﬁcant correlation was seen between gestational age and epsilon expression in samples ranging from 17-34 weeks gestation (R=0.3, p=0.18). Epsilon globin gene expression was not identiﬁed in non-pregnant adult samples (n=4).

Conclusions: Epsilon globin gene expression was evident in all maternal samples tested to date, and was not present in non-pregnant adults. We speculate that epsilon globin gene expression may serve as evidence for the presence of fetal RNA, and would therefore serve as a positive control for the adequacy of fetal DNA isolated from maternal plasma.

39 DO CORD BLOOD BILIRUBINS PREDICT THE NEED FOR TREATMENT IN NEONATES AT RISK FOR HYPERBILIRUBINEMIA?

Bradley L1, Walker V2, Roy D2, Grogan T3, Elashoff D3, Calkins K1. 1University of California, Los Angeles, Los Angeles, CA; 2University of California, Los Angeles, Los Angeles, CA and 3University of California, Los Angeles, Los Angeles, CA.

Purpose of Study: Neonates with blood group incompatibility are at high risk for hemolytic disease of the newborn (HDN), requiring phototherapy, longer hospital stays, readmission, and kernicterus. Limited evidence supports use of cord blood bilirubin (CBB) concentrations to predict need for phototherapy. The objective of this study was to determine if a specific CBB concentration predicts the need for phototherapy in a population at high risk for HDN.

Methods Used: This is a single center retrospective case-control study where CBB testing is routinely performed when neonates are born to mothers with blood types O or Rh negative or who have positive antibody screens. Inclusion criteria for the study included ≥ 35 weeks gestation, CBB obtained at birth, and ≥ one serum total bilirubin concentration prior to discharge from the nursery. Cases received phototherapy and controls did not. Cases were matched 1:3 with controls by treating physician and gender.

Summary of Results: Ninety six percent of cases (n=24) and 97% of controls (n=63) were born to mothers with blood type O. There was no difference in hyperbilirubinemia risk factors between the groups. Eight three percent of cases and 60% of controls had positive Coomb’s tests (p=0.2). The mean ±SD CBB for cases was higher than controls (2.4±0.5 vs 1.8±0.4, p<0.001). Cases received a mean of 27±13 hours of phototherapy, and 8% were admitted to the NICU for hyperbilirubinemia. A CBB of 2.3 mg/dL had a 71% sensitivity, 89% positive predictive value, and 90% negative predictive value for assessing the need for phototherapy.

Conclusions: In this study, the mean CBB concentration was significantly higher in neonates who received phototherapy. CBB concentrations may help predict the need for phototherapy in a population at risk for HDN. Prospective studies are recommended.

40 EFFICACY AND SAFETY OF BLUE-GREEN LIGHT FOR PHOTOTHERAPY

Linfield DT, Lin D, Schulz S, Vreman HJ, Wong RJ, Stevenson DK. Stanford University School of Medicine, Stanford, CA.

Purpose of Study: Phototherapy using light with a bandwidth of 430 to 490 nm is the most common treatment for neonatal hyperbilirubinemia. In recent in vitro studies, we found that narrow spectrum blue-green (BG) light-emitting diode (LED) light at 498 nm was the most effective in degrading bilirubin (Vreman et al, EPAS2011: 673, 2011). Using genetically jaundiced, Gunn rat pups, we now evaluated the in vivo efficacy and safety of BG light phototherapy.

Methods Used: 3- to 7-day-old homozygous (j/j) and heterozygous (J/j) Gunn rat pups were placed in chambers supplied with air at 20 mL/min. Control pups were kept in the dark, while the treatment groups were exposed for 2 to 3h to either narrow band blue (450 nm) or BG (498 nm) LEDs normalized to a photon level of 4.2x10^12 moles as measured by an Ocean Optics S2000 Spectrometer. Efficacy was assessed by calculating the rate of bilirubin degradation using transcutaneous bilirubin (TeB) measurements taken with a Minolta/Air-Shields JM-101 Jaundice Meter before and after light exposures. Safety was assessed as fold changes in rates of total body carbon monoxide (VeCO2) and carbon dioxide (VeCO2) excretion, weight loss, and liver lipid peroxidation (LP) during light exposures. After exposure, pups were sacrificed and livers harvested for LP measurements as indexed by tissue CO production using gas chromatography.

Summary of Results: Pups exposed to blue light had a higher, but not statistically significant, rate of bilirubin degradation compared to those exposed to BG light (1.3 vs 1.0 mg/dL/h, respectively). Our comparison of safety parameters between both light sources demonstrated that fold changes in VeCO2, VeCO2, and weight loss from baseline levels were not significantly different between pups exposed to either light. In addition, fold changes
in liver LP of light-exposed pups were not significantly different from that of controls.

Conclusions: We therefore conclude that BG (498 nm) light appears to be as effective and safe as blue (450 nm) light. Further studies are warranted to confirm these findings clinically.

DATA SUMMARY.

<table>
<thead>
<tr>
<th>Light Source</th>
<th>Bilirubin Degradation Rate (mg/dL/h)</th>
<th>Fold Change in VeCO2</th>
<th>Fold Change in VeCO2</th>
<th>Wt 1 Loss (mg/b)</th>
<th>Fold Change in LP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue</td>
<td>1.3±0.3 (n=4)</td>
<td>1.1±0.1 (n=11)</td>
<td>1.2±0.3 (n=7)</td>
<td>33±54 (n=9)</td>
<td>1.4±0.8 (n=5)</td>
</tr>
<tr>
<td>Blue-Green</td>
<td>1.6±0.1 (n=3)</td>
<td>1.1±0.2 (n=17)</td>
<td>1.2±0.2 (n=12)</td>
<td>44±80 (n=13)</td>
<td>1.2±0.2 (n=5)</td>
</tr>
</tbody>
</table>

Values are shown as mean±SD.

41 CHEMOPREVENTION OF NEONATAL JAUNDICE USING POLYMERIC PARTICULATE DELIVERY OF ZINC PROTOPORPHYRIN

Wong RJ1, Espadas C2, Inayathullah M1, Lechuga-Ballesteros D2, Kalish F1, Rajadas J2, DK Stevenson1, 1Stanford University, Stanford, CA and 2Stanford University, Stanford, CA.

Purpose of Study: Heme oxygenase (HO) is the rate-limiting enzyme in the degradation of heme to produce bilirubin. Because hemolysis can lead to increased bilirubin production and cause neonatal jaundice, the use of HO-inhibitors, e.g. metalloporphyrins (Mps), may be an ideal preventive strategy. Tin mesoporphyrin has been studied in human neonates, but its property as a photosensitizer and ability to induce HO-1 limits its clinical use. We have shown that zinc protoporphyrin (ZnPp) is a promising Mp as it is naturally occurring, not phototoxic, and potent, but its use is also limited since it is not orally absorbed. To this end, we designed formulations of ZnPp using polymeric particulate delivery systems (micro- or nanoparticles) to improve its stability and enhance gastric absorption. Our objective was to test these preparations for oral bioavailability and subsequent in vivo potency and phototoxicity in a newborn mouse model.

Methods Used: 3d-old mice were given vehicle or 30 µmol/kg of ZnPp-Phosphat (-PO4), ZnPp-Polymer (-Poly), or ZnPp-Lipid formulations by direct intragastric (IG) injections. After 3h, pups were sacrificed and livers were harvested for measurements of HO inhibitory potency. HO activity was calculated as pmol CO/h/mg fresh weight and then expressed as mean ±SD % of control values. To evaluate phototoxicity, pups were treated similarly and then immediately placed under fluorescent tube (2 cool white/1 blue TL52) light for 3h. Overall survival of pups was monitored for 1 wk.

Summary of Results: Even though, ZnPp-PO4 was found to be the most potent (80%) in vitro, its potency significantly decreased after IG administration. The ZnPp-Poly was the most potent, but it was phototoxic resulting in 90% mortality within 48h. Importantly, we observed that the ZnPp-Lipid formulation was also potent, but showed no phototoxicity.

Conclusions: Because the ZnPp-Lipid formulation was effective in inhibiting liver HO activity after IG administration and had no phototoxicity, we thus conclude that it has potential for use in the treatment of neonatal jaundice.

<table>
<thead>
<tr>
<th>Inhibitory Potency (% of Control Liver HO Activity)</th>
<th>Control</th>
<th>ZnPp-PO4</th>
<th>ZnPp-Poly</th>
<th>ZnPp-Lipid</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Survival</td>
<td>100±2%</td>
<td>60±12%*</td>
<td>350±33%*</td>
<td>46±4%*</td>
</tr>
</tbody>
</table>

*p<0.05 vs Control, n=5-15 for each group

42 ANGIOGENESIS: EPIGENETIC MODIFICATION AND SIGNALING MECHANISMS

Prest JD, Goyal R, Longo L. Loma Linda University, Loma Linda, CA.

Purpose of Study: To a great extent, despite extensive morphological study, the underlying molecular mechanisms of angiogenesis remain unknown. The present study examined the effects of long-term hypoxia (LTH) on sheep frontal cortex capillary density, the molecular mechanisms involved in hypoxia-induced angiogenesis in these vessels, and the different mechanisms involved in angiogenesis in fetal and adult sheep cerebral arteries.

Methods Used: Long-term hypoxic sheep were sheltered at an altitude of 3801 m at White Mountain Research Station, Bishop, CA for 110 days. At this altitude their blood PO2 fell from 102±2 to 59±2. Normoxic sheep were maintained at Neberker Ranch, Lancaster, CA (300 m). Frontal cortex samples from normoxic and hypoxic sheep were compared using immunofluorescence imaging to examine the effects of LTH on angiogenesis, and the molecular mechanisms involved. Angiogenically induced fetal (FA) and adult (AA) sheep carotid arteries were compared with non-induced fetal (FC) and adult (AC) arteries and analyzed with immunofluorescence imaging to examine the molecular pathways and epigenetic modification involved in fetal and adult angiogenic mechanisms.

Summary of Results: Hypoxic sheep frontal cortex demonstrated a significant increase in angiogenesis when compared to normoxic control. In capillary endothelium, LTH induced an increase in Extracellular Regulated Kinase 1/2 (ERK 1/2) phosphorylation and Vascular Endothelial Growth Factor (VEGF) expression. However, we noted no change in histone H3K27 trimethylation (me3) or H3K9 acetylation with hypoxia. AA demonstrated increased ERK 1/2 phosphorylation, histone H3K4me3, and histone deacetylase 1 and 2 (HDAC 1/2) expression compared to AC. However, decreased HDAC1 and HDAC2 was noted in AA smooth muscle. FC demonstrated increased HDAC1, HDAC2, and histone H3K4me3 when compared to AC. FA demonstrated increased HDAC1, HDAC2 and histone H3K4me3, but decreased HDAC 1/2 phosphorylation when compared to AC.

Conclusions: In sheep frontal cortex, ERK 1/2 phosphorylation and VEGF pathways are implicated in hypoxia-induced angiogenesis. Differences in active molecular mechanisms in AC, AA, FC and FA may account for the differences in angiogenic activity. A better understanding of these mechanisms may provide new targets for the treatment of cancer, ischemic heart disease, and other angiogenic-based diseases.

43 ACCURACY OF MRI-DETERMINED PROTON DENSITY FAT FRACTION FOR ESTIMATION OF HEPATIC STEATOSIS IN EX-VIVO HUMAN LIVER


Purpose of Study: The purpose of this study was to assess the accuracy of MRI-determined proton density fat fraction (MRI-PDFF) and histologically-determined fractional fat (FF) in estimating hepatic steatosis in ex-vivo human liver using biochemically-determined triglyceride concentration ([TG]) as the reference standard.

Methods Used: We obtained ten anonymous explanted whole livers from the National Disease Research Interchange. Donors were selected based on history of fatty liver disease or having risk factors for fatty liver. Two-dimensional axial images were obtained at 3T using a spoiled gradient-recalled-echo sequence with low flip angle and TR = 120ms to minimize T1 dependence. PDFF maps were generated offline from source images pixel-by-pixel with a reconstruction algorithm that corrects for T2* signal decay and multi-frequency interference effects of fat. Since liver fat spatial distribution may be non-uniform, we measured MRI-determined proton density fat fraction (PDFF) values at five separate locations within each liver. At each location, two sets of biopsies were obtained: one set for biochemical analysis
to determine [TG] and the other set for histological analysis to determine FF per surface area. Spearman’s correlations were computed for [TG] and MRI-PDFF, and [TG] and histologically-determined FF. The bootstrap-based 95% confidence intervals were computed. The difference between correlations was assessed using bootstrap.

**Summary of Results:** MRI-PDFF, histologically-determined FF, and [TG] ranged were -0.4 to 21.8 %, 0-70 %, and 1.5 to 22.9 mg/100g respectively. Spearman’s correlation between [TG] and MRI-PDFF, and [TG] and histologically-determined FF were r = 0.971 (95% CI: 0.951, 0.994), and r = 0.905 (95% CI: 0.812, 0.974) respectively. The difference between correlations was 0.067 (95% CI: -0.029, 0.208) (p-value = 0.19).

**Conclusions:** In this ex vivo study and using biochemically-determined [TG] as the reference standard, MRI-PDFF correlation with [TG] was higher than histologically-determined FF correlation with [TG]. This difference was not statistically significant and further study with a larger sample size is needed to fully assess this issue. Overall, this study can be considered as the first step in a multistep process to validate MRI-PDFF as a biomarker of hepatic steatosis.

**44**

**CORNEAL DEFORMATION CAUSED BY TOPICAL LOADED MANGANESE-ENHANCED MRI**

McCormick MA1, Chung C2, Sun S3,2,1, Loma Linda University. Loma Linda, CA, 1Loma Linda University, Loma Linda, CA and 2University of California, Riverside, CA.

**Purpose of Study:** Manganese-Enhanced MRI (MEMRI) can be used to non-invasively quantify axonal and cross-synaptic transportation in vivo. Topical loading of a Mn2+ contrast agent can be used for the early detection of Alzheimer’s disease and glaucoma. A previous study suggested one application of topical-loaded MEMRI may be safe; however, corneal deformation may occur after 7 biweekly repeated applications. In this study, we aimed to answer two questions: 1. How many topical loadings are necessary to produce corneal deformation? 2. Because the Mn2+ solution is slightly acidic (pH = 5), is corneal deformation caused by Mn2+ or the low pH?

**Methods Used:** C57BL/6 female mice were separated into two groups to receive 1 M MnCl2 or pH-matched (pH = 5) HCl solution (N = 6). 5 μl MnCl2 or HCl was applied to the corneal surface and removed after one hour. All eyes received the same solution biweekly for 6 applications. Corneal thickness was imaged using Spectral Domain Optic Coherence Tomography two weeks after each topical loading. Prior to OCT imaging, mice were anesthetized with an intra-peritoneal injection of 100 mg/kg ketamine hydrochloride and 10 mg/kg xylazine. Volumetric images were acquired with 1000 A-scans per B-scan, 100 B-scan frames, and 1024 samplings/A-scan in depth.

**Summary of Results:** Both the Mn2+ and HCl treated eyes exhibited a ~20% decrease of corneal thickness after 4 applications. The corneal thickness of both groups returned to normal after 6 topical treatments, while the cornea appeared opaque compared to controls.

**Conclusions:** Our previous study showed corneal thickening and opacity after 7 biweekly Mn2+ loadings. New results suggest corneal thinning followed by thickening after repeated applications. More importantly, the pattern of corneal thinning suggests that low pH (pH = 5) is the predominant factor causing deformation; Mn2+ might not cause an adverse corneal effect. It is not uncommon to see a low pH with therapeutic topical ophthalmic solutions; however, the duration of corneal contact with these solutions is much shorter, and human tears may dilute the solution to prevent discomfort.

**45**

**COMPARATIVE EFFECTIVENESS OF GUIDELINE DEFINITIONS AND CLINICAL JUDGMENT IN IDENTIFYING SEPSIS IN THE EMERGENCY DEPARTMENT**

Brown TN1, Yeung D1, Ghelani A1, Nguyen H1,2, Loma Linda University School of Medicine, Loma Linda, CA, 1Loma Linda University Medical Center, Loma Linda, CA and 2Loma Linda University Medical Center, Loma Linda, CA.

**Purpose of Study:** The purpose of our study was to compare the agreement of physician diagnoses relative to the 1991 and 2001 internationally accepted definitions of sepsis, severe sepsis, and septic shock.

**Methods Used:** This study was an observational cohort of adult patients presenting to the Emergency Department (ED) with a chief complaint suggestive of infection over a six-week period, with a daily enrollment schedule from 7 am to 10 pm. Patients were classified as non-sepsis, sepsis, severe sepsis, or septic shock based on the 1991 definition, 2001 definition, and the physician diagnosis as documented in the medical chart. Agreement statistics were performed.

**Summary of Results:** Of 1,275 enrolled patients, 228 patients of age 49.7 ± 21.4 years were identified as having a source of infection. Temperature, heart rate, and white blood cell count were significantly higher in patients with infections, compared to those without (p < 0.01). Agreement between physician diagnosis and the 1991 and 2001 definitions were poor, with kappa = 0.1 and 0.1, respectively. The prevalence of the non-sepsis diagnosis was 83.3% by physician, 51.3% by the 1991 definition, and 45.6% by the 2001 definition. The odds ratio for a non-sepsis diagnosis by physician was 4.74 (95% CI: 3.01, 7.53) times that of the 1991 definition, and 5.96 (95% CI: 3.78, 9.46) times that of the 2001 definition. Severe sepsis had the greatest discrepancy, with a prevalence of 1.3% by physician, 18.4% by the 1991 definition, and 17.5% by the 2001 definition. The odds ratios for a severe sepsis diagnosis by physician were 0.06 (95% CI: 0.01, 0.19) and 0.06 (95% CI: 0.01, 0.20) times that of the 1991 and 2001 definitions, respectively.

**Conclusions:** Compared with the international definitions, physician diagnosis of sepsis lacks agreement such that severe sepsis is under-recognized by clinical judgment alone. These results raise concern that early treatments for these high-risk patients may be delayed due to inaccurate clinical diagnosis. An intervention is warranted to increase the application of sepsis guideline definitions to better identify ED patients with this potentially fatal condition.

**46**

**DOES HEART-KIDNEY TRANSPLANT CONFER PROTECTIVE BENEFITS IN IMMUNE RESPONSES?**

Liu F, Yu Z, Hamilton M, Kobashigawa J. Cedars-Sinai Medical Center, Los Angeles, CA.

**Purpose of Study:** Combined heart-kidney transplantation is occurring more often. In this dual organ transplantation, the more vascular organ (kidney) appears to protect the heart transplant due to complex immunologic properties. Previous reports of heart-kidney transplant have not compared similar immunosuppression regimens. Therefore, it has not been firmly established whether this combined organ heart transplant actually decreases first year rejection in the transplanted donor heart under similar immunosuppression regimens.

**Methods Used:** Between 1997 and 2012, we evaluated 28 heart-kidney transplants and assessed first year rejection and survival. These first year rejection episodes were compared to heart alone transplanted patients under similar immunosuppression regimens. All patients received induction therapy with anti-thymocyte globulin and were maintained on tacrolimus/mycophenolate immunosuppression during the first year after transplant.

**Summary of Results:** There were 28 heart-kidney transplants, which were compared to 226 heart alone transplanted patients. First year rejection, both cellular and antibody-mediated, was comparable between the two groups. There was also no difference in first year survival between the two groups.

**Conclusions:** Heart-kidney transplant patients do not appear to have a protective effect from rejection compared to heart alone transplant patients.
47
TOXOPLASMA SEROLOGY AND OUTCOMES AFTER HEART TRANSPLANTATION: CONTENTION IN THE LITERATURE
Purpose of Study: Toxoplasma serology is routinely assessed prior to heart transplantation (HTXs). It has been suggested that toxoplasma serology either positive or negative may lead to poor outcome after transplant (Arora, J Am Coll Cardiol 2007;50:1967-72 and Doesch, Transpl Int 2010; 23:382-389). Arora reported that toxoplasma seropositive status in HTX patients (pts) was associated with an increased mortality risk. However, Doesch reported that toxoplasma seronegative status was associated with increased mortality risk. Therefore, we assessed our pts for pre-transplant toxoplasma serology and assessed their post-transplant outcomes.
Methods Used: Between 1995 and 2012, we assessed 785 HTX pts and divided them into those that were toxoplasma positive and those that were toxoplasma negative at baseline. 5-year post-transplant outcomes including 5-year actuarial survival, 5-year freedom from non-fatal major adverse cardiac events (NF-MACE), and 5-year freedom from cardiac allograft vasculopathy (CAV) were assessed. Serology mismatch (donor positive to recipient negative, donor positive to recipient positive, donor negative to recipient positive, donor negative to recipient negative) subgroups were also assessed.
Summary of Results: There is no difference between outcomes of toxoplasma negative versus toxoplasma positive serology pre-transplant patients. In subgroup analysis, there was a statistically significant difference in 5-year actuarial survival in the donor positive to recipient negative group compared to the donor negative to recipient negative group (72.2% vs. 87.3%, p=0.048). It is unclear whether all deaths are Toxoplasma Gondii related, as no autopsies were performed.
Conclusions: Toxoplasma serology prior to HTX does not appear to impact post-transplant outcome. However, in subgroup analysis, toxoplasma seronegative pts who received toxoplasma seropositive hearts had a poorer 5-year actuarial survival post-transplant compared to toxoplasma seronegative patients who received toxoplasma seronegative hearts.

48
SEVERE, FATAL MULTISYSTEM MANIFESTATIONS IN A PATIENT WITH DOLICHOL KINASE-CONGENITAL DISORDER OF GLYCOSYLATION
MT Liu1, BG Ng2, JS Rush1, T Wood3, MJ Basehorn3, M Hedge3, RC Chang3, JE Abdenour2, HH Freeze2, RY Wang4. 1David Geffen School of Medicine at UCLA, Los Angeles, CA; 2Sanford Burnham Medical Research Institute, La Jolla, CA; 3University of Kentucky College of Medicine, Lexington, KY; 4Greenwood Genetic Center; Greenwood, SC; 5Emory University School of Medicine, Atlanta, GA and 6CHOC Children’s Specialists, Orange, CA.
Case Report: Congenital disorders of glycosylation are a group of metabolic disorders with an expansive and highly variable clinical presentation caused by abnormal glycosylation of proteins and lipids. Dolichol kinase (DOLK) catalyzes the final step in biosynthesis of dolichol phosphate (Dol-P), which is the oligosaccharide carrier required for protein N-glycosylation. Human DOLK deficiency, also known as DOLK-CDG or CDG-Ib, results in a syndrome that has been reported to manifest with dilated cardiomyopathy of variable severity. A male neonate born to non-consanguineous parents of Palestinian origin presented with dysmorphic features, genital abnormalities, malformations and multi-systemic dysfunction. This patient expands the phenotype of DOLK-CDG to include anatomic malformations and multi-systemic dysfunction.

49
THYROTOXICOSIS-INDUCED FETAL HEART FAILURE
Sharifi M, Rea C, Navabi K, Bouchonville MF, Kaspner P. University of New Mexico Health Sciences Center, Albuquerque, NM.
Case Report: The prevalence of hyperthyroidism in pregnancy is 0.1% to 0.4% with Graves' disease accounting for 85% of cases. Prompt treatment of this condition is essential for preventing fetal complications. We present an unfortunate case of fetal thyrototoxicosis related to poor follow-up and adherence to medical therapy.
A 26-year-old female, 30 weeks and five days pregnant who presented to the emergency room with tachycardia and decreased fetal movement. A diagnosis of Graves' disease had been made in the first trimester but the patient had not adhered to treatment for at least two weeks prior to her current presentation. Labs at this time included a free T4 >8 ng/dl (reference 0.7-1.6) and undetectable TSH (reference 0.358-3.740 IU/l). She was immediately started on methimazole and propranolol. Fetal US demonstrated tachycardia and marked cardiomegaly with third spacing concerning for heart failure. No fetal goiter was noted. TSH receptor antibodies were more than 40 IU/L (reference <=1.75), thyroid stimulating immunoglobulins (TSI) were 491% basal activity rate (reference <=122), and thyroid peroxidase antibodies were 85.9 IU/ml (reference <35). A cesarean section was performed sixteen days after admission due to fetal decelerations. The newborn was diagnosed with hyperthyroidism at birth with TSH of 0.013 IU/l and free T4 of 2 ng/dl and treatment with methimazole and propranolol was initiated. Sentinel echocardiograms since the delivery have demonstrated gradual improvement of the heart failure.
This case underscores the importance of proper recognition and management of Graves' disease in pregnancy. Close fetal monitoring with ultrasoundography is important to assess fetal response to maternal thionamide therapy, particularly in the setting of elevated maternal titers of TSH receptor antibodies. We will present a review of the literature pertaining to the pathogenesis of fetal thyrotoxicosis and fetal hyperthyroidism. Moreover, we will review current consensus guidelines for surveillance of TSH receptor antibodies, fetal monitoring, and indications for umbilical blood sampling.

Poster Session I
Community Health Projects
2:30 PM Thursday, January 23, 2014
50
AN EFFECTIVE SUMMER ENRICHMENT PROGRAM TO GARNER THE INTEREST OF A DIVERSE POPULATION OF YOUTH TOWARDS HEALTH CAREERS
Purpose of Study: The need for enrichment programs that expose a diverse population of youth to health careers is urgent. In this report, we describe the effectiveness of a unique and highly interactive enrichment program in garnering the interest of a diverse population of high school students towards a career in health care.
Methods Used: To give youth a glimpse of life in medical school, we designed a very structured summer enrichment program that mimics the medical school's interactive curriculum. The workshops included but were not limited to cadaver lab, bedside ultrasound, suturing, robotics, patient interviews, and splinting. The students were accepted through an application process. We encouraged participation of those underrepresented in medicine (URIM) by providing scholarships. A feedback survey was distributed at the
end of the program to measure the effectiveness of the program in helping them with their future goals and professional development as well as the effectiveness of the workshops. A 5-point scale was used, 1 = least effective or 5 most effective).

Summary of Results: During the summers of 2012 and 2013, 280 high school students participated in the program and 22% were URM. Of 280, 257 (92%) complete evaluations were collected. The average rating of the workshops ranged from 3.4 to 5.0, with cadaver lab and patient interview each having the highest rating of 4.76. As a result of this program, students gave an average rating of 4.7 out of 5 regarding their motivation to pursue a career in medicine, rating of 4.59 for understanding evidence based medicine, a rating of 4.45 for comfort in interviewing patients, and a rating of 4.43 for interest in mentoring in the future.

Conclusions: The Summer Premed Program at UC Irvine School of Medicine was very successful in promoting the interest of a diverse population of youth towards a career in medicine. Long-term follow-up of the participants’ career choices is needed.

51

RAPID ASSESSMENT OF MOBILE CLINICS PROGRAM IN RURAL MALAWI
Caradonna L1, Debay M2,1 Loma Linda University, Loma Linda, CA and 1Loma Linda University, Loma Linda, CA

Purpose of Study: The Community Health Department (CHD) of Malamulo Hospital (MH) in Malawi, Africa has been operating a mobile clinic program with support from the Integrated HIV/AIDS Prevention and Family Planning Promotion Project from 2001 until the end of 2011. The program has continued since then at a decreased level of activity with MH as the main source of funding. We developed a standardized, rapid assessment in order to gather key information on the current CHD mobile clinic activities in order to demonstrate the usefulness of these clinics when reapplying for funding of the program.

Methods Used: An assessment tool was developed to evaluate the 17 mobile clinics for services offered, catchment area and population, resources used and utilization of services. The clinical assessment tool was implemented during systematic visits of the 17 mobile clinic locations. In addition, a retrospective review of available project documentation from the hospital and government records was performed. Interviews of MH staff, government health workers and government officials involved with the program were conducted as well.

Summary of Results: A total of 17 clinics were evaluated over a five-week period. A consistent finding among all of the clinics was a significant decrease in the number of health workers and volunteers present at the clinics. The nearest health facility for 76.5% of the sites was MH. 11.8% of the sites had a regular health facility to meet in when the clinics were being conducted while the other 88.2% met outside or in public structures. Family planning and health education services were the only two services that were offered at all of the sites while HIV testing was offered at 41.1% of the sites. The coverage area of all of the mobile clinics was 30,979 people. As compared with the functioning of the clinic two years ago, the mobile clinics program is operating at a lowered capacity in all regards of the assessment.

Conclusions: The mobile clinics program is running at a very low capacity due to underfunding and lack of incentives for volunteers and workers. Health literacy is the degree to which individuals have the capacity to obtain, process and understand basic health information and services they need to make appropriate health decisions. In the United States, limited health literacy disproportionately affects the poor, minorities and those with limited education and English proficiency. Low health literacy is associated with greater hospitalizations and emergency room visits and poorer health outcomes. Harborview Medical Center (HMC) in Seattle, WA serves a culturally, ethnically and socioeconomically diverse patient population at greater risk of having low health literacy. The purpose of this project was to increase the health literacy of HMC patients through health education.

Methods Used: In coordination with the Community House Calls Program (CHCP) at HMC, I identified relevant health education topics for a Somali community (liver disease and hepatitis) and a Cambodian community (kidney disease). A literature review determined background medical information and evidence-based interventions and teaching strategies shown to increase health literacy. I worked with community groups, family medicine physicians, and the CHCP in organizing health education talks for both communities in Seattle. The presentations were interpreted and a family medicine physician helped field questions.

Summary of Results: The Somali health presentation was given to 12 women at Daryel, a wellness group for Somali women. All participants were actively engaged in the presentation and subsequent conversation, and were able to teach back relevant points regarding the importance of hepatitis testing, disease prevention, and educating others in their community. There was a miscommunication with the Cambodian Sewing Group regarding the date and time of their presentation, so the presentation was rescheduled for a later date.

Conclusions: Low health literacy requires significant attention in Seattle in order to increase health understanding and decrease the associated poor health outcomes and individual healthcare costs. In order to make a significant impact, health providers must use a systematic and evidence-based approach to provide culturally-sensitive, patient-centered health information based on the skills, knowledge, culture and language of the intended audience.

53

EXPANDING COMMUNITY EDUCATION OF DENGUE VECTOR PREVENTION BY DISTRIBUTION OF EDUCATIONAL FLYERS
Dennis T. University of Washington, Seattle, WA.

Purpose of Study: Dengue is a significant disease in the city of Iquitos, Peru, with over 80% of the population testing positive for dengue between the years 1999 and 2005. The city is often subjected to dengue epidemics, due to a high urban density, poor water distribution and a tropical climate. The goal of this project was to increase community compliance with known dengue vector control protocols.

Methods Used: An educational pamphlet was created for distribution in addition to ongoing house-to-house efforts to eliminate the primary dengue vector, the A. aegypti mosquito. The flyer was distributed throughout the city by community public health workers. The flyers supplemented verbal information that was given to the population by the health workers in an attempt to increase compliance with mosquito elimination protocols. The flyers were incorporated into a government document that is already glued to the inside door of every house in an attempt to reduce waste.

Summary of Results: The flyers were first handed out in a test case to 600 houses to see how they were received by the community. With no community objection and significant worker support, the flyers were then adopted by the Morona Cocha neighborhood Dengue Prevention Program and presented to the head of Dengue Prevention in Iquitos. The flyers are being considered for incorporation into the house-to-house Dengue Prevention Protocol for all of Iquitos. The template for the flyers was left with the dengue prevention supervisor both as a digital and hard copy.

Conclusions: Flyers were distributed to 3,000 houses and will possibly be distributed to the majority of the population in Iquitos. It is difficult to determine the impact of the flyers; however, it is another source of education to minimize the impact of dengue on the city of Iquitos. The dengue health workers believed it was a useful tool for teaching the population. The project should be sustainable, as long as the flyers remain a part of the Dengue Prevention Protocol.
54 EVALUATING AND BUILDING ORGANIZATIONAL CAPACITY FOR A HEALTH EDUCATION PROJECT IN THE REMOTE SPITI VALLEY OF INDIA


Purpose of Study: Since 2007, students from University of British Columbia have worked in Northern India to improve student health at a boarding school. This included a health education program on diarrheal diseases, personal hygiene, and sanitation. In 2012, UBC students trained students from grades nine and ten to form a Student Health Council (SHC). The SHC promotes sustainability by independently delivering health education in the local language. Evaluations showed that SHC seminars significantly improved peer health knowledge. This year, UBC evaluated logistical outcomes of the SHC one year after its implementation: 1) Has the SHC continued to deliver health modules regularly in UBC’s absence? 2) Is there an established structure for electing a new SHC annually to replace graduating members? 3) What organizational changes would ensure the program operates independently?

Methods Used: UBC students monitored the current SHC peer teaching program using a SWOT analysis through meetings with the SHC, school principal, and school director. The SHC was observed during the education sessions, and follow-up meetings were held with the SHC, principal, and director to plan operational improvements and future goals.

Summary of Results: Since its inception in 2012, the SHC had successfully delivered one of the four health education modules. Delayed school opening and organizational difficulties had prevented delivery of subsequent modules, rescheduling sessions, and electing junior members. Under UBC’s guidance, the SHC elected and trained junior students, and they delivered all modules to four classes. A new organizational structure was developed with community collaboration to enable the SHC to operate without UBC’s facilitation; two SHC members were elected as leaders, and three teachers were selected to administer the SHC.

Conclusions: While local community members can effectively deliver health education, a lack of clear leadership can prevent the execution of educational sessions. Building strong organizational structure is necessary to leverage local capacity. During transition periods, foreign teams can facilitate the development of organizations while local members deliver curriculum. In the future, UBC will evaluate the success of the new SHC structure.

55 IMPROVING NUTRITION IQ: RESULTS OF AN INTERACTIVE PEER-TO-PEER INTERVENTION IN A HIGH-SCHOOL SETTING

Espinoza MH, Alquizon G, Aranda I, Trice A, Kinman R23, 1 Fresno High School, Fresno, CA; 2 University of California, San Francisco-Fresno, Fresno, CA and 3 Children’s Hospital Central California, Madera, CA.

Purpose of Study: Forty-three percent of fifth, seventh, and ninth grade students in Fresno County public schools are either overweight or obese, which can result in serious health problems both now and in the future. Weight gain results from excess calories consumed, including both food and/or beverages. Given that 1) sugar-laden drinks can result in increased amounts of calories consumed, and 2) the average adolescent in California consumes one soda per day, we designed a project to educate students at a large urban high school in Fresno about the amount of sugar contained in commonly consumed beverages.

Methods Used: Forty-one students at Fresno High School were asked to rank a group of five beverages (Gatorade, Monster, Pepsi, water, and vitamin water) according to their favorite beverage. Gatorade was ranked the most popular by 37% of students, followed by Pepsi, vitamin water, water, and Monster. Students were then shown the amount of sugar in these beverages, and asked if they wished to re-rank their beverage choices.

Summary of Results: Post-demonstration rankings differed greatly from pre-demonstration rankings, with water ranked the most likely to be consumed by 61% of students, followed by vitamin water, Gatorade, Monster, and Pepsi. Of the drinks ranked, the sugar content was highest in Pepsi, followed by Monster, Gatorade, vitamin water, and water.

Conclusions: These data reveal that an interactive project such as this can result in healthier beverage choices by adolescents. Our hope is that educating adolescents in healthier choices will allow them to make healthier beverage choices so that they not only decrease their risk for obesity and future health problems, but also improve their self-esteem and self-confidence by achieving a more healthy weight.

56 INCREASING KNOWLEDGE OF REPRODUCTIVE HEALTH THROUGH TARGETED EDUCATION IN OLLANTAYTAMBO, PERU

Gadzik E. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Despite the availability of free family planning services in local health clinics, there is low utilization of these services in Ollantaytambo, a rural district in the sacred Valley of southern Peru. Gender inequality, misinformation, lack of awareness of services, lack of partner support, and geographic obstacles remain significant barriers to care. This project aimed to increase knowledge of reproductive health and family planning through sustainable, community-based education.

Methods Used: Reproductive and sexual health education was delivered to primary school students, university students, promoters (community health workers), and adults. Information was delivered in 2-3 hour interactive lessons for students, and a daylong interactive workshop for promoters and adults. All attendees completed a pre-test to assess prior levels of knowledge. Post-tests will be completed with all promoters 2 weeks following training to gage retention. All students and attendees demonstrated comprehension of the material by re-teaching topics to their classmates.

Summary of Results: A total of 10 promoters, 6 adult community members, 11 primary school students, and 9 university students received education about the reproductive system, contraception, pregnancy, and family planning. Partnerships were developed with a network of schools and community organizations seeking long-term, regular reproductive health education. All curricula and educational materials were given to Sacred Valley Health (SVH) for use in future health campaigns. SVH committed to including comprehensive reproductive health education in all future promoter training cycles and school health campaigns.

Conclusions: This project increased awareness of anatomy, puberty, conception, benefits of family planning, local options for contraception, sexually transmitted infections, and communication in healthy relationships. This education will be sustained SVH’s promoter program in coordination with schools, universities, government health clinics, and community groups in Ollantaytambo. It will be important to complement reproductive health topics with education on gender roles, autonomy, self-esteem, communication, decision-making, and healthy relationships.

57 INCREASING PHYSICAL ACTIVITY IN ADULTS THROUGH ADOPTION OF A COMMUNITY WALKING GROUP IN SOUTH BEND, WASHINGTON

Jacobsen A. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: The city of South Bend is located in Pacific County with an adult diabetic rate of 11.9% and adult obesity rate of 30.6%. Both of these rates are alarmingly higher than WA state as a whole. Individuals with diabetes and obesity would benefit from regular physical activity, but South Bend is without a gym or fitness center. This prevents easy access to exercise. The purpose of this project is to provide adults in the community with a cost effective and convenient way to exercise together as well as provide education on the health benefits of walking.

Methods Used: A walking group was created by first contacting a member of the community who was willing to lead the group. The First Lutheran Church of South Bend was partnered with, which provided a consistent meeting place. Advertising for the walking group was accomplished through meeting with local pastors, the public health department of South Bend and contacting patients of the hospital’s diabetic counselor. It was decided that the bi-weekly group walks would take place along the river trail in South Bend. A Pubmed literature review identified three key components to
successful walking groups: having goals, being taught the benefits of exercise and decreasing unpleasant stimuli. A brochure was created to educate the walking group participants on the benefits of walking and how to set walking goals. Pedometers were also recommended to keep track of the number of steps individuals were taking each day.

Summary of Results: There were seven participants at the first walking group meeting including four diabetic patients. Participants created weekly walking goals for themselves and then walked two miles along the scenic river trail. Participants showed enthusiasm about the group and some remarked that it was the furthest they had walked in a long time.

Conclusions: Physical activity is necessary for a healthy lifestyle, yet most adults of South Bend lack access to an exercise facility. It seems realistic to expect an improved level of physical activity through implementing a walking group in the city. The community displayed an eagerness to reach their walking goals and recruit other participants. In the future, an indoor walking venue will be found for use in the winter months.

58

DEVELOPMENT OF A COMMUNITY HEALTH WORKER PROGRAM FOR NORTHERN INDIA

Lamarche M1, Hunter K1, Mason E1, Sidhu N1, Suen MW2, Kapoor V3. 1UBC, Vancouver, BC, Canada; 2UBC, Vancouver, BC, Canada and 3UBC, Vancouver, BC, Canada.

Purpose of Study: Health care delivery in India faces many challenges, a significant one being the geographical isolation of its villages. AMAN and VIMARSH are two non-governmental organizations (NGOs) in the northern Indian state of Uttarakhnad (UKD) who focus on women’s empowerment through literacy and health education. Over the past 4 years, UBC students have been working with the NGOs to deliver health workshops to remote villages in UKD as well as provide training programs for women’s groups. These programs were piloted in the community with a view to implement a sustainable plan for knowledge dissemination through the use of Community Health Workers (CHWs). Recently, the World Health Organization (WHO) released a review of CHW programs worldwide. In order to increase the likelihood of a successful CHW program in UKD, it is necessary to identify key areas of the selection process and training that could align with Indian culture and values and compliment existing government health services.

Methods Used: We performed a Medline search for “Community Health Workers”, “Community Health Services” or “Community Health Centers”, AND “India”; AND “Child Welfare”, “Maternal Welfare” or “Infant Welfare”. 133 studies were identified and 18 studies included for review. We reviewed these papers for relevant information to supplement the framework laid out by the WHO review.

Summary of Results: We identified several key findings that can assist in building an India specific CHW program in UKD. Many of these findings focused on the specifics of the selection process, health topics to be covered, different methods for delivering the information, as well as role definitions for the CHWs.

Conclusions: In order to make a CHW program for northern rural India, we completed a systematic literature review of similar Indian programs. After identifying key components, we provided our Indian NGO partners with a summary of guidelines for developing a CHW program in UKD. Many of these findings focused on the specifics of the selection process, health topics to be covered, different methods for delivering the information, as well as role definitions for the CHWs.

59

A COMMUNITY BASED INITIATIVE: PEER MENTORING TO TEACH HEALTHY HABITS


Purpose of Study: Education about healthy habits through peer mentoring has not been explored in the literature. The objective of the Healthy Habit Initiative at UC Irvine School of Medicine was to determine whether an interactive session using a cascading mentorship is effective in teaching elementary students about healthy habits.

Methods Used: Under the direction of one faculty, undergraduate and high school students designed a curriculum to teach elementary students about the food pyramid and the importance of exercise. The program required the active participation of the elementary schools students. A survey was distributed after each session to evaluate the effectiveness of the program.

Summary of Results: One faculty, two undergraduate students and nine high school students conducted the sessions in six different elementary schools. 242 elementary school students participated in the program. A comparison of responses by elementary students before and after the session is shown below. The workshops increased the knowledge of elementary students about healthy eating and importance of exercise. The college and high school student mentors expressed that their interest in life-long civic engagement and confidence increased as a result of this project.

Conclusions: The Healthy Habit Initiative based on peer mentorship was very effective in teaching very young students about the food pyramid and the importance of exercise. The program also inspired a sense of life-long civic engagement in the high school and college student mentors.

Comparison of the Responses Pre and Post Session

<table>
<thead>
<tr>
<th>Questions</th>
<th>Pretest N=242% answered correctly</th>
<th>Post-test N=143% answered correctly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you know about the food pyramid? (answered yes)</td>
<td>69%</td>
<td>95%</td>
</tr>
<tr>
<td>What food group is recommended with most serving?</td>
<td>9%</td>
<td>57%</td>
</tr>
<tr>
<td>What food group is recommended with least serving?</td>
<td>78%</td>
<td>81%</td>
</tr>
<tr>
<td>What is the recommended duration of physical activity per day?</td>
<td>50%</td>
<td>82%</td>
</tr>
</tbody>
</table>

60

THE ASSOCIATION BETWEEN NEIGHBORHOOD PHYSICAL DISORDER AND ALLOSTATIC LOAD

Liu A1, Vassar S2,3, Barron J2,3, Sankare I2,3, Brown AF2,3. 1DGSOM at UCLA, Los Angeles, CA; 2Clinical and Translational Science Institute, Los Angeles, CA and 3UCLA, Los Angeles, CA.

Purpose of Study: Allostatic load (AL) is a measure of cumulative biologic risk that has strong associations with health outcomes, including chronic disease risk, morbidity, and mortality. Although neighborhood disorder has been associated with poor health outcomes, the mechanisms for this relationship are not well understood and little work has been done in community settings. To better understand these associations and the underlying mechanisms, we described the distribution of AL and examined its relationship with neighborhood physical disorder in a low-income community in South Los Angeles.

Methods Used: The Healthy Community Neighborhood Initiative (HCNI) is a collaborative effort to improve health and health care in a South Los Angeles community disproportionately affected by preventable chronic conditions. The project fielded a community assessment consisting of 1) a household survey, 2) neighborhood observations, and 3) community asset mapping. Survey data obtained from the residents was linked to data from the neighborhood observations. AL scores were calculated with cardiovascular, metabolic, and inflammatory biomarkers as sums of clinical cutpoints and z-scores for each biomarker. Neighborhood observations of the street segments where these participants lived were combined to calculate physical disorder scores.

Summary of Results: These analyses include data from 65 residents who lived on 58 unique street segments in this community. Residents of neighborhoods with low disorder (bottom 50%) had a mean AL of 2.35 (95% CI: 1.92, 2.79) and those living in neighborhoods with high disorder (top 50%) had a mean AL of 2.82 (95% CI: 2.35, 3.28). Using z-score sums, residents living in neighborhoods with lower disorder had an AL of -0.52 (95% CI: -1.72, 0.68) and residents in more dispersed neighborhoods had an AL of 0.28 (95% CI: -0.71, 1.26).
Conclusions: While not statistically significant, we found a trend towards higher AL scores in more disordered neighborhoods, suggesting that residents of more disordered neighborhoods have higher levels of stress. We were constrained by a small sample size, and additional data is needed from larger cohorts to better understand the mechanisms underlying associations between neighborhood disorder and health.

61 NUTRITION AND GARDENING EDUCATION FOR YOUTH IN WHITE SALMON, WASHINGTON
McEntee K. University of Washington School of Medicine, Spokane, WA.
Purpose of Study: As with many small communities, White Salmon, WA is challenged by poverty and food insecurity. A large portion (20.4%) of its inhabitants fall under the poverty line (compared to 12.5% in Washington state), and 65% of children born in Klickitat County qualify for the WIC program. The Klickitat County WIC Coordinator described families subsisting on Top Ramen and processed foods, and this theme was often repeated: access to healthy, affordable food is a large barrier to proper nutrition and health in the White Salmon community. The goal of the project was to heighten curiosity and broaden knowledge about fruits and vegetables, while also empowering youth to increase their access to fresh foods by basic gardening education.
Methods Used: In order to develop the project, I spoke with various Public Health officials and health care providers to confirm the need for improved nutrition in White Salmon. The White Salmon Community Youth Center offered to partner with the project as a venue. I performed a literature review to inform the project, and found support for an interactive, garden-based nutrition workshop for youth.
Summary of Results: A total of 14 youth from 1st - 6th grade attended the workshop held at the White Salmon Community Youth Center. Supplies were donated by Vanguard Nursery and Dr. Witherite, a local family physician. Fifteen varieties of fruits and vegetables were arranged on a table, and participants played interactive games identifying the produce by sight and taste, highlighting important points about healthy living—such as exercise and eating less processed food. All students participated in a blindfolded taste test game, and there was much less resistance to eating vegetables than anticipated. The workshop concluded with hands on gardening education; each participant planted and took home their own container garden of peas and green beans.
Conclusions: The strengths of this intervention were the hands-on, interactive approach to teaching nutrition. Although no outcome metrics were used, it was subjectively clear that all the students had lots of fun, and the concept of eating fruits and vegetables was encouraged as a fun and exciting thing, not just a moral “should.” A future workshop like this might also benefit from a focus group with the youth to identify knowledge gaps and barriers to eating fresh produce.

62 DETERMINING BARRIERS THAT PREVENT INCREASED EXERCISE AND FRUIT/VEGETABLE INTAKE IN WILMINGTON, CA
Mejia M. Charles Drew School of Medicine and Science, Los Angeles, CA and 2David Geffen School of Medicine, Los Angeles, CA.
Purpose of Study: To assess potential exercise and nutrition barriers that prevent those living in Wilmington, CA from having a BMI of less than 25.
Methods Used: Approximately 100 participants at a local health fair on July 20, 2013 filled out a registration from that included numerous demographic information. The participants’ height and weight were also measured to determine BMI, and then asked 5 questions regarding their exercise and fruit/vegetable intake. SPSS was used to analyze the survey data and determine correlation between survey questions and education level, income, health insurance status, BMI and having a regular doctor.
Summary of Results: Among those who reported 0 days/wk of exercise, there was a statistically significant difference between those who were overweight that did not exercise compared to those who were normal and obese (p<0.01). There was also a statistically significant difference across all three groups in regards to level of education for those who reported 0 days/wk of exercise. Those with less than an 8th grade level of education were less likely to exercise (p<0.001). For those who exercised less than three days per week, many cited working long hours as a reason for not exercising more often. Among those who did not prepare food at home, many mentioned having the food prepared quickly and enjoyed eating out with friends and/or family as reasons for not making food at home.
Conclusions: Numerous barriers prevent individuals in Wilmington, CA to consume the correct amount of fruits and vegetables in their diet and get an appropriate amount of exercise. Further investigation into the causes of obesity in underserved areas is warranted to help tailor health interventions that educate these individuals about increasing exercise and food and vegetable consumption, in addition to policy measures that support a healthier surrounding environment.

63 FRISBEE GOLF FAMILY DAY: A CHILDHOOD OBESITY INTERVENTION IN DAVENPORT, WA
Metzger P. University of Washington School of Medicine, Seattle, WA.
Purpose of Study: According to the 2012 Washington State Healthy Youth Survey, 19 percent of eighth grade students in Lincoln County are overweight and 6 percent are obese. In 2011, the Lincoln County Public Health Coalition created the 54321 Let’s Go LinCo! program to reduce the number of children who are overweight or at risk of becoming overweight. The primary aims of this project were:
1. To promote the 54321 Let’s Go LinCo! message in Davenport, WA during the summer
2. To engage with parents and children in a conversation about developing healthy behaviors
3. To improve lifelong community health outcomes by reducing youth obesity.
Methods Used: The Lincoln County Public Health Department determined that the existing 54321 Let’s Go LinCo! program would benefit from reinforced messaging during the summer. A literature search found that a single health-education event linked to a long-term, community-based obesity intervention could contribute to reductions in childhood obesity rates. We designed a 5-hole Frisbee golf course in Davenport City Park. Each hole had a theme based on 1 of the 5 recommendations in the existing 54321 program. The course required participants to land a Frisbee in a “hole” and engage in a discussion focusing on the health behavior at each hole. The course was open on a Friday afternoon from 4:30-6:30pm during the city’s Farmer’s Market to encourage participation.
Summary of Results: 20 participants comprised of 5 families completed the course. 3 of the 5 families had at least one parent that played with their children. Community volunteers were stationed at each hole and conducted health-education demonstrations or challenges in association with the 54321 program recommendations. The Lincoln County Public Health Office provided 54321 program informational pamphlets, and volunteers handed out buttons with the 54321 program logo to further promote the program’s message.
Conclusions: Childhood obesity is a national health challenge that will affect lifelong health outcomes. Community interventions like the 54321 Let’s Go LinCo! program have been shown to reduce childhood obesity. In keeping with the 54321 model, the Frisbee golf course was both an engaging athletic activity, and the challenges at each hole provided facts about healthy behaviors for future conversations within families regarding healthy choices.
become a growing concern with 50 new confirmed infections since the beginning of this year. Furthermore, studies have shown that tattoos performed in non-sterile settings carry a risk of HCV transmission. Therefore, the purpose of this study is to increase tattooing safe practices through educating the low income/homeless population on the risk factors and proper techniques of the art.

Methods Used: A review of the literature revealed that there is a significant association between receiving tattoos in a non-sterile fashion and HCV. The papers cited home tattoos, tattoos received in shops using improper sterile technique, and receiving tattoos in jail were risk factors for contracting HCV. With this information, a partnership with a local homeless shelter (Samaritan House) and their annual event (Homeless Connect) that provides services to the low income and homeless was made.

Summary of Results: Tattoo shops in the area with certification were provided materials for workers and customers to read regarding safe tattoo practices. The event served 635 people, and an information booth was set up at this event that attracted 15 individuals, and 10 expressed a lack of knowledge in the safety hazards of tattoo application. Furthermore, Temple Décor, a local tattoo shop, volunteered information on their safety technique for the event and agreed to continue to provide safety materials for their customers.

Conclusions: HCV is a chronic illness that is becoming of growing concern in the community of Kalispell. Education about preventing the spread of HCV by cleaning needles during drug use has been widespread; however, education about safe tattoo practices has been lacking in the effort to prevent further spread of HCV. This project confirmed that the tattoo shops in the area and the population of Kalispell have shown a willingness to learn and help educate those seeking tattoos on the need for safe tattoo practices.

INCREASING AWARENESS AMONG YOUNG MOTHERS ON OPIOID USE DURING PREGNANCY AND ITS IMPACT ON INFANT CARE

Paolilla L.J. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Opioid dependency is a growing issue across many communities in the United States. Rural areas have experienced a higher burden, an earlier onset of use, and greater risk for long-term dependency. In Clallam County (Washington), opioid-related deaths per 100,000 people are almost double the state average and have increased over 50% in the last ten years. Opioid exposure during pregnancy can lead to dependency in newborns, known as Neonatal Abstinence Syndrome (NAS), characterized by infant hyperirritability, indigestion, and breathing difficulties. Infants with NAS experience higher rates of maternal neglect and developmental delay. The goal of this project is to increase awareness among young mothers and provide techniques on how to care for affected infants.

Methods Used: Common characteristics of Neonatal Abstinence Syndrome and effective strategies of care for opioid-affected newborns were incorporated into a one-page informational sheet. This was provided to area individuals at high-risk for opioid use during pregnancy in an effort to improve education of the health consequences for the developing baby. Intensive discussion in Port Angeles area support center focused on educating individuals that may care for infants with NAS.

Summary of Results: During a community event hosted by The Answer For Youth (TAFY), seven couples were approached and were counseled on the symptoms of Neonatal Abstinence Syndrome and care techniques for affected infants. The average number of children per couple was 1.9. Fifty-seven percent of participants had used a recreational drug in the past, with methamphetamine being the major agents. Of the 13 adults present, only one thought they may have been learned about NAS previously, but all found the education valuable.

Conclusions: Increasing rates of opioid use during pregnancy in Clallam County threaten the health of many mothers and babies, and will require well-coordinated intervention. Participants expressed limited knowledge of how opioid use during pregnancy could impact the health and care of the developing infant, but found information valuable. Early education of mothers and prospective mothers on the risks of opioid use during pregnancy is an important component of controlling and ultimately preventing Neonatal Abstinence Syndrome.

COPD PREVENTION IN AN AGRICULTURAL SETTING THROUGH EDUCATION IN BAKER, MONTANA

Schafer M. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: The mortality rate in Fallon County, MT due to COPD is 73% (69.9/100,000) higher than the national average (40.8/100,000). Smoking, although a major cause of COPD is not the only cause, and many occupational exposures such as farming and ranching are also risk factors for developing COPD. Fallon County has a largely agriculturally based economy and many farmers and ranchers are generally not aware of the risks of occupational exposures and the measures that can be taken to prevent acquiring COPD. This project was intended to create awareness of other potential causes of COPD and methods of prevention in an agricultural environment.

Methods Used: A literature review was completed to determine evidence based risk factors for acquiring COPD and what preventative measures could be used and presented to the public in order to help them prevent exposure to agricultural causes of COPD. With the support of Fallon Medical Complex (a multi-use health facility in Baker, MT that provides a hospital, clinic, nursing home, independent living, dentistry, chiropractic and physical therapy in one building) an advertisement was placed in the weekly county newspaper. The information was also broadcast by the local radio station describing the time and place of the presentation.

Summary of Results: While the results of this public educational forum are not known, the public meeting was encouraging. Around thirty community members were present and many perceptive questions were asked. Several people expressed that they had relatives and friends with COPD, so it was an issue that hit home for many. Two community members were especially curious about preventative measures that could be taken. Many more had COPD themselves and were more interested in treatment options.

Conclusions: COPD is a major health issue in Fallon County as well as the state of Montana. Smoking and an economy with a large base in agriculture are contributors to the diseases prevalence. Public education on prevention as well as cooperation from healthcare providers, clinics and other organizations with an interest in public health may play important roles in COPD mortality reduction.

EVALUATION OF DAIRY GOAT PROJECT TO IMPROVE THE NUTRITIONAL AND ECONOMIC BENEFIT OF LOCAL GOATS IN RURAL KENYA

Schaefer M. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: The Global Health Initiative (GHI) at the University of British Columbia is partnered with Partners in Community Transformation (PCT) in Western Kenya to deliver sustainable livelihood projects with the aim of improving community health and socio-economic well-being. Based on an analysis of community needs, the GHI-PCT alliance designed several projects aimed to target these disparities including a dairy goat project directed at increasing community nutrition and economic wealth. To ensure sustainability, this project demands a thorough evaluation of project outcomes, challenges, and potential for growth.

Methods Used: The dairy goat project created 27 buck stations within the community, where residents can bring local goats to be serviced to create milk-producing offspring. Since the initiation in 2010, we have expanded the project to include government funding and external training by the Ministry of Agriculture and the Dairy Goat Association of Kenya. During the summer of 2013, three GHI students conducted a qualitative analysis of the dairy goat project through visits to these buck stations. The stations were evaluated on goat and housing structure maintenance, including successes, failures, and challenges.

Summary of Results: There were many challenges identified including problems with shared responsibility for feeding and cleaning, infection control, birthing, and feeding offspring. This prompted the creation of revised goatkeeping guidelines for 4 of the sites and increased site visits from PCT are expected during the next year for us to continue evaluating progress. Proper education and training for the goat keepers has proved to be a fundamental step in the success of this project.
Conclusions: The goal of the GHI-PCT dairy goat project is to establish a sustainable means to improve the nutritional and economic benefit of the local goats. A step to greater success and expansion will entail community sensitization to continue to relay the benefits of the project for community members and to encourage the use of the back stations. Moving forward, we hope that this will be the last year of funding for this project, as it is expected that the project will become fully self-sustainable.

68

IMPROVING PRENATAL EDUCATION AND SUPPORT IN GILLETTE, WYOMING
Shickich M. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Gillette is coal-mining town in Northeast Wyoming. Home to many young individuals in their peak reproductive years, Gillette has a birth rate double the national average. With a large transient population due to the mining, many young pregnant couples arrive with limited knowledge of local resources, limited social support, and little to no health insurance. Under-resourced pregnant women in the community face additional challenges including costly prenatal care, lack of sliding scale fee clinics, and complicated federal assistance applications. Local programs exist to help women navigate these obstacles, but are underutilized. This project sought to connect under-resourced pregnant women to basic prenatal education, local prenatal resources, and social support.

Methods Used: Guided by the relevant literature, and in partnership with the Public Health Department, a community gathering was designed to educate under-resourced women about pregnancy basics and local support services, and assist in building social support. The event was advertised with fliers at locations frequented by the target population and was hosted at two times to decrease barriers to attendance. The semi-structured talk was modeled after the successful “Centering Pregnancy” concept that utilizes interactive group prenatal education and incorporated adult learning theory.

Summary of Results: Hosted at the local Public Health Department in partnership with the Department’s prenatal program, the talk included an educational handout and a presentation guiding an interactive session. The talk was facilitated with an emphasis on group discussion. The six attendees were primarily local nurses and public health staff who obtained information about prenatal care resources for their clients. To ensure that the information reached the target population, all presentation materials were made available for attendees to distribute to their clients.

Conclusions: Gillette is home to many pregnant women with multiple barriers to prenatal care. Many of these barriers prevented the target population from attending an event designed for them. As such, the talk was redirected to the population in attendance. Local health providers engaged in a lively discussion surrounding prenatal care in the community. The target population was reached indirectly through the education and engagement of health providers.

69

A SIMULATION MODEL FOR SYMBIOTIC MULTI-SPECIES COEVOLUTION IN A COMMUNITY CONTEXT
Tian L1, Liu Y1,2,1Shenyang University, Shenyang, China and 2Shenyang University, Shenyang, China.

Purpose of Study: Natural selection tends to enable living organisms to adapt to their environments by the processes of interaction. In recent years, symbiosis as a rich source of potential engineering applications and computational model has attracted more and more attentions in the adaptive complex systems and evolution computing domains.

Methods Used: In this work, we implement an entire symbiotic simulation model which consists of both heterogeneous and homogeneous coevolution aspects in formulating our symbiotic simulation models. We introduced several symbiotic species each possesses a number of individuals into this coevolution model to represents the “biological community”. The coevolution process in our model is hierarchical and contains three levels. Clearly we model more details of the social behaviors in nature ecosystems and tie this model closer to natural evolution.

Summary of Results: Inspired by different symbiotic coevolution forms in nature, the simulation performs four versions of the proposed model to mimic mutualism, commensalism, parasitism, and competition mechanism, respectively. The simulation results are encouraging: all the algorithms have markedly superior search performance in terms of accuracy, robustness and convergence speed on all benchmark functions. We also simulated the coevolution process of a number of distinct species in our biological community model, and the simulation result is consistent with the natural phenomenon (i.e., the biological diversity is sustained after many coevolutionary gene-rations, and the adaptive abilities of the interacting individuals / species are greatly increased.)

Conclusions: The models of evolution that are being used in evolutionary and swarm intelligence algorithms are becoming increasingly complex. Hence, this work proposed a symbiotic multi-species coevolution model. The model has been instantiated as four novel multi-species optimizers. The simulation results capture some important aspects of the dynamics of biological coevolution that some evolutionary biologists believe takes place in nature.

Acknowledgement: This work was supported in part by the International S&T Cooperation Program of China (STSCP) under Grant 2011DAF01810-5, the Program for New Century Excellent Talents in University of Ministry of Education of China under Grant NCET-12-1012.

69A

MISUSE AND ABUSE OF PRESCRIPTION OPIOIDS: AN EDUCATIONAL INTERVENTION FOR AT-RISK ADULTS IN DILLON, MT.
McCormick R. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: In Montana, more citizens die from overdose of prescription medications than in car crashes, or from all other illegal drugs combined. The most common of these misused and abused prescription medications are opioid analgesics. In rural towns like Dillon, MT the burden is even worse. Those at highest risk for misuse of and addiction to prescription opioids are patients with a history of chemical dependence, mental health problems, or victims of abuse. To address one of these at-risk groups, an educational intervention targeted at members of the Southwest Montana Chemical Dependency Group (SMCDG) was carried out. The purpose of the intervention was to improve health literacy, and thus reduce future prescription opioid abuse behavior.

Methods Used: Social service and healthcare professionals of Dillon were interviewed and confirmed that prescription opioid abuse is a significant problem in the community, and that the protocol for prescribing opioids and educating patients on the risks of opioid use is inconsistent. Literature on adult learning theory and the efficacy of adult education to improve health literacy was reviewed. Then, a health education presentation on the use and abuse of prescription opioids was given to clients at the SMCDG. A follow-up discussion was led, and an informational handout on prescription opioid risks was distributed and left with the SMCDG for reproduction.

Summary of Results: Eleven clients of the SMCDG attended the evening educational talk. The group members participated in discussion asking questions and sharing personal stories. Positive feedback was received from a short survey completed at the end of the talk. All participants reported learning at least some new information from the presentation, and the majority reported that their learning would be helpful in avoiding future abuse and misuse of opioids.

Conclusions: This educational intervention was successful in the sense that participants showed up, listened, and engaged; but it is hard to how much their behavior might change as a result. In the future, it would be helpful to design a parallel intervention educating prescribers on patient screening and education in order to further close the gaps between prescribed pain medi-cine and safe compliance.

Poster Session I
Developmental Biology
2:30 PM
Thursday, January 23, 2014

70

EFFECTS OF ENROFLOXACIN ON CYP450s IN MICE
Li Y1, Lu L2,1, Lin J, Qiu J1, Ai X1, Wang X1. 1Shanghai Jiaotong University, Shanghai, China and 2Sichuan Agricultural University, Yaan, China.
Purpose of Study: Enrofloxacin (EF) is an antibacterial agent that has been worldwide used in veterinary medicine and animal breeding. However its effects on drug metabolizing enzyme of liver is unclear. This study was to explore the effects of EF on the activity of some important enzymes in CYP450 family and their protein expressions in mice.

Methods Used: In vivo test, the experimental mice were intraperitoneal injected EF as 5 (low dose group), 25 (middle dose group) and 125 (high dose group) mg/kg-1 respectively, once per day for 5 days. In vitro test, EF were added to the mice hepatic microsome incubation systems as the final concentration of EF in the solution were 5 (low dose group), 25 (middle dose group) and 125 (high dose group) mmol-1 respectively. Then the microsome mixture was incubated at 37 degrees centigrade for 1h. The mouse liver microsome was extracted by low temperature differential centrifugation. The contents of CYP450 and b5 were detected by CO reducing differential spectroscopy and b5 scanning spectra. The activities of CYP1A2, CYP2B6, CYP2C9, CYP2E1 and CYP3A4 were detected by fluorescence method. The expression of CYP1A2, CYP2B6, CYP2C9, CYP2E1 and CYP3A4 in mice was detected by Western-Blot.

Summary of Results: The low dose EF had no effect on the content of mice hepatic microsomal P450 and b5 (P>0.05) compared with the control both in vivo and vitro test. However, the middle and high dose EF had significant inhibition effects (P<0.05). All the low, middle and high dose EF treatments had significant inhibition effects on the activities of mice CYP1A2, CYP3A4, CYP2C9 (P<0.05). The low dose EF had significant inhibition effect on the activities of mice CYP2E1 (P<0.05). The activities of mice CYP2E1 were extremely significant induced by the middle and high dose EF (P<0.01).

Conclusions: The content of mice micromomal protein, CYP450 and b5, and the activities was protein expression of CYP1A2, CYP2B6, CYP2C9, CYP2E1, CYP3A4 could be affected by EF. These effects were EF dose dependent, and also related to the different enzymes.

71 MEDICAL IMAGE SEGMENTATION USING BIO-INSPIRED APPROACHES

Liu Y1,2, Ha K1, Tian L2, Zhu Y1, Chen H1. 1Chinese Academy of Sciences, Shenyang, China and 2Shenyang University, Shenyang, China.

Purpose of Study: Image segmentation is of great importance in the field of medical imaging. The result of medical image segmentation is a set of areas that collectively cover the entire image, or a set of contours extracted from the image that have a special pharmacological meaning.

Traditional image segmentation methods fall into five categories: pixel based segmentation, region based segmentation, edge based segmentation, edge and region hybrid segmentation, and clustering based segmentation. However, these types of image segmentation algorithms commonly suffer from the problems of computational costs and long time consume.

Methods Used: In this work, we introduce a new bio-inspired image segmentation algorithm based on pulse coupled neural network (PCNN) and particle swarm optimization (PSO). The image was firstly segmented by PCNN, and then the PSO algorithm was used to automatically set parameters of PCNN, so that the segmentation performance would be adjusted adaptively.

Summary of Results: The experiments of segmentation of different brightness and contrast based on PCNN-PSO on a set of gray-scale medical images are performed. With the new image segmentation method based on PCNN-PSO, the segmentation results mainly depends on the intrinsic properties of the image. The detail of the image is very clear, and the image's shape is obvious, and there was no isolated point. Apparently, this algorithm greatly increases the flexibility and efficiency of PCNN and makes it possible for the application of PCNN in image segmentation to be implemented in hardware.

Conclusions: In another simulation study, we converted the RGB image into HSV space. Here, H represents different colors, S represents the density of color, and I represents the luminance of color. We eliminated the relevance of each component and applied the proposed PCNN-PSO to each vector. Then we can take advantage of the excellent technical effect on grayscale images to color image segmentation. The Experimental results also show the bio-inspired method's usefulness with high segmentation accuracy.

Acknowledgement: This work was supported in part by the International S&T Cooperation Program of China (IStCP) under Grant 2011DFA09180-15, the Program for New Century Excellent Talents in University of Ministry of Education of China under Grant NCET-12-1012.

72 HAND ASYMMETRY IN BREAST-FED VS. FORMULA-FED CHILDREN

Nouri G, Martin J. Western University of Health Sciences, Pomona, CA.

Purpose of Study: Studies have shown asymmetry in various anatomical structures but there is little known about the causes of this asymmetry. Earlier studies have suggested that asymmetrical digit ratios in adults maybe an indicator of early steroid hormone exposure, possibly in breast milk. In order to investigate the existence and causes of asymmetry in children, we compared hand and finger measurements in three groups of children, those who were breastfed exclusively, formula-fed exclusively and a combination of both. Since breast milk contains estrogen which is not present in formula, we hypothesized that there will be a significant hand asymmetry in breast-fed subjects.

Methods Used: A total of 97 subjects between the ages of 18 months and 18 years were measured. Child-feeding history was obtained from the parents or guardians from a questionnaire, as well has height, weight, and birthdays by reviewing their medical records. Measurements of digits 2 and 4, hand width, and hand length were taken from hand scans.

Summary of Results: With all males and females combined, there was a significant rightward hand length asymmetry in older children, with right hand length to stature ratios higher than the left. However, feeding regimen did not affect this positive correlation between age and asymmetry. Females that were formula fed had significant leftward asymmetry in hand length and differed from formula fed males in hand length asymmetry. Also, males had significantly higher right 4th digit ratios that were adjusted for stature.

Conclusions: The findings suggested that rightward hand asymmetry becomes more prominent with age, but feeding regimen does not affect this positive correlation. This could be due to the increasing hormone levels as a child ages, and these hormones could have a greater effect on the right hand than the left. There was significant rightward 4th digit asymmetry in exclusively breast-fed males and leftward hand length asymmetry in exclusively formula-fed females. A possible explanation for this difference between males and females is that the estrogen in breast milk had different effects on males versus females, since females may have more estrogen receptors in different parts of the body than males. It can also be concluded that breast milk prevents the development of leftward asymmetry in female children.

73 MOLECULAR CLONING AND CHARACTERIZATION OF SMAD2 AND B-CATENIN FROM STEM-LIKE LARYNGEAL CARCINOMA CELLS

Zhao Z1, Wang Y1, Lv X2, Nie Y2, Wu J1,2. 1Sichuan University, Chengdu, China and 2Xinjiang Medical University, Urumqi, China.

Purpose of Study: Recent studies on the pathobiology of laryngeal squamous cell carcinoma have led to the discovery of a small population of cancer cells that is highly tumorigenic, capable of self-renewal, and behave as stem-like cells. Epithelial-mesenchymal transition (EMT) appears to be involved in the process leading to the acquisition of stemness by tumor cells. As key components of TGF-β induced EMT signal transduction pathways, Smad2 and β-catenin are crucially involved in the development of invasion and metastases, and act as possible mediators of cell-cell communication that occurs between stem-like cells and hosts. Therefore, we have now cloned and characterized the complete complementary DNA (cDNA) molecule encoding Smad2 and β-catenin from stem-like cells of the human laryngeal squamous cell carcinoma.

Methods Used: Stem-like cells have been isolated and identified laryngeal squamous cell carcinoma using markers such as CD133 and CD44 expression, and aldehyde dehydrogenase (ALDH) activity. DNA encoding Smad2 and β-catenin were isolated using RT-PCR from laryngeal stem-like cancer cells. Their expression were detected at the transcriptional and protein levels in laryngeal stem-like cancer cells and tissues of laryngeal squamous cell carcinoma by Western blotting and immunofluorescence. Both of Smad2 and β-catenin were localized in moderately and poorly differentiated laryngeal cancers higher than in their adjacent tissues.

Summary of Results: The positive expression of Smad2 was mainly positive in cytoplasm and membrane of laryngeal stem-like cancer cells, and β-catenin
was localized in the cytoplasm and/or nucleus, the expression of Smad2 was positively correlated to the cytoplasmic expression of phospho-β-catenin (r=0.511, P<0.01), but had no correlation to the nuclear expression of phospho-β-catenin (r=0.134, P>0.05).

Conclusions: We have cloned and characterized Smad2 and β-catenin from laryngeal stem-like cancer cells. Smad2 and β-catenin may mediate TGF-β-induced EMT and subsequent invasion and metastases, suggesting that inhibition of those small molecules is a possible therapeutic target for prevention of laryngeal squamous cell carcinoma.

74

THE COLLECTION EFFICIENCY OF A LOW COST LASER MICRO-DISSECTION SYSTEM FOR PURE BIOLOGICAL SAMPLE PREPARATION

Yi, D Motic China Group CO., Xiamen, China.

Purpose of Study: Laser micro-dissection (LMD) is both a method and a system that is widely used in the field of life science to obtain purified samples for downstream experiments. Though a LMD is an essential tool for pure sample preparations, it is highly expensive with a typical price of about US$200K, hence is not affordable for an ordinary laboratory. This study is to evaluate the collection efficiency of a low-cost LMD.

Methods Used: Motic LMD consists of an inverse biological microscope AE31, a high-precision high-speed automatic stage that is capable of smooth movement in all three dimensions (X, Y and Z), a high-energy (120μJ) diode laser system with the capability of automatic adjustment of energy level and pulse frequencies, a control box for the generation of smooth cutting curves, an user-friendly software, a high resolution color camera, and a sample collecting arm which can simultaneously hold multiple poly-chain-reaction (PCR) cover slips of two sizes: 50μl and 20μl. There are typically three sequential steps for pure sample collections using a laser micro-dissection system, the first one is to prepare glass slides covered with a thin membrane, the second step is to place the biological sample which is typically either frozen or paraffin-embedded tissues on the membrane covered glass slide, the third step is to use a laser micro-dissection system to actually select, cut and collect a group of pure cells for downstream experiments.

Summary of Results: After finishing cutting all of the 20 user selected ROIs, the user manually adjusts the collector arm in the X, Y, and Z directions, primarily in the Z direction to move it into focus of a 4X objective to visually observe collection results, and find there are 19 pieces out of the 20 user selected ROIs being collected, leaving only one large sample of size near 3000μm remain on the glass slide. This study demonstrate a collection efficiency of 95%.

Conclusions: Motic LMD provides high collection efficiency that satisfies user requirement of purifying sample collection for downstream experiments. Several separate studies are conducted to further validate that the collected samples are of good quality for downstream DNA/RNA/protein experiments.

Acknowledgement: This work is partially supported by the Chinese National Science & Technology Pillar Program with contract # No.2012BAI23B04.

Poster Session I
Endocrinology and Metabolism

2:30 PM
Thursday, January 23, 2014

75

ASSOCIATION OF LICHEN PLANOPILARIS WITH THYROID DISEASE IN A CLEVELAND CLINIC POPULATION: A RETROSPECTIVE CASE-CONTROL STUDY

Brankov N, Atanaskova-Mesinkovska N, Bergfeld WF. Cleveland Clinic, Cleveland, OH.

Purpose of Study: Clinically, we see many thyroid disease patients with lichen planopilaris (LPP) at Cleveland Clinic and studies are limited on its association. The objective of this study was to determine the prevalence of thyroid diseases in patients with LPP.

Methods Used: This was a retrospective case-control study using data from the medical records of LPP patients (n = 166) and age- and sex-matched controls (n = 81) evaluated at the Cleveland Clinic Department of Dermatology, from 2000 to 2013. Demographic factors, such as age, sex, and race were recorded. The presence of thyroid disease at first evaluation and subsequent follow ups were recorded.

Summary of Results: Thyroid gland disease or history of thyroid disease was found in 33% (n = 57) of the 166 LPP patients and in 11% (n = 9) of the control subjects (p = 0.0001). When confined to hypothyroidism only, this disease was found in 29% (n = 48) of the LPP patients and 9% (n = 7) of the control subjects (p = 0.0003). The majority of hypothyroid LPP patients had a prior hypothyroid diagnosis (n = 41, 85%); however, LPP was diagnosed preceding hypothyroid diagnosis in 15% (n = 7) of the hypothyroid LPP patients.

Conclusions: Patients with LPP have increased associations with thyroid disease, in particular hypothyroid conditions, which suggests that LPP patients should be screened for thyroid disorders. In the future, further investigations of the mechanisms of this association might be worthwhile in understanding the pathogenesis of LPP.

76

GIANT ADRENAL MYELOLIPOMAS IN A PATIENT WITH CONGENITAL ADRENAL HYPERPLASIA

Navabi K, Shariff M, Bouchonville MF, Kapsner P. University of New Mexico Health Sciences Center, Albuquerque, NM.

Case Report: Adrenal myelolipomas are rare benign tumors of the adrenal gland composed of mature adipose tissue and bone marrow elements. They are typically nonfunctioning, less than 4 cm, and most often discovered incidentally during autopsy or on imaging studies performed for other reasons. Although their exact incidence is unknown, autopsy studies have shown it varies from 0.08 to 0.4% and that they account for 3 to 5% of all adrenal tumors. We report a 29-year-old female with a history of congenital adrenal hyperplasia (CAH) attributed to 21-hydroxylase deficiency treated with prednisone and fludrocortisone presenting with recurrent left upper quadrant and flank pain. Physical exam was remarkable for an androgynous appearing woman without virilization. Vital signs showed normal blood pressure and tachycardia. Left sided abdominal tenderness was present. Laboratory data showed 17-OH progesterone 717 ng/dL (< 139 ng/dL), plasma renin activity 22.7 ng/ml/hr (0.5-4.0 ng/mL/hr) and normal electrolytes.

Serial abdominal CT scans performed over several years showed bilateral adrenal nodularity consistent with CAH and the development of bilateral adrenal myelolipomas in 2011. Most recent CT scan showed a heterogeneous left adrenal mass with soft tissue and gross fatty components, consistent with a giant myelolipoma, measuring 80 x 37 mm at the largest diameter (previously 77 x 34 mm). The right, adrenal gland showed a smaller lobulated mass, characteristics also consistent with a myelolipoma, measuring approximately 5 cm, not significantly changed in size comparing to previous years.

While myelolipomas of the adrenal gland are rare, giant myelolipomas occur even less frequently with only case reports in the literature. Giant adrenal myelolipomas may be associated with CAH. We will review the literature regarding giant adrenal myelolipomas, their pathogenesis and possible association with CAH as well as recommended therapy.

77

A CASE OF ADRENAL AND EXTRA-ADRENAL PHEOCHROMOCYTOMAS/PARAGANGLIOMAS ASSOCIATED WITH ONCOCYTIC ADRENOCORTICAL NEOPLASM

Tabrizi M1, Bouchonville MF1, Hanson J2, LeBlanc M2, Kapsner P1.1 University of New Mexico School of Medicine, Albuquerque, NM and 2 University of New Mexico School of Medicine, Albuquerque, NM.

Case Report: Paraganglioma is a rare tumor originating from extra-adrenal chromaffin cells and pheochromocytoma arises from chromaffin cells of the adrenal medulla. Early diagnosis and surgical planning are crucial, as these tumors secrete catecholamines and may be adjacent to large vessels. Adrenal oncocytic neoplasms are rare and mostly benign, usually presenting as incidental, large adrenal masses for which surgery is the main therapy. The
combination of adrenal and extra-adrenal pheochromocytomas/paragangliomas associated with oncocytic adrenocortical neoplasms in one patient is a very rare condition.

We report a case of a previously healthy 19 year-old female presenting with intermittent episodes of headache, blury vision, palpitations, back and abdominal pain who was found to have a catecholamine-secreting tumor. 24 hr urine norepinephrine was 1528 mcg (reference 0-18 mcg/day) and normetanephrine was 5628 mcg (reference 82-500 mcg/day). CT with contrast revealed a left adrenal nodule with heterogeneous soft tissue masses adjacent to the duodenum and bilateral renal veins. PET-CT showed a FDG avid left adrenal mass and two separate FDG avid retroperitoneal masses. MIBG scan showed increased radiopharmaceutical uptake in the left adrenal gland as well as multiple areas of extra-adrenal uptake in the abdomen and retroperitoneum.

The patient underwent an open left adrenalectomy and retroperitoneal lymph node dissection. Pathologically, there was a microscopic pheochromocytoma (0.7 cm) as well as multiple extra-adrenal paragangliomas. A separate oncocytic adrenocortical neoplasm was found demonstrating focal fat invasion, nuclear atypia, calcification, and ossification. Additionally, a posterior caval mass and a left periadrenal mass were revealed to be oncocytic adrenocortical neoplasms. Four lymph nodes were benign.

We will present a review of the literature including pathology, genetic testing, prognostic indicators and therapeutic interventions related to pheochromocytoma/paragangliomas and oncocytic adrenocortical neoplasms.

Poster Session I
General Internal Medicine and Aging
2:30 PM
Thursday, January 23, 2014

78
QUANTITATIVE ASSESSMENT OF FACIAL PARALYSIS USING FORMAL CONCEPT ANALYSIS IN BIOMEDICAL THERMAL IMAGES
Liu X1, Zhang Z2, Luan J1, 1Northeastern University at Qinhuangdao, Qinhuangdao, China and 2Yanshan University, Qinhuangdao, China.
Purpose of Study: Facial paralysis is the loss of voluntary muscle movement of one side of the face, it physically, aesthetically and emotionally devastated to an individual. This study was to establish an approach for automated computerized assessment of thermal images of facial paralysis, in order to facilitate the physician’s decision making.

Methods Used: This study presented a novel approach for objective assessment of facial paralysis based on infrared thermal imaging and formal concept analysis. First, the facial thermal images were pre-processed to identify six potential regions of bilateral symmetry by using image segmentation techniques. Finally, we explored the relationships between the statistical averages of those temperature differences and the House-Brackmann score for objective assess the degree of facial nerve damage using formal concept analysis.

Summary of Results: The facial temperature distribution of the patients with facial paralysis exhibited a contralateral asymmetry, and the bilateral temperature differences of the facial regions were greater than 0.2 degree centigrade, whereas in normal healthy individuals these temperature differences were less than 0.2 degree centigrade. Furthermore, if one of the temperature differences of bilateral symmetry on facial regions was greater than 0.2 degree centigrade, and all were less than 0.5 degree centigrade, facial paralysis could be determined as for the mild to moderate.

Conclusions: Infrared Thermal imaging is an effective technique for detecting small temperature changes due to facial paralysis, it is non-invasive, objective and reliable for quantitative assessment of facial paralysis.

IDENTIFYING THE RELATIONSHIP BETWEEN THYROID DISEASE AND ALOPECIA AREATA, LICHEN PLANOPILARIS, AND FRONTAL FIBROSING ALOPECIA
Nguyen TQ Goh C. UCLA David Geffen School of Medicine, Los Angeles, CA.
Purpose of Study: Alopecia, or the loss of hair, can be scarring or nonscarring and can be related to a variety of factors including thyroid hormone dysfunction. While a history of thyroid disease has been linked to alopecia areata (AA), the role of thyroid disease has not been conclusively established in other types of alopecia such as lichen planopilaris (LPP) and frontal fibrous alopecia (FFA). This study explores the association between thyroid disease and AA, LPP, and FFA and to determine whether there is an increased risk of thyroid dysfunction in these patients.

Methods Used: A retrospective cohort study was performed to identify patients with AA, LPP or FFA from the UCLA Hair Disorders Clinic from September 2010 to July 2013. A control group of patients without alopecia was selected from the UCLA Dermatology Clinic from the same provider. A systematic chart review was performed to evaluate for thyroid disease, gender, age, and type of hair loss.

Summary of Results: There were 113 alopecia patients: AA (n=50), LPP (n=35), and FFA (n=28) with a mean age of 50.47 years (n=113) and a mean TSH value of 2.18 mIU/L (n=62). There were 31 controls with a mean age of 49.48 years and TSH value of 1.93 mIU/L. There were 8 AA (16%; p=0.7046), 7 FFA (25%; p=0.9487), 6 LPP (17.4%; p=0.7754), and 5 Controls (15.13%).

Conclusions: Compared to the general population, patients in all groups, including the control group, had a higher prevalence of thyroid dysfunction. It is unclear, therefore, if an increased prevalence of thyroid dysfunction can be attributed to the increased risk of thyroid disease, although AA has been previously associated with thyroid disease. Further exploration of this question with a larger patient population may elucidate any possible association. Screening for thyroid disease in patients with AA, LPP, and FFA may be considered.

Poster Session I
Neonatology General
2:30 PM
Thursday, January 23, 2014

80
NEUROBEHAVIORAL PERFORMACE OF INFANTS IN THE NEONATAL INTENSIVE CARE UNIT
Crane T, Neece C, Tagge E. Loma Linda University, Loma Linda, CA.
Purpose of Study: Infant neurodevelopmental evaluation is becoming increasingly important for a large number of infant scenarios, including extreme prematurity, perinatal asphyxia and following exposure to general anesthesia. The purpose of this study was to review the neurobehavioral performance of infants in a busy urban Level III NICU which specializes in extreme prematurity, high volume of neonatal surgery and early experience with a neonatal neuro-intensive care nursery.

Methods Used: The NICU Network Neurobehavioral Scale (NNNS), developed by the NIH, examines the neurobehavioral organization, neurological reflexes, motor development, and signs of stress in infants as young as 30 weeks gestation. Over the course of three months, hospital staff were trained and certified in the administration of the NNNS. Infants were then assessed after entry into a prospective study (IRB #5120144) examining the relationships between parental mental health and infant outcomes.

Summary of Results: Thirty-five consecutive infants underwent the NNNS evaluation. Their results were compared to published normative values. Of the thirteen NNNS subscales, the mean scores of eight were similar to the normative values (within one standard deviation). Means for the other five decreased, by more than one standard deviation from the normative values. On average, these infants scored very high on lethargy (90th-95th percentile), very low on stress/abstinence (5th-10th percentile), and low on arousal, handling, and attention (10th - 25th percentile).

Conclusions: The relative NNNS subscale scores can provide valuable insight into the current neurobehavioral state of infants and by doing so allow healthcare professionals to better determine the necessary treatment for infants on a very individualized basis. Furthermore, recent studies suggest...
that the scales provide predictive value into many aspects of the infants’ development from medical outcome to behavioral characteristics. Details about what future characteristics of the infant may be predicted by general deviations from the normative subscale values.

81

LONGITUDINAL EVALUATION OF INFANT HEALTH IN THE NICU USING THE NEONATAL THERAPEUTIC INTERVENTION SCORING SYSTEM

Massatt S Tagge E, Loma Linda University School of Medicine, Loma Linda, CA.

Purpose of Study: The severity of infant illness in the NICU is a largely un-expected field. Severity Scoring Systems are a tool often employed to assess infant health by using different parameters to determine the severity of a patient’s condition. These scoring systems have been used extensively in research, but not as clinical tools. As a clinical tool, they could potentially be a valuable resource in tracking the overall trend of decline or improvement in patients over time.

Methods Used: In our study, we used the Neonatal Therapeutic Intervention Scoring System (NTISS), which is based on the number and type of therapies being used on an infant at any given time. The therapies are each assigned a value based on therapeutic complexity, and the total sum of all these values for a given 24-hour period gives the NTISS score. The therapies are divided into the categories of respiratory, cardiovascular, drug therapy, monitoring, metabolic/nutrition, transfusion, vascular access, or procedures. Our patient population consisted of 54 babies in the NICU of the Loma Linda Medical Center.

There were equal numbers of males and females, and an average gestational age of 35 weeks. Scores were determined for the days of admission and discharge, as well as for a set of 5 consecutive days in between.

Summary of Results: The overall average NTISS score for the day of admission was 17 (range 7-53; SD = 9); 11.5 for the 5 consecutive days (range 4-48; SD = 8); and 7 for the day of discharge (range 4-32; SD = 7). There was a slight decline in NTISS score during the five consecutive days. Healthy babies had a score of 4 (due to minimum NICU requirements), while our worst case had a score of 53. In a comparison of patients who were deceased vs. alive at discharge (4 vs. 51 patients), the deceased patients showed a significant increase in score during the 5 consecutive days, while scores decreased for patients who survived.

Conclusions: Patients in the NICU generally follow a trend of gradual improvement from admission to discharge from the NICU, but there is a significant trend of worsening condition for those patients that do not ultimately survive. The small variation in scores for consecutive days indicates that fewer scores would suffice to determine the overall trend for a patient. This would simplify the potential clinical application of NTISS.

Poster Session I

Surgery

2:30 PM
Thursday, January 23, 2014

82

IS ISOTRETINOIN USE A RISK FACTOR FOR KELOID FORMATION? AN ILLUSTRATIVE CASE SERIES

Bowman S, Lewis P G Mattison, Chidester J, Gupta S. Loma Linda University School of Medicine, Redlands, CA.

Case Report: Since its 1982 FDA approval, isotretinoin has primarily been used to treat acne vulgaris, particularly severe cystic acne that carries potential psychosocial elements. The history of isotretinoin is fraught with claims of various side effects including teratogenicity, neurosychogenic effects, and potential damage to multiple systems. A debated correlation is keloid development following use. Though scar reduction with isotretinoin use has been noted in several studies, few reports describe keloids ensuing during or after use. Reports exist of keloid appearance following laser or dermabra- sion with parallel isotretinoin therapy. Even fewer, describe spontaneous keloid formation with isotretinoin therapy. This case series presents 5 patients who developed keloids following isotretinoin use without any family or personal history of keloids.1:Caucasian male age 21 started isotretinoin 8 days after sustaining an abrasive lesion on his shoulder from a motorcycle accident. Treatment included isotretinoin cessation, Kenalog injections, and laser therapy prior to subsequent excision.2:Caucasian female age 23 took isotretinoin for approximately 5 months prior to ceasing use due to spontaneous keloid formation of the back, chest, and shoulders. Keloid treatment included Kenalog injection, laser Vbeam therapy, and topical Imiquimod 5%. She has ongoing treat-ment.3:Caucasian male age 21, took isotretinoin for 7 months during which he spontaneously developed keloids at the angle of the mandible. Treatment included topical Imiquimod 5%, Kenalog injections, and fractional laser ther-apy on the face and neck.4:Caucasian male age 23, presented at age 16 with severe keloids of his chest and back following the use of isotretinoin for refractory acne vulgaris. Treatment included laser and Kenalog injections.5: African-American male age 24 with keloids of the cheeks, upper neck, ears and shoulders. Imiquimod and Vbeam were utilized with mild improvement of periauricular and cheek keloids.

This case series presents 5 patients who developed keloids after isotretinoin use. Keloid onset varied from concurrently with isotretinoin use to 7 months after cessation. Although rare, the possibility of keloid for-mation should be considered it patients who take or have taken isotretinoin.

83

THE EFFECT OF THE TIMING OF HARD PALATE REPAIR ON MAXILLARY GROWTH IN THE PATIENT WITH A UNILATERAL CLEFT LIP AND PALATE: A SYSTEMATIC REVIEW

Gerke B, Hiersche M, Jones J, Lewis P, Martin M. Loma Linda University, Loma Linda, CA.

Purpose of Study: Recommendations regarding the timing of surgery in cleft palate repair revolve around a compromise between two competing concerns: maxillary growth and speech development. To date, the optimal timing of cleft palate repair regarding maxillary growth has not been well elucidated. Our purpose was to evaluate the timing of hard palate repair on facial growth via a systematic review of the literature.

Methods Used: A systematic review of the literature was performed using the search terms “facial growth,” “cleft palate,” “timing,” and “timing of pal-ate repair” from 1954 to 2013 via PubMed. Additional resources were cross referenced in selected articles for inclusion. All controlled studies in English that provided objective measures of palatal growth in relation to the timing of repair and met inclusion criteria were selected. Care was taken to only select papers involving patients with unilateral, nonsyndromic cleft lip and palate, that compared similar techniques.

Summary of Results: 48 studies met the inclusion criteria and were all non-randomized, retrospective reviews. 35 studies were cross-sectional, while 13 were longitudinal in design. Analysis was performed by casts in 14 papers, by cephalometry in 26 and by both in 8 studies. In addition four relative sys-tematic reviews/meta-analyses were identified. Based upon the paucity of data, variable methods and heterogeneous nature of the selected literature a formal meta-analysis was not possible at this time, limiting broadly applica-ble conclusions.

Conclusions: Based on the heterogeneity in the literature, definitive recommendations regarding the appropriate timing of cleft surgery and opti-mal maxillary growth are not possible. Prior literature has noted this defi-cency in cleft literature, advocating for prospective, controlled, long-term trials to provide definitive data. The myriad of treatment algorithms, variable cleft pathology, necessary long-term year follow-up and ethical obstacles make a randomized-controlled trial with sufficient power difficult to perform. Thus, we propose algorithms that direct the timing of cleft palate repair should focus on tangible end points and outcomes.

84

ENERGY EVALUATION AND VISUALIZATION OF LASER FIBER CLEAVING TECHNIQUES

Vussantachart J, Yeo A, Maldonado J, Martin J, Lee M, Engbretsen S, Aloyouf M, Olgin G, Lightfoot M, Li R, Baldwin D. Loma Linda University, Loma Linda, CA and Loma Linda University, Colton, CA.

Purpose of Study: Commercially-available reusable laser fibers have the po-tential to reduce surgical waste and costs associated with urologic surgeries
utilizing the holmium laser. However, unlike disposable fibers, reusable laser fibers require proper cleaving of the silica core to maintain an optimal working life. The purpose of this paper is to quantify the effect of different cleaving tools on energy output of the laser fiber and demonstrate changes in appearance with microscopy.

Methods Used: The manufacturer tip of a new Lumenis 365 μm Reusable SlimLine laser fiber was used to obtain baseline energy transmission values. The fiber was then cleaved using the manufacturer-recommended cleaving tool (Lumenis), a competitor’s cleaving tool (Cook Medical), suture scissors and a 15 blade scalpel. A Lumenis VP100 holmium laser was set at a power output of 3 Watts (0.6 J at 5 Hz), and energy output was measured for 5 seconds. The fibers were cleaved with each tool 7 times, and 3 measurements were taken for each trial. The fiber tips were then imaged with a dissecting microscope and scanning electron microscope for visual characterization. A single-factor analysis of variance was used for statistical analysis with alpha set to 0.05.

Summary of Results: The manufactured tip transmitted 3.0 W (100 ± 0.9%) of the energy output of the generator and was used as a control. The recommended tool had the next highest average output (98.2 ± 1.4%), followed by the 15 blade scalpel (84.8 ± 2.9%), the competitor’s cleaving tool (78.1 ± 6.9%), and finally the suture scissors (58.0 ± 7.3%). Analysis of variance showed a significant difference between energy transmitted by the different techniques (p<0.001). The microscope imaging showed that the manufacturer tip had a smooth, flat surface and rim. The recommended tool had a similar surface but defects along the rim. The other tools had defects on the surface and rim.

Conclusions: Cleaving techniques produce a significant effect on the energy transmitted through a reusable laser fiber. The manufacturer-recommended cleaving tool had the most consistent and highest average energy output. This tool should be routinely used in the maintenance of reusable laser fibers.

Behavior and Development 1
Concurrent Session
3:30 PM
Thursday, January 23, 2014
85
CHARACTERISTICS OF CHILDREN WITH AUTISM BORN PREMATURELY
Scoble J1, Hansen R2, Krakowiak P1, Underwood M1, Hertz-Picciotto I1, Angkustsiri K1, 1University of California, Davis, Children’s Hospital, Sacramento, CA; 2University of California, Davis, Medical Center, Sacramento, CA; 3University of California, Davis, Sacramento, CA.

Purpose of Study: Infants born prematurely are at risk for developmental delays, and recent studies suggest an association with autism. Our aim was to compare the characteristics of children with autism (AU) who were born preterm with those born at term. We hypothesized that premature AU children would have worse Autism Diagnostic Observation Schedule (ADOS) autism severity and social affect (SA) scores, but exhibit no differences in restrictive and repetitive behavior (RRB) than those children born at term. We also hypothesized that premature AU children would have lower cognitive, language, and adaptive scores than those born at term.

Methods Used: The Childhood Autism Risks from Genetics and Environment study is a population-based case-control study developed to address environmental and endogenous risk factors for autism. The current analysis included 419 children ages 3-5 years with a diagnosis of AU confirmed by the ADOS and Autism Diagnostic Interview-revised (ADI-R). Cognitive and language developmental quotients (DQ) were assessed with the Mullen Scales of Early Learning (MSEL) and adaptive function was evaluated via the Vineland Adaptive Behavior Scale (VABS). Children were grouped by gestational age (<37 wk, n=44; and >37wks, n=375).

Summary of Results: Preliminary analysis shows similar autism severity in children born at term and prematurely (7 vs. 6.6; p=0.1). There was no significant difference in ADOS SA (14.2 ± 15; p=0.2) or RRB (19.3 vs. 20; p=0.2) scores. MSEL DQs were also similar between term and preterm. Premature AU children exhibited lower adaptive functioning, with significantly lower composite VABS scores than AU children born at term (59 vs. 63.8; p=0.03).

Conclusions: Preterm children with AU did not show significant differences in autism severity, social affect or restrictive and repetitive behaviors than those born at term. Cognitive and language scores were not significantly different between groups, but the preterm children showed more difficulty with adaptive functioning. This population may represent a subset of children with autism who exhibit more difficulty with daily living skills.

86 INTERACTIVE EFFECTS OF COPY NUMBER VARIATION AND MATERNAL INFECTION ON AUTISM IMPAIRMENT
Mazina V1,2, Bernier R2, 1University of Washington School of Medicine, Seattle, WA and 2University of Washington, Seattle, WA.

Purpose of Study: Epidemiological data have suggested maternal infection and fever to be associated with increased risk of autism spectrum disorder (ASD). Animal studies show that gestational infections perturb fetal brain development and result in offspring with the core features of autism and have demonstrated that behavioral effects of maternal immune activation (MIA) are dependent on genetic susceptibility. The goal of this study was to explore the impact of pathogenic copy number variant (CNVs) and prenatal maternal infection on clinical severity of ASD within a dataset of prenatal history and complete genetic and phenotypic findings.

Methods Used: We analyzed data from the Simons Simplex Collection sample including 1971 children with a diagnosis of ASD aged 4 to 18 years who underwent array CGH screening. Information on infection and febrile episodes during pregnancy was self-reported through telephone interviews. ASD severity was clinically measured through parent-report interview and questionnaires.

Summary of Results: We found significant interactive effects between presence of CNVs and a history of maternal infection or fever during pregnancy on autistic symptomatology, such that individuals with CNVs and history of maternal infection demonstrated increased rates of social communicative impairments and repetitive/restricted behaviors. Interactive effects were significant on all ASD measures (Table 1). In contrast, no significant interactions were found between presence of CNVs and prenatal infections on cognitive and adaptive functioning of individuals with ASD.

Conclusions: Our findings support a gene-environment interaction model of autism severity, in that individuals with putative causative CNVs are more susceptible to the effects of MIA in pregnancy on behavioral outcomes, and suggest that these effects are specific to ASD rather than to global neurodevelopment.
88 AUTISM SEVERITY IN CHILDREN EXPOSED TO MONOLINGUAL VERSUS BILINGUAL ENVIRONMENTS
Purpose of Study: To compare autism severity scores in children exposed to monolingual vs. bilingual environments. Given that atypical language development is a defining feature of autism spectrum disorder (ASD) and often the first presenting symptom, we hypothesized that exposure to multiple languages would result in more severe Autism Diagnostic Observation Schedule (ADOS) scores.
Methods Used: Participants were part of the CHARGE (Childhood Autism Risks from Genetics & Environment) Study, an ongoing population-based case-control study of children ages 2-5 years old. Analysis was limited to 543 families who used English and/or Spanish to communicate with their children. Language exposure was assessed using the Multiple Language Questionnaire. Monolingual (n=518) was defined as primary language spoken to child ≥75% of the time with <25% of a secondary language. Bilingual children (n=25) were exposed to both languages at least 25% of the time. Autism severity scores [Gotham et al., 2009] were calculated from ADOS raw totals, with higher scores indicating greater autism severity. The Social Affect (SA) and Restricted Repetitive Behaviors (RRB) subscales of ADOS were also analyzed. ADOS scores were compared across groups using ANCOVA, adjusted for maternal education & birth place, and Mullen Scales of Early Learning composite score.
Summary of Results: Mean autism severity scores were not significantly different between monolingual and bilingual groups (see table).

<table>
<thead>
<tr>
<th>Language Exposure</th>
<th>Mean Autism Severity Score</th>
<th>SE</th>
<th>P-value</th>
<th>P-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monolingual:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100% English n=404</td>
<td>7.56</td>
<td>0.16</td>
<td>[ref]</td>
<td>[ref]</td>
<td>[ref]</td>
</tr>
<tr>
<td>75-99% English n=86</td>
<td>7.19</td>
<td>0.19</td>
<td>0.7595</td>
<td></td>
<td></td>
</tr>
<tr>
<td>75-100% Spanish n=28</td>
<td>7.31</td>
<td>0.34</td>
<td>0.8978</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilingual:</td>
<td>7.74</td>
<td>0.33</td>
<td>0.7415</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Contrary to our hypothesis, this analysis suggests that bilingual exposure is not related to more severe autism symptoms. This information could help reassure parents that their native language does not impact severity of autism symptoms and help them arrive at language practices that are congruent with families’ needs.

89 CHANGE IN EXPRESSED EMOTION AS A MARKER FOR INTERVENTION EFFECTIVENESS IN PARENTS OF INDIVIDUALS WITH HIGH FUNCTIONING AUTISM
Steinfeld M1, Jalnapurkar I2, Singh K1, Leckliter I1, Schneider A2, Gunther J1, Roa D1, Solomon M2, UC Davis, Sacramento, CA; 1UC Davis, Sacramento, CA; 2UCLA, Los Angeles, CA.
Purpose of Study: The concept of expressed emotion refers to the emotional climate between family members in their home environment. High levels of expressed emotion have a detrimental impact on the functioning of family members with neuro-developmental disorders including schizophrenia, ADHD and autism. The aim of this pilot study was to examine whether the Five Minute Speech Sample (FMSS) measure of expressed emotion (EE) would reflect changes in EE as a result of parent participation in a psycho-educational support group conducted as part of an evidence-based child social skills training group program. We hypothesized participation in the parent group would be associated with a shift from high EE to low EE as measured by the FMSS.
Methods Used: Parents of 38 verbal children ages 6-19 years (mean age 11.32 years) with a community diagnosis of autism spectrum disorder (ASD) completed the FMSS, which is a 5 minute semi-structured interview which can only be coded by trained raters. The interviews were audiotaped, transcribed and coded for the content and tone of parent-child relationship. The parents were rated on the levels of criticism (CRIT) and emotional over-involvement (EOI) displayed in their narratives about their children at the beginning and again at the end of the 25 week social skills intervention program and linked psycho-educational parent support group.
Summary of Results: The analysis showed a significant decrease in the proportion of parents who expressed high levels of CRIT and EOI from pre-participation to post participation in the social skills and parent group intervention.
Conclusions: The parents were able to complete the FMSS and many enjoyed doing so. Based on these initial results, it appears that the FMSS is sensitive to functioning in families of children with ASD and can be used as a measure of intervention outcome for them.

90 GROSS MOTOR FUNCTION IMPROVES AFTER MYOFASCIAL STRUCTURAL INTEGRATION THERAPY IN YOUNG CHILDREN WITH SPASTIC CEREBRAL PALSY
Buyssa CA1, Loi E1, Hansen AB2, Price KS1, Jaramillo TM1, Pico E1, Feldman BM1, Stanford University, Palo Alto, CA; 2Providence Milwaukie, Portland, OR; 3Rolling Children, Palo Alto, CA; 4University of California, San Francisco, San Francisco, CA and 5Children’s Hospital and Research Center Oakland, Oakland, CA.
Purpose of Study: To assess whether Myofascial Structural Integration as a complementary treatment improves gross motor function in children with spastic cerebral palsy.
Methods Used: The study is a randomized controlled trial (RCT) with a subsequent open label crossover design. Children < 4 years with a diagnosis of spastic CP were enrolled. Exclusions: recent injection of botulinum toxin and active seizures. Participants continued pre-existing therapies. Children were assigned to treatment (n=8) or waitlist-control group (n=8). All children (N=16, pooled sample) were assessed at baseline, pre-treatment, and post-treatment. Study intervention was a standard course of MSI, performed weekly for ten weeks, by one clinician. A trained physical therapist evaluator, unaware of treatment phase, assessed response to treatment. Primary outcome measure was the Gross Motor Function Measure-66, a standardized measure of gross motor function. For this age and degree of disease-involvement, we anticipated GMFM scores in the 20-90 range (higher scores indicate higher function).

Summary of Results: In RCT phase, repeated measures ANOVA suggested a beneficial effect of MSI (initial treatment group mean GMFM change M=1.60, waitlist control group mean GMFM change M=−29). In the open label phase, using the pooled sample, paired t-test analysis showed no significant change in GMFM score comparing baseline to pre-treatment assessments (M=1.33, p=0.169) but a significant change in pre-treatment to post-treatment scores (M=1.62, p=0.046).
Conclusions: Myofascial structural integration therapy was associated with better GMFM scores in young children with spastic cerebral palsy. Though the magnitude of change was modest, it was measurable beyond that observed in development over time with standard of care therapies.

91
TRANSITION OF HEALTH CARE FOR YOUTH WITH SPECIAL HEALTH CARE NEEDS (YSHCN)-USING EMR FOR TRAINING PEDIATRIC RESIDENTS
Mahajan G1, Hansen R2, Romano P3, Shaikh U4, 1UC Davis School of Medicine, Sacramento, CA; 2UC Davis School of Medicine, Sacramento, CA and 3UC Davis School of Medicine, Sacramento, CA.
Purpose of Study: Health care transition for youth with special health care needs (YSHCN) is rarely addressed systematically. A quality improvement intervention to train pediatric residents in transition planning using an EMR template and evaluate its efficacy was completed.
Methods Used: All pediatric residents attended a brief presentation on health care transition for YSHCN and were given a list of their patients in need of transition services based on ICD9 codes and age. Residents were divided into 2 groups based on their day of continuity clinic. The intervention group was provided additional training in the use of an electronic medical record (EMR) template to facilitate transition and received access to the template. Bimonthly review of EMR records for all identified YSHCN was performed. Outcome measures included whether 1) transition planning was discussed during an appointment with their resident primary care physician, 2) the EMR transition template was used, 3) a portable medical summary was created, and 4) accurate documentation of visit type for purposes of coding was made. Families of both groups were surveyed by mail to evaluate their perception of the quality of transition planning provided at their visit.
Summary of Results: 21 of 39 patients (53.8%) in the intervention group and 14 of 32 patients (43.7%) in the control group kept appointments with their primary care pediatric resident. There was very strong evidence that the intervention increased the probability that transitioning would be discussed at their appointment (p-value = 0.0115). The EMR template was used 76% of the time and a portable medical summary was created 42.8% of the time. A higher billing code accounting for physician time spent was used 62% of the time. Multiple barriers to transition planning were identified by both pediatric residents and families.
Conclusions: Additional training increases the likelihood of discussing transition, and using an EMR template supports systematic transition planning. Residents, supervising faculty and families need more knowledge, time and support for transition planning for YSHCN.

92
THINNING OF THE LEFT ROSTRAL ANTERIOR CINGULATE AND LEFT MEDIAL ORBITOFRONTAL CORTEX IN ADOLESCENT FEMALES WITH ANTISOCIAL SUBSTANCE DEPENDENCE
Boulos P1, Dahwani M2, Sakai J3, 1University of Colorado School of Medicine, Aurora, CO and 2University of Colorado School of Medicine, Aurora, CO.
Purpose of Study: Some individuals have onset of substance use disorders early in adolescence, develop multiple substance use disorder diagnoses, and have severe persistent courses. Youths in this population are likely to have a number of precursors, associated cognitive deficits, and characteristic co-morbidities such as conduct disorder. We have previously termed this Antisocial Substance Dependence. Although such youths exhibit more impulsivity, risk-taking, and problems of inhibition, relatively little is known about brain differences seen in such youths. This is especially true among adolescent females.
Methods Used: We recruited 22 patients from a university-based treatment program for youths with serious substance and conduct problems and 21 community controls, all female and aged 14-19 years. We obtained T1 structural brain images using a General Electric 3T MRI scanner and assessed for group differences in cortical thickness across the entire brain using FreeSurfer’s QDEC program and for three regions-of-interest bilaterally (total of 6 comparisons). These regions of interest were defined by the Desikan’s atlas, chosen based on a priori predictions from the literature, and included: 1) medial orbitofrontal cortex; 2) rostral anterior cingulate cortex; 3) middle frontal gyrus. Age and IQ were entered as nuisance factors for all analyses.
Summary of Results: Using a vertex-level threshold of p < 0.005 and Monte Carlo Simulation-determined cluster threshold we demonstrated on whole-brain analyses that one region, including the left rostral anterior cingulate cortex and extending into the left medial orbitofrontal region (355.84 mm² in size) was significantly thinner in patients. Region-of-interest analyses showed no significant difference in any of the 6 regions.
Conclusions: Adolescent females with Antisocial Substance Dependence have significantly thinner left rostral anterior cingulate and left medial orbitofrontal cortices. These regions have been hypothesized to be associated with poor behavioral control in past studies.

Global Health
Concurrent Session
3:30 PM Thursday, January 23, 2014
93
EVALUATION OF A MALNUTRITION MANAGEMENT PROGRAM IN GUJARAT, INDIA
Patel R, Maloney C, Nkoy F, Fassl B. University of Utah, Salt Lake City, UT.
Purpose of Study: More than 50% of India’s children are reported malnourished resulting in adverse socio-economic, cognitive, developmental, and health consequences. The government of India launched a pilot malnutrition management program (MMP) for children identified with severe acute malnutrition (SAM) - to date no information exists about its effectiveness. This is the first study to describe long and short-term weight and health outcomes of children admitted for nutritional rehabilitation in a child malnutrition treatment center (CMTC).
Methods Used: This study took place in Sinar, Gujarat, India. We included all children admitted for SAM management to the CMTC from 7/2011-10/2012. Children completed a 10-day inpatient treatment course, including medical, educational and nutrition interventions. We reviewed hospital records to determine compliance with SAM management guidelines and nutritional/weight parameters. Weight-for-age z-scores were calculated using the World Health Organization growth norms. Following discharge, we conducted household visits to determine interval changes in weight and health status. We obtained social, family and household characteristics and comorbidities from the hospital record and a validated household survey. Data analysis is descriptive.
Summary of Results: 139 children were admitted for SAM management (51% male, mean age: 26 months). 111/139 (80%) of the children were from the lowest caste group; 50% of mother's were illiterate. The mean monthly household income was below $30 US. The median z-score admission weight was -5.03 (range: -3.3 to -8.7). The median z-score discharge weight was -4.625 (range -2.9 to -9.2) with a mean weight gain of 3.8%. All children completed the 10-day MMP, 0 met weight discharge criteria (1 SD or 15% weight gain). Minimum follow-up was for 6 months and we identified 94/139 (69%) children. There were no medical records for 2/94 that expired. Follow up weights showed a median z-score of -4.766. Comorbidities were reported at the time of the interview, including: diarrea 20% (19/94), acute respiratory infection 35% (35/94), and fever 26% (24/94).
Conclusions: Modifications to the current MMP are needed to effectively address SAM in children.

94
CONGREGATION-BASED INTERVENTION IN RESOURCE LIMITED SETTINGS: IMPLEMENTATION CHALLENGES & LESSONS LEARNED
Akondeng C1, Ezanoulo EE2, Ogidi A3, Osaj A4, Obiene M4, Ehiri J5, 1University of Nevada Las Vegas, Las Vegas, NV; 2University of Nevada school of medicine, Las Vegas, NV; 3University of Arizona, Tucson, AZ and 4PeTR-GS, Enugu, Nigeria.
Purpose of Study: The Healthy Beginning Initiative (HBI) is a congregation-based approach to implement evidence-based interventions for Prevention of
Mother-to-Child HIV Transmission (PMTCT) at the community level. We report challenges and lessons learned in implementing this initiative in south-east Nigeria with the hope that the experience would help to inform programs in other resource limited settings.

Methods Used: Focus group sessions and questionnaire survey of 15 HBI program staff. We assessed challenges related to: 1) Recruitment [study site selection; Church recruitment; Church randomization; Staff recruitment and training]; 2) Intervention [Participant enrollment, completion of pre-natal survey, laboratory testing], and 3) Retention [post-partum follow-up, completion of post-partum survey; post-partum laboratory testing, data entry and study close out].

Summary of Results: We identified five major challenges: 1) In dealing with initial concerns raised by priests and leaders of churches randomized to control group, we implemented the intervention at those churches at the end of the research program. 2) Low literacy level among Church Health Advisors (CHAs) posed a challenge that required targeted training. 3) Male partners of the pregnant women demanded men-focused intervention to improve their own health. Addressing this demand increased cost of intervention. 4) Surrounding church’s high demand to participate, led to an increase in the number of participating churches and a need to decentralize scale-up to give room for establishment of “model” centers.

Conclusions: Involvement of churches and church leaders, integration of program into local celebrations associated with pregnancy and child birth, and coverage of screening for other locally endemic maternal and child health infections (in addition to HIV) helped to eliminate stigma and increase participation. Programs using HBI model to promote birth outcomes through screening and linkage to care should first establish a model site to train CHAs before activating several implementation sites.

96

RURAL MEDICINE ELECTIVES AS A VEHICLE TO ENGAGE RURAL COMMUNITIES WITH THE GLOBAL STEM CELL NETWORK: A PILOT STUDY

Fingirut W. University of British Columbia, Vancouver, BC, Canada.

Purpose of Study: The global stem cell and marrow network is a database that physicians use to find potential stem cell donors for their patients who need stem cell or bone marrow transplants. In Canada, individuals between the ages of 17-35 can sign up to be potential stem cell donors online or at a stem cell drive, where they provide a medical history, swab their cheeks to provide a tissue sample, and consent to join the Canadian stem cell donor database: OneMatch Stem Cell Registry, Canadian Blood Services. For the past two years, OneMatch has trained medical students at the University of British Columbia (UBC) to run stem cell drives independently.

At UBC, all medical students are required to complete a rural medicine rotation in a community in British Columbia or in the territories. The purpose of this pilot was to determine feasibility for UBC medical students to run a stem cell drive in their rural community, during the rural elective.

Methods Used: The pilot was completed by a medical student placed in Inuvik, Northwest Territories, Canada for the rural elective (population 3,500). The student was previously trained by OneMatch to run stem cell drives independently. Permission was obtained by the local health authority to run the drive. A drive was held at a local grocery store, during afternoons and evenings between August 23-30, 2013, and lasting 20 hours total. This drive specifically targeted young, multi-ethnic males (i.e. Canadian Aboriginals) as this demographic is most underrepresented on the Canadian stem cell donor registry. The drive target was to sign up 20 people to be potential stem cell donors. Social media was used to advertise.

Summary of Results: In all, 44 individuals under age 35 were signed up to be potential stem cell donors, including 32 males. 26 were of an ethnicity other than Caucasian.

Conclusions: This pilot demonstrated that combining stem cell drives with medical student rural electives is feasible and may be an effective strategy to facilitate rural community participation in the global stem cell donor database. As well, operating stem cell drives in rural communities in Canada may offer a unique opportunity to engage individuals from key ethnic groups to become potential stem cell donors, including Inuit, First Nations, and Metis Aboriginals of Canada.

97

ADDRESSING BARRIERS TO CERVICAL CANCER SCREENING IN RURAL UGANDA

Scodeller C. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Cervical cancer is the most common and deadly female malignancy throughout much of the developing world. Despite inexpensive screening options for low-resource settings, less than five percent of women in Uganda are screened during their lifetime. As a result, the majority of patients present with late-stage disease and an accompanying poor prognosis. A growing body of literature addresses barriers patients face to regular screening. However, the challenges rural health workers face in the field are not well defined. Therefore, the aim of this project was to identify cervical cancer knowledge, attitudes, and practices among rural health workers in Uganda, while simultaneously raising awareness and education at the participating health center.

Methods Used: A loosely structured, open-ended focus group interview with health workers was held at St. Monica Health Centre Katende, a rural level three health center in the Mpigi District of Uganda. The interview included one clinical officer, two nurses, two midwives and one lab assistant. Following the interview, misconceptions were corrected, training material was distributed, and a CMF course was taught by the Uganda Cancer Institute.

Summary of Results: Health workers accurately identified cervical cancer as the most common and deadly female malignancy in Uganda, but they lacked knowledge about the risk factors contributing to the disease burden. The health center aimed to educate women about cervical cancer during mothers’ postnatal appointments. However the health workers reported that patients rarely show up for these visits. No health worker had performed a
vaginal exam post training, citing insufficient skills as the major barrier. All health workers involved in the focus group interview participated in a CME course and received training and reference material.

**Conclusions:** Health workers faced multiple barriers in screening patients for cervical cancer. More robust training and education practices are needed to effectively combat the cervical cancer disease burden in rural Ugandan communities. The results of this investigation will inform government cancer outreach programs at the Uganda Cancer Institute. However, follow-up studies must be performed to better characterize the barriers identified in this investigation.

**98 PHOTOVOICE: ENGAGING YOUTH IN RURAL UGANDA IN ARTICULATING HEALTH PRIORITIES THROUGH PARTICIPATORY ACTION RESEARCH**

Ho P1, Esau D1, Blair G1, Duffy D1, O'Hara N1, Kapoor V1, Ajiko M2. 1University of British Columbia, Vancouver, BC, Canada and 2Soroti Regional Referral Hospital, Soroti, Uganda.

**Purpose of Study:** While 80% of Uganda’s population lives in a rural community, only 27% of available health services are provided in rural areas. Although access to health services in rural Uganda has been increasing, this study aims to document the personal health priorities of the youth in Soroti, Uganda. Engaging community members in understanding their own health status is an effective mechanism for health improvement, and aids in appropriate resource planning for a country’s health system.

The use of a participatory action research method to evaluate the self-reported health priorities of Soroti youth allows them to express their concerns, empowers them to advocate for their own health and informs decision-makers of gaps in health information and services.

**Methods Used:** Photovoice is a community-based research method that uses photography to gain insight into personal health perspectives. Participants between the ages of 13-17 were recruited from four secondary schools in Soroti. Each participant was provided with a 27-exposure disposable camera. Participants were asked to capture photos of aspects of their lives that improve or detract from their health. After one week, the cameras were returned and the photos developed. Each participant reviewed their photographs in an interview with a member of the study team, answering a set of questions to provide insight into the health priorities of the participants.

**Summary of Results:** Thirty-two students were recruited and 512 photos were developed in the study. Each photo was assigned one or more health themes. The most common themes reported in the photos were hygiene, nutrition and water. Insight was gained into the health determinants between genders, ages and schools. Individual comments made during the interview were used to draw conclusions regarding the health determinants of the study population.

**Conclusions:** Photovoice is effective in providing insight into health perspectives of Soroti youth that may not have been obtainable through conventional methods. These findings will contribute to further community health education and influence Ugandan public health policy and resource allocation.

**99 COMMUNITY HEALTH WORKERS IN NAKURU DISTRICT, KENYA: IMPROVING HEALTH PROGRAM EFFICACY THROUGH CONTINUING EDUCATION**

Cross ZK. 1University of Washington, Seattle, WA and 2University of Washington, Seattle, WA.

**Purpose of Study:** Community health worker (CHW) programs are a cost-effective means of delivering health education and primary care to resource-poor, underserved areas. Project objectives included 1) development of resource manuals, 2) implementation of pilot training sessions, and 3) establishment, in collaboration with a clinical student and resident rotation program, of a continuing education protocol.

**Methods Used:** The project was carried out in two communities in rural Kenya, selected for the presence of existing CHW programs: Karagita slum and Karate village. No continuing education has been provided since limited initial CHW training was completed in 2009 (Karagita) and 2011 (Karate). CHWs were interviewed about local health issues, resources, and barriers to carrying out CHW duties. A comprehensive list of topics was generated, and used to design training sessions and materials. Resource manuals tailored to community needs were developed. Three topics were addressed in training sessions: HIV, tuberculosis, and diarrheal and opportunistic infections.

**Summary of Results:** CHWs reported worker shortages, little or no compensation, lack of materials, and low morale. Each training session reached between six and sixteen CHWs. Pre- and post-training surveys were administered at each meeting (free response and Likert scale), with self-reported qualitative feedback demonstrating that confidence and topic knowledge increased with training. Manuals were well-received, and will be kept at the community dispensaries. CHWs wrote that the handouts provided were helpful, and expressed a desire for additional training sessions.

Teaching materials detailing key contacts and topics have been provided to the locally-based UW Internal Medicine Global Health Chief Resident.

**Conclusions:** The goals of this project - to provide reference manuals, initiate a training program, and establish a continuing education protocol - were met. With the participation of rotating students and residents, future training sessions will be held. Communication between the CHWs and students/residents will be critical, in order to maintain community engagement.

The project has long-term potential, and training resources can be added as needed. This is a low-budget intervention that is welcomed by the CHWs.

**100 EXPLORING HEALTH IDEAS AND PRIORITIES IN A REMOTE HIMALAYAN COMMUNITY SCHOOL IN INDIA USING MIXED QUALITATIVE METHODS**


**Purpose of Study:** For seven years, University of British Columbia students have been involved in projects to improve health outcomes at a boarding school in the rural Spiti Valley of Himachal Pradesh, India. These initiatives have included annual health screening, greenhouses, health education, and water chlorination. To inform future projects and inspire grassroots initiatives, this qualitative study was undertaken to determine the community’s health ideas and needs.

**Methods Used:** Three age-appropriate qualitative methodologies explored concepts of health and health priorities. Eleven grade ten students, thirty grade five students, fifteen teachers, two school administrators, a school nurse, and six caretakers were randomly selected from a pool of volunteers. School administrators and the school nurse were interviewed, and teachers and caretakers participated in focus group discussions. Grades five and ten students engaged in participatory drawing and photography, respectively. The data was coded and analysed for themes and intra- and inter-group differences.

**Summary of Results:** Nutrition, the environment, and personal hygiene were considered key health determinants. Ideas about disease differed by age group; children viewed microorganisms and social factors (alcohol, smoking) as causing disease, whereas many adults held traditional beliefs. Participants varied intra- and inter-group in their use of traditional medicine, Buddhist health beliefs, and Western medicine for disease prevention and treatment. Limited resources, lack of access to healthcare, water and food contamination, poor sanitation, food insecurity, inadequate waste disposal, and a lack of greenery were principal community health concerns. Participants valued culturally relevant, sustainable medical projects and educational initiatives.

**Conclusions:** Mixed qualitative methods effectively assess health perspectives from community members of various age groups and empower the community to visualize and vocalize health concerns. These findings will inform health initiatives undertaken by the Spiti community, UBC, and other foreign groups. Understanding community-identified health concerns is crucial to the development and implementation of culturally appropriate global health projects in collaboration with local communities.

**101 INDIGENOUS FARMING PILOT AS WAY TO REDUCE POVERTY IN RURAL KENYA**


**Purpose of Study:** Partners in Community Transformation (PCT) is a community-based organization in the Kisumu region of Western Kenya. In
We assembled a library of seventeen CAR vectors that linked activation or costimulatory domains to distinct recognition domains specific for tumor associated EGFR, CD19, or ROR1 molecules. Human CD8+ T cells transduced with CARs encoding recognition and costimulatory domains for CD19, ROR1 and/or EGFR, and dual expressing cells were purified by cell sorting. Target cells expressing one or more of the CD19, ROR1, and/or EGFR target molecules were analyzed for recognition by CAR-modified T cells using cytotoxicity, cytokine release, and proliferation assays.

Summary of Results: We identified a group of 15 dedicated individuals who then attended a training session administered by the Kenyan Ministry of Agriculture and received seeds for five indigenous vegetables. This was followed by a farming demonstration of the appropriate procedures for planting the crops with group participation. The owner of the land used for demonstration has already started growing these crops successfully and he will offer the other participants support through training.

Summary of Results: This project will be evaluated through surveys and site visits administered by PCT to the 15 farmers to assess crops planted, successes and challenges. Once these farmers are successfully harvesting, they will be involved in training other community members as well as selling their seeds to keep this project sustainable.

Conclusions: The indigenous farming pilot project has a lot of potential as a sustainable way to increase nutritional status and reduce poverty in the Kisumu region in conjunction with other GHI-PCT projects. For example, workshops educate community members about the nutritional benefits of the various crops and their incorporation into a balanced diet. Another important project trains community members in group savings and loans to provide financial security and resilience for subsistence farmers. Overall, this pilot project is an important addition to the projects run by PCT and will support through training.

Conclusions: Delivering activating and costimulatory signals in trans is an attractive strategy to impose selectivity for tumor cell recognition because T cell proliferation and cytotoxicity should be limited to cells simultaneously expressing both cell surface antigens. Our CAR library offers a novel way to target two tumor antigens using gene-modified T cells and may reduce toxicity when one antigen is expressed on normal host tissue.

103 COMBINATORIAL ANTIGEN RECOGNITION BY ENGINEERED T CELLS
Salter AI, Liu L, Riddell SR. 
University of Washington, Seattle, WA; 
Fred Hutchinson Cancer Research Center, Seattle, WA; 
University of Washington, Seattle, WA.

PURPOSE OF STUDY: A combinatorial approach to develop tumor-recognizing CAR T cells to include both antigenic epitopes may be more efficient in recognizing known tumor cell antigens (e.g., CD19) than targeting a single epitope with high specificity. The ability to rationally combine antigens may expand the therapeutic breadth of CAR T cell therapies. Here we describe the development of a combinatorial library of 21 CARs, each recognizing two distinct tumor antigenic epitopes.

METHODS: We assembled a library of Seventeen CAR vectors that linked activation or costimulatory domains to distinct recognition domains specific for tumor associated EGFR, CD19, or ROR1 molecules. Human CD8+ T cells transduced with CARs encoding recognition and costimulatory domains for CD19, ROR1 and/or EGFR, and dual expressing cells were purified by cell sorting. Target cells expressing one or more of the CD19, ROR1, and/or EGFR target molecules were analyzed for recognition by CAR-modified T cells using cytotoxicity, cytokine release, and proliferation assays.

SUMMARY OF RESULTS: A combinatorial library of Seventeen CAR vectors that linked activation or costimulatory domains to distinct recognition domains specific for tumor associated EGFR, CD19, or ROR1 molecules. Human CD8+ T cells transduced with CARs encoding recognition and costimulatory domains for CD19, ROR1 and/or EGFR, and dual expressing cells were purified by cell sorting. Target cells expressing one or more of the CD19, ROR1, and/or EGFR target molecules were analyzed for recognition by CAR-modified T cells using cytotoxicity, cytokine release, and proliferation assays.

CONCLUSIONS: Delivering activating and costimulatory signals in trans is an attractive strategy to impose selectivity for tumor cell recognition because T cell proliferation and cytotoxicity should be limited to cells simultaneously expressing both cell surface antigens. Our CAR library offers a novel way to target two tumor antigens using gene-modified T cells and may reduce toxicity when one antigen is expressed on normal host tissue.
The uncleanable control probe had lower Cy5/Cy7 that was identical between tumor and normal tissue (1.27±0.07 vs. 1.26±0.08). The same was true for model (B). In model (C), 8119 metastases in the liver (5.0±0.35, n=32 metastases) had higher ratios than normal liver tissue (1.49±0.1, P<10^-13) for the cleavable RACPP. In model (D), Cy5/Cy7 was significantly higher for LNs with 8119 cancer cells than uninfected LNs. Mice injected with the uncleanable RACPP had low ratios in all LNs. The RACPP detected metastatic cancer cells when LNs were partially invaded (<10%). With a discrimination threshold ratio of 1.2, RACPPs had 100% specificity (16/16) and sensitivity (6/6) for detecting LNM.

Conclusions: RACPPs offer a significant advance in cancer detection over nonratiometric protease sensors. Surgical use of RACPPs could decrease the surgery time and incidence of positive margins and streamline decision-making by providing the LN invasion status in real time.

105

ARE CYSTIC Glioblastoma tumors derived FROM Low-GRADE gliOMAS?

J Piu, Sarmiento J1,2, Nulto M2, Ortega A2, Ly D2, Mukherjee D2, Fan X2, Black KL1, Patil CG1, 1UCLA David Geffen School of Medicine, Los Angeles, CA, and 2Cedars-Sinai Medical Center, Los Angeles, CA.

Purpose of Study: Controversy exists regarding the prognostic significance of cystic features in newly diagnosed glioblastoma (GBM) and the pathological origin of cystic GBMs. We aimed to determine (1) whether cystic GBMs develop from low-grade gliomas by evaluating IDH1 status and (2) evaluate differences in overall survival between patients with cystic and non-cystic GBM.

Methods Used: We retrospectively reviewed the records of 351 consecutively newly-diagnosed adult GBM patients treated at a single institution from October 1997 to November 2011. Among these patients, we sought to identify those with tumors with a large cyst cavity that comprised at least 50% of the total tumor volume. IDH1 mutation status was determined by immunohistochemistry. Descriptive statistics were reported by subgroups of patients with cystic and non-cystic tumors. Comparison of the overall survival between these cohorts was conducted using the Kaplan-Meier survival estimates.

Summary of Results: Out of a total of 351 newly diagnosed GBM patients, 27 (7.7%) patients had cystic GBMs and 324 (92.3%) patients had non-cystic GBM. Tumor samples from all 27 cystic GBM patients were analyzed for IDH1 mutations with immunohistochemistry. Two (7.4%) of the 27 tumor samples showed IDH1 mutations. There were no significant differences between the two cohorts with respect to age, gender, peroperative KPS, tumor size, extent of resection, or radiation and temozolomide received post-operatively. The median overall survival in months for the cystic cohort was 15.0 (95% CI 6.1-30.8) and 18.2 (95% CI 15.6-20.1) for non-cystic patients (log-rank p=0.77).

Conclusions: The low frequency of IDH1 mutation status in our cystic cohort strongly suggests that most newly diagnosed cystic GBMs do not arise from malignant transformation of previously undiagnosed cystic low-grade gliomas. Furthermore, there is no difference in overall survival between cystic and non-cystic newly diagnosed GBM patients.

106

PROSPECTIVE PHASE II TRIAL OF INTRA-ARTERIAL YTTRIUM-90 radioEmbolization FOR METASTATIC LIVER TUMORS

McKay TJ1, Geschwind J2, 1University of Washington, Seattle, WA and 2Johns Hopkins Medical Institute, Baltimore, MD.

Purpose of Study: The liver is a common metastatic site for many primary malignancies. These liver lesions often become the dominant life-threatening burden in metastatic disease. Resection is currently the only curative option for the disease, yet fewer than 20% of patients are candidates for surgery due to tumor size, location, and multifocality. Yttrium-90 (Y90) radioembolization has shown safety and efficacy in treating primary hepatic malignancies. The purpose of the present study is to evaluate the safety and efficacy of Y90 radioembolization as a treatment for metastatic liver tumors.

Methods Used: Patients (n=50) with unresectable metastatic liver tumors, who failed or were intolerant of standard first-line therapy, were enrolled in this prospective single-arm, single-center study. Y90 coated glass beads were delivered under fluoroscopic guidance intraarterially into the right, left, or both hepatic lobes. Patients received follow up with MRI at 1, 3, 6, 9, and 12 months post treatment. Patients were stratified by tumor type and for analysis. Primary endpoint was time to untreated survival (TTUP). Secondary endpoints were overall survival and tumor response. TTUP and survival were calculated with Kaplan-Meier analysis. Tumor response was evaluated from MR imaging using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 and v1.3 and WHO criteria.

Summary of Results: The median TTUP (in months) for neuroendocrine (n=9), colorectal (n=12), and other (n=14) tumors were 9.9, 2.7, 3.9, respectively. The overall survival (in months) for neuroendocrine, colorectal, and other tumors were 11.9, 4.4, and 7.7, respectively. Median TTUP and overall survival for carcinoïd tumors (n=15) were not met at the censor date. To date, 7/50 patients have undergone tumor response analysis at 6 months post treatment, with 1/7 patients showing complete response, 3/7 showing partial response, 3/7 showing stable disease, and 0/7 showing disease progression. This early analysis supports a 100% disease control rate.

Conclusions: Y90 radioembolization yields good survival in patients with metastatic liver disease and leads to significant local tumor control. This procedure offers excellent therapy for metastatic tumors which can be interpersed with other therapies.

107

CHARACTERISTICS OF LONG TERM SURVIVORS TREATED ON ONCOLOGY PHASE I STUDIES

Kaur GB1,2, Ramanathan R1,2,3, Von Hoff D1,2,3, Weiss G1,3, Jameson G1,3, Maia C1,2, White E1,3, Downhour M4,5, Slater M1,2, Translational Genomics Institute, Scottsdale, AZ, 1University of Arizona College of Medicine, Tucson, AZ, and 2Scottsdale Healthcare, Scottsdale, AZ.

Purpose of Study: Phase I first in human clinical trials are restricted to patients with advanced incurable cancers without any treatment options. The life expectancy for these patients is 3-5 months and few survive > 12 months. Eligible patients need to have an estimated life expectancy of >12 weeks. Phase I studies were thought of as the last resort for advanced cancer patients, however, with molecular target selection of agents in individual patients, we are increasingly seeing long term survivors. This study aims to elucidate the characteristics of those patients which survived >12 months.

Methods Used: The medical records of patients entered onto phase I clinical trials in 2008 and 2009 were reviewed. IRB approval was obtained for review of patient characteristics.

Summary of Results: 30 patients were identified (approx 8% of patients seen in 2008-2009) with >12 months survival from study entry. The median age was 63.4 years (range 54-84). Performance status: ECOG 0 in 60 % and ECOG 1 in 40 %. 66% were male. Tumor types were: prostate 17%, pancreas 13%, basal cell 10%, breast 10% and lung 7 %. The remainder (43%) included liposarcoma, small bowel, ovarian, uterine, cervical, appendiceal , gastric, colon, neuroendocrine and adrenal tumors. The median survival of this group (n=30) is 27.9 months from start of the first phase I trial. Tumor involvement: 13% locally advanced, 70% had one organ (usually liver), 13% had 2 organs involved and 3% had 3 organs involved. The majority (90%) were treated with a first in human molecular targeted agent. The agents were TKI (20%), P3K (15%) and a variety of other molecular inhibitors (cMET, H1F1-α, Anti-myosatin, Hedgehog, W, HSP-90ee-c1, CHK2, CDK etc).

Conclusions: A subset of patients (about 9%) treated with molecular targeted agents have prolonged (>12 months) survival, which is encouraging. A good performance status and <1 organ involvement correlates with survival. In the near future, patients will have a genomic profile to select individualized therapy. In our program, molecular profiling with whole genome sequencing, CGH etc is already being introduced to appropriately select biomarkers for therapy.

108

USING VIRTUAL PATIENTS AND ONLINE LEARNING MODULES TO ENHANCE ONCOLOGY EDUCATION IN THE UNDERGRADUATE MEDICAL CURRICULUM

Verna P1, Thau E1, Li S2, Hamilton S1, Lai L1, Lee A1, Ingledew P1,2, 1University of British Columbia, Vancouver, BC, Canada and 2BC Cancer Agency, Fraser Valley Center, Surrey, BC, Canada.

Purpose of Study: The incidence of cancer continues to increase. Despite this, oncology education during medical school is sparse. As a result many
graduating medical students feel unprepared to care for oncology patients. To address the significant gaps in oncology undergraduate education, project goals were to develop online learning modules supplemented by virtual patients to enhance oncology instruction during undergraduate medical training.

**Methods Used:** To develop a curriculum for the online resources, the Kern approach was employed. A needs assessment of third-year medical students at a single medical school was conducted. Following analysis of the survey, development of online resources began in 2009; medical students scripted online modules and virtual patients. Reviews were conducted by practicing oncologists, and a web-based platform was selected to disseminate material. Kirkpatrick’s hierarchy of evaluation has been used as an evaluation framework.

**Summary of Results:** In the initial steps of curriculum development, over half (82/156) of third-year medical students completed the needs assessment, revealing that 50% of students had not interacted with cancer patients during their clerkship year and 62% felt their ability to discuss oncology issues with patients was poor or fair. All respondents expressed interest in online oncology modules. Between 2009 and 2013 a core group of ten medical students and one attending oncologist worked to script, review, and publish 10 online modules supported by virtual patient cases. The online modules were integrated into the oncology curriculum at a single medical school in late 2011. Ongoing evaluations have shown a high level of satisfaction. Modules improved the student’s perceived knowledge of oncology and comfort dealing with oncology patients. An evaluation of the impact of the modules on learning continues.

**Conclusions:** While there are gaps in oncology education, this represents a novel intervention to address deficiencies. Research continues to evaluate the online modules and enhance this robust educational resource. Long-term goals are to disseminate this resource to medical students at a national and international level.

---

**STEREOTACTIC BODY RADIATION THERAPY FOR HEPATIC TUMORS**

Tang M1, Lee P2. 1David Geffen School of Medicine at UCLA, Los Angeles, CA and 2David Geffen School of Medicine at UCLA, Los Angeles, CA.

**Purpose of Study:** Stereotactic body radiation therapy (SBRT) is a new technique for delivering high doses of focal radiation in few fractions (1–5). We examined potential predictive factors for local control and overall survival in patients with hepatic tumors treated with SBRT, including tumor size, primary versus secondary, prior chemotheraphy, and biologically effective dose (BED).

**Methods Used:** A retrospective chart review was conducted for patients with hepatic tumors treated with SBRT from August 2009 to June 2013. The data were analyzed using a univariate and multivariate COX regression model.

**Summary of Results:** The study included 67 patients with 73 tumors. The 2-year local control and overall survival rates were 0.64(95% CI 0.31-0.85) and 0.39 (0.22-0.56). Gender, age, and tumor size had no significant association with overall survival (p=0.49-0.90). Patients with primary liver tumors—hepatocellular carcinoma, cholangiocarcinoma—had lower overall survival than patients with secondary liver lesions (univariate analysis: hazard ratio= 2.35, 95% CI 1.07-5.17, p = 0.03). Chemotherapy prior to SBRT predicted lower overall survival (HR= 1.26, 95%CI 1.00-1.58, p=0.05). Higher BED was weakly associated with longer survival (HR 0.983, 95% CI 0.969-0.998, p= 0.025). No factors significantly predicted local control.

**Conclusions:** SBRT is an effective treatment option for unresectable hepatic tumors. The primary site and history of chemotheraphy were predictive of overall survival for this cohort of SBRT patients.

---

**THE COMBINATION OF MER AND FGFR INHIBITION SIGNIFICANTLY INHIBITS NON-SMALL CELL LUNG CANCER CELL LINE PROLIFERATION**

Newton TP1, Cummings CT1, Kirkpatrick G1, Heasley L2, Graham D1. 1University of Colorado School of Medicine, Aurora, CO and 2University of Colorado School of Dental Medicine, Aurora, CO.

**Purpose of Study:** Although therapies targeting recently identified oncogenic drivers of non-small cell lung cancer (NSCLC) have been developed, a minority of tumors have been responsive. Therefore, a need still exists to identify other oncogenic drivers. Mer and FGFR are receptor tyrosine kinases that exhibit aberrant over-expression in many human malignancies, including NSCLC. Because Mer and FGFR signal primarily through complementary pathways involved with survival and proliferation (PDK-akt and MEK-ERK, respectively), dual inhibition of FGFR and Mer may offer a benefit for NSCLC. In this study we assayed the in vitro effect of UNC-2025 (Mer inhibitor) combined with AZD-4547 (FGFR inhibitor) on NSCLC cell lines.

**Methods Used:** Seven NSCLC cell lines were cultured for 14 days in soft agar overlaid with media containing DMSO vehicle control or increasing doses of UNC-2025 and/or AZD-4547. Cell colonies were stained with NBT and counted using the Gel Count Colony Counter and software. A replating assay was also performed: cells were seeded in 24-well plates, treated for 48 hours with inhibitors, lifted with EDTA, re-seeded in 6-well plates at 2000 cells/well, and incubated in normal media for 7 days. Colonies were stained with crystal violet and counted as above. Downstream signaling effects were evaluated via immunoblotting.

**Summary of Results:** In the soft agar and replating assays, Colo699 and H460 NSCLC cell lines were inhibited by UNC-2025 and AZD-4547 both as single agents and as a combination; the combination decreased proliferation more than either single agent alone. Immunoblotting revealed downregulation of pro-survival proteins (Cyclin D1, survivin, Bcl-xl) after 72h of treatment, and down-regulation of downstream effectors (p-akt, p-ERK) after 2h of treatment.

**Conclusions:** In our in vitro cell line models of NSCLC, the combination of UNC-2025 and AZD-4547 had an inhibitory effect greater than single agent efficacy. This was accompanied by down-regulation of downstream pro-survival proteins. This data warrants continuing preclinical investigation of this strategy for NSCLC treatment, including testing of murine in vivo models.
TARGETED RESPONSE IN PANCREATIC CANCER IN FUNCTIONAL IMAGING

Lee JY1, Serkova N1, Weekes C2.

Purpose of Study: Pancreatic cancer is the 4th most fatal U.S. cancer, with the lowest 5-year survival rate (4.8%) of any cancer sub-type. Recent clinical trials have shown targeted signal transduction inhibitor (STI) therapies to have promising results. However, cancer commonly develops drug-resisting mutations, requiring treatment with an additional inhibitor targeting multiple malignant pathways and oncogenes. This project utilizes two drugs targeting a commonly constitutively-active signaling pathway in pancreatic cancer and targeting the cancer support system.

Additionally, traditional objective response monitoring (CT, MRI) to STI therapy can be inadequate for primary site evaluation due to the characteristic desmoplastic reaction and inflammatory response. STI therapies are commonly cytostatic, necessitating additional imaging techniques to supplement the traditional size measurement to more completely understand treatment response. This project measures metabolic response (FDG-PET), cellularity changes (DWI-MRI), and tumor volume changes (MRI) to combination STI treatment.

Methods Used: Panc-159 tumors were bilaterally grown in the hind flank of athymic mice. PET studies were performed at baseline, mid-study, and end of study. For PET studies, after 4 hours of fasting, injection with approximately 150μCi of radioactive tracer via tail vein and 1-hour uptake incubation, animals were anesthetized with isoflurane for scanning. Total tumor activity was determined as standardized uptake values: total tumor activity divided by the decay-corrected injected dose delivered. DWI-MRI imaging was conducted under isoflurane at baseline, early treatment response, and late treatment response. Imaging analysis was used to calculate tumor volume and apparent diffusion coefficient (cellularity).

Summary of Results: At mid and end of study, only the combination treatment had a statistically significant lower tumor growth rate. At end of study, the combination treatment had a statistically significant tumor cellularity decrease, and STI drug 1 and combination groups had a statistically different glucose uptake decrease.

Conclusions: While not completely cytostatic, combination treatment was able to retard tumor growth and decrease tumor cellularity and glucose uptake.

PERINATAL NICOTINE EXPOSURE-INDUCED BONE MARROW-DERIVED MENSECHYMAL STEM CELL MYOGENIC DIFFERENTIATION IS MEDIATED BY TRANSCRIPTION FACTOR ZIP521 AND MIR-30D


Purpose of Study: Bone marrow-derived mesenchymal stem cells (BMDMSCs), by differentiating into specific cell-types, play a critical role in lung injury/repair. However, if perinatal nicotine exposure affects the lipogenic potential of BMDMSCs is unknown. Furthermore, whether a targeted intervention, e.g., modulation of BMDMSCs lipogenic potential via specific miRNA targeting blocks nicotine-mediated BMDMSC effects, is also unknown. Zip521 is a central cell lineage determinant of mesenchymal stem cells, which through a complex network of physical and functional interactions, antagonizes Runx2. We hypothesized that perinatal nicotine exposure drives BMDMSCs miRNA profile towards a myogenic phenotype, blocking their lipogenic potential through Zip521 and miRNA-mediated regulation of Runx2.

Methods Used: Sprague Dawley dams were given 1 mg/kg nicotine (s.c.) once daily from e6 to postnatal day 21, when pups were killed and BMDMSCs isolated. Expression of the key myogenic markers [fibronectin and α-smooth muscle actin (α-SMA)] and adipogenic markers [adiponectin and PPARγ] were analyzed by RT-PCR and Western blot analysis. The expression of selected key myogenic and adipogenic regulatory miRNAs by mir-Q method, as well as the expression of Zip521 and RUNX2, were examined by q-PCR.

Summary of Results: Perinatal nicotine exposure resulted in decreased lipid staining, along with decreased adiponectin, LPL and PPARγ expression by BMDMSCs, but markedly increased myogenin and α-SMA expression, indicating perinatal nicotine-induced lipofibroblast-to-myofibroblast transdifferentiation (p<0.05 for all). In addition, with nicotine exposure, both Zip521 (0.5-fold) and MiR-30d (0.6-fold) were down-regulated (p<0.05 vs. control), accompanied by RUNX2 up-regulation and PPARγ down-regulation, providing novel mechanistic insights into nicotine-mediated increased myogenic, but inhibited adipogenic differentiation of BMDMSCs.

Conclusions: Perinatal nicotine exposure resulted in the down-regulation of both Zip521 and miR-30d, known negative regulators of RUNX2, resulting in inhibited PPARγ expression, providing fresh mechanistic insights and novel targets to modulate nicotine/smoke exposure during pregnancy-induced pathologies in the affected offspring. Supported by NIH HD51857, HD71731.

PERINATAL NICOTINE EXPOSURE MODULATES PPARγ EXPRESSION EPIGENETICALLY

Gong M, Vyas A, Liu J, Rehan V. LABIOMED, Torrance, CA.

Purpose of Study: Nicotine (NIC) induces down-regulation of PPARγ signaling, which is known to be regulated by DNA methyltransferase (DNMT1) and the epigenetic modifying enzyme, methyl CpG binding protein 2 (MeCP2). However, if how NIC-induced epigenetic alterations modulate PPARγ expression are not known. Using a well-established rat model of perinatal NIC-induced lung damage, we aimed to determine whether NIC-induced down-regulation of PPARγ is epigenetically regulated.

Methods Used: Pair-fed pregnant rat dams received either placebo or NIC (1 mg/kg, sc) in 100 μl volumes once daily from e6 until postnatal (PND) 21. At PND21, lung and testicular tissue were collected and processed for PPARγ promoter methylation studies using methylation-specific-PCR. Protein and mRNA levels of PPARγ, fibronectin, αSMA and MeCP2 were analyzed by Western blot analysis and q-PCR. To determine if NIC-induced down-regulation of PPARγ could be restored by DNA methylation inhibitor, 5-aza-2’-deoxycytidine (AZA), human embryonic lung fibroblasts, WI-38 cells, were used. Chromatin immunoprecipitation was also performed to determine histone modifications and the recruitment of DNMT1 and MeCP2 to PPARγ promoter.

Summary of Results: We found that in vivo conditions, NIC increased PPARγ promoter methylation, accompanying decreased PPARγ protein level (p<0.05 vs. control) in both lung and testicular tissue. Nicotine-induced increase in PPARγ promoter methylation as well as DNMT1 and MeCP2 protein levels were also observed in cultured WI-38 cells. Inhibition of DNA methylation by treating WI-38 cells with AZA blocked the NIC-induced decrease in PPARγ and increase in fibronectin and αSMA levels. Using ChIP-qPCR, we found enhanced NIC-induced physical interaction between PPARγ promoter and H3K9Me3 and MeCP2.

Conclusions: Nicotine exposure, under both in vitro and in vivo conditions, results in increased PPARγ promoter methylation, accounting for the NIC-induced decrease in PPARγ expression, likely mediated via the recruitment of DNMT1 and MeCP2 to PPARγ promoter. Our findings suggest important new mechanistic insights into NIC’s epigenetic regulation of PPARγ, providing novel prognostic/therapeutic targets for perinatal smoke-induced lung damage. Supported by NIH HD51857, HD71731.
lung mechanics, while female rat pups are unaffected. Maternal tobacco smoke (MTS) exposure also results in IUGR. However, the effects of MTS-induced IUGR on lung mechanics, specifically compliance and resistance, are unknown. **Objective:** We hypothesized that MTS alters lung compliance and resistance in rat offspring.

**Methods Used:** Maternal rats received tobacco smoke exposure from gestational day 11 to term. Pups were delivered at term and cross-fostered to a control dam until they were weaned at postnatal day 21 (d21). At d21, rats were anesthetized and paralyzed, and closed chest, lung static compliance and lung resistance mechanics were measured using the FlexiVent System.

**Summary of Results:** MTS significantly increased lung compliance in female (118 ± 4%, p=0.02), but not male rat offspring. Lung resistance was not affected by MTS in either male or female rat offspring.

**Conclusions:** MTS-induced IUGR leads to long-term increase in lung compliance in female rats. Given our previous findings of impaired lung mechanics male offspring in a model of sIUGR, we speculate that the programming of gene expression patterns in response to IUGR is sensitive to the cause of IUGR.

---


**PHYSIOLOGIC EFFECTS OF INSPIRATORY VERSUS EXPIRATORY TIDAL VOLUME TARGETING IN A NEWBORN ANIMAL MODEL.**


**Objective:** To evaluate the effect of inspiratory versus expiratory tidal volume targeting on lung compliance and resistance in newborn pigs.

**Methods Used:** Newborn pigs (1741±220 gm) were randomized to mechanical ventilation modes that use inspiratory (VaC) or expiratory tidal volume targeting (PAC+VG) to achieve an 8ml/kg breath (Avea ventilator, CareFusion, San Diego, CA). Pigs underwent 20-minute treatment blocks in both ventilation modes and with varying ETT leak: none, 30%, and 60%. Conclusions: PAC+VG resulted in marked alkalosis. This may be a result of the leak compensation algorithms or because the larger inspiratory volume delivered contributed more to ventilation than leak.
provide a novel mechanism to match ventilation to perfusion in the lung. Therapies targeting muscarinic receptors could improve both lung perfusion and ventilation, thereby helping patients with diverse airway or pulmonary vascular diseases. Support from NSF, NIH, and the Macpherson society.

### 119

**ELEVATED IGF-1 LEADS TO ALVEOLAR SIMPLIFICATION IN THE LUNG AT 3 DAYS OF VENTILATION OF PRETERM LAMBS**


**Purpose of Study:** Insulin-like growth factor-1 (IGF-1) is a morphogen that participates in lung development normally. IGF-1 expression is increased in the lung of mechanically ventilated (MV) preterm babies whose death was attributed to neonatal acute respiratory failure or chronic lung disease. Histopathologically, the lungs had alveolar simplification, evident as thick, cellular walls between distal airspaces and few secondary septa. Our studies using preterm lambs indicate that MV also leads to more proliferation, and less apoptosis, VEGF, and VEGF-receptor 2. Whether IGF-1 causes these effects is not known. We hypothesized that IGF-1 causes alveolar simplification.

**Methods Used:** Preterm (PT) lambs, treated with antenatal steroids and postnatal surfactant and caffeine citrate, were managed by (1) MV alone, (2) MV + nebulized IGF-1 receptor antagonist, (3) nasal high-frequency nasal ventilation (HFNV) alone, or (4) HFNV+IGF-1 receptor agonist (n=4 each). Treatment was 1/d on days of life 2 and 3. We assessed alveolar formation structurally and biochemically.

**Summary of Results:** MV for 3d led to thick, cellular walls of distal airspaces and few secondary septa. Blocking IGF-1 receptors during MV resulted in thinner walls and more secondary septa. In contrast, HFNV for led to thin, less cellular walls and many secondary septa. Unexpectedly, adding IGF-1 receptor agonist during HFNV did not lead to thicker and more cellular walls, and few secondary septa. However, it led to more proliferation, and less apoptosis, VEGF, and VEGF-R2. Blocking IGF-1 receptors during MV led to opposite effects.

**Conclusions:** We conclude that IGF-1 causes alveolar simplification through structural and molecular effects. Current experiments are using a higher dosage of IGF-1 agonist during HFNV to test whether alveolar simplification also occurs. Our results provide potential for blocking IGF-1 receptors during MV of preterm neonates.

---

### 120

**FETAL MARKERS OF SEVERITY IN CONGENITAL DIAPHRAGMATIC HERNIA (CDH) PREDICT PERSISTENCE OF PULMONARY HYPERTENSION (PH)**

Wai K1, Lusk L2, Basta A1, Moon-Grady AJ2, Filly RA3, Keller RL2. *UCSF, San Francisco, CA.*

**Purpose of Study:** CDH results in morbidity and mortality due to lung hypoplasia and persistence of PH. While fetal markers of CDH severity predict mortality, less is known about morbidity. We assessed these markers as predictors of neonatal PH.

**Methods Used:** We conducted a retrospective study of fetuses with left-sided CDH cared for after birth at UCSF (2002-12). We reviewed medical records for fetal and neonatal clinical data and excluded those with major anomolies. Clinical echocardiograms (Echo) were performed weekly for up to 6 wks until PH resolved off support or hospital discharge. Fetal ultrasound (AB and RF) and neonatal Echos (AMG and KW) were re-read. Fetal stomach position (degree of herniation) was classified from least to most abnormal: abdominal, anterior left chest, mid/posterior left chest, or retrocardiac (right chest), and liver position as abdominal or thoracic. Lung-to-head ratio (LHR) was determined at 20-29 wks GA. PH was assessed by Echo using ductus arteriosus level shunt (direction and velocity), interventricular septal position, then TR jet velocity. Time to PH-free survival (d) was determined when pulmonary artery pressure was estimated as <2/3 systemic blood pressure and evaluated by Cox proportional hazards, adjusting for GA at birth and fetal surgery and censoring at death or 100d.

**Summary of Results:** Fetal markers were evaluable in patients as follows: LHR (n=53), liver position (n=112) and stomach position (n=80). Fetal markers correlated strongly with PH-free survival (Table).

**Conclusions:** Fetal markers of CDH severity are strongly associated with time to resolution of PH in CDH, which is useful in prenatal counseling. These relationships may help identify fetuses for intrauterine interventions to mitigate PH.

**Fetal Markers of CDH Severity and PH-free Survival (d)**

<table>
<thead>
<tr>
<th>Fetal markers</th>
<th>%Resolved PH</th>
<th>Age at which 50% of patients are alive and PH-Free</th>
<th>HR (PH vs. PH-free)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LHR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;1 (n=36)</td>
<td>85%</td>
<td>15</td>
<td>0.27 (0.12-0.62)</td>
</tr>
<tr>
<td>≤1 (n=23)</td>
<td>46%</td>
<td>21</td>
<td>ref</td>
</tr>
<tr>
<td>Liver position</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aneurysmal</td>
<td>88%</td>
<td>11</td>
<td>ref</td>
</tr>
<tr>
<td>Operative</td>
<td>60%</td>
<td>15</td>
<td>0.38 (0.24-0.61)</td>
</tr>
<tr>
<td>Thoracic</td>
<td>100%</td>
<td>9</td>
<td>ref</td>
</tr>
<tr>
<td>Stomach position</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>94%</td>
<td>15</td>
<td>0.27 (0.12-0.61)</td>
</tr>
<tr>
<td>Mid/posterior</td>
<td>62%</td>
<td>17</td>
<td>0.10 (0.04-0.24)</td>
</tr>
<tr>
<td>Retrocardinal</td>
<td>47%</td>
<td>22</td>
<td>0.06 (0.02-0.20)</td>
</tr>
</tbody>
</table>

---

### 121

**LONGITUDINAL PLASMA ENDOTHELIN-1 LEVELS IN PREMATURITY INFANTS WITH AND WITHOUT BRONCHOPULMONARY DYSPLASIA**

Johnson C1, Chitkara R1, McCarthy E1, Finerman JR2, Sun C2, Kim L1, Hintz SR1, Van Meurs KP1, Punn R1, Mills CE1, Feinstein JA1, Stanford University, Palo Alto, CA and 2UCSF, San Francisco, CA.

**Purpose of Study:** Bronchopulmonary dysplasia (BPD) is a major cause of morbidity and mortality following premature birth, and may be associated with subsequent pulmonary hypertension (PH). Endothelin-1 (ET-1) has been implicated in the pathobiology of PH, with elevated levels found in term infants with PHHN and CDH. Longitudinal changes in ET-1 levels, the role of ET-1 in the development of BPD, and levels of ET-1 in premature infants remain to be elucidated. Thus, the objective of this study was to evaluate ET-1 levels and determine whether a relationship exists with the development of PH in premature infants, with and without a diagnosis of BPD.

**Methods Used:** We performed a prospective study of infants born at <30wks gestational age (GA) without major anomalies, or congenital infection. Plasma ET-1 levels were drawn at <1wk of age and every 4wks until 36wks postmenstrual age (PMA), when an echocardiogram was also performed for PH. ET-1 levels were measured by ELISA and echocardiograms were scored for PH by masked pediatric cardiologists using a standardized scoring tool.

**Summary of Results:** 15 patients (mean GA 27±2wks) were enrolled. Average ET-1 levels peaked at 29-32wks PMA (~29wks - 28.4±13.4 pg/ml, 29-32wks - 46.7±25.5 pg/ml, 32-36wks - 36.5±13.5 pg/ml). In infants without BPD, ET-1 levels appeared to peak at ~30wks PMA, regardless of chronologic age. Infants with BPD did not follow this trend, instead exhibiting persistently elevated or late increases in ET-1. Four of five patients diagnosed with BPD had ET-1 levels >40.0 pg/ml at 36wks, and median levels were...
higher for infants with BPD vs. those without; however, this difference was not significant likely due to small sample size (p= 0.085). PH by echo was not present in any subject.

Conclusions: In this small cohort of preterm infants, ET-1 levels were substantially higher than those reported for term infants with PPHN and CDH, and trended higher at 36wks PMA for infants with BPD vs. those without. Since infants with BPD are known to be at increased risk for PH, persistently elevated or increasing ET-1 levels may correlate with the development of BPD and serve as a marker for subsequent PH risk. A large prospective study is required to investigate this hypothesis.

Neuroscience I

Concurrent Session

3:30 PM
Thursday, January 23, 2014

122
BLOOD EXOSOMES: ANALYSIS OF ISOLATION VARIABLES AND A SOURCE OF BIOMARKERS FOR ALZHEIMER'S DISEASE

Harms C1, Crofton A1, Oh N1, Howard K1, Sanchez N1, Zabel M1, Antes T2, Sethi J3, Kirsch W1. 1 Loma Linda University, Loma Linda, CA and 2System Biosciences, Mountain View, CA.

Purpose of Study: To improve exosome isolation methods by analyzing variables that may affect isolation quantity and quality and to determine if blood exosomes are a source of Alzheimer's Disease (AD) biomarkers. Better diagnostic tests for AD are needed since definitive diagnosis remains possible only at autopsy. Exosomes are endosome-derived membrane-bound circulating microparticles normally found in most biological fluids. They contain protein and mRNA, may play a role in cell-cell signaling, and have already proven useful as a source of cancer biomarkers. Exosomes may simplify the diagnosis of AD as well. Given the heterogeneity of blood, studying an exosome blood fraction may simplify discovery and use of blood-based AD biomarkers and further elucidate mechanisms of AD.

Methods Used: Exosomes were isolated from serum and plasma from human volunteers (with LLU IRB approval) using polymer-based exosome isolation reagents. Variables hypothesized to affect exosome isolation quality and quantity such as reagents used, time of collection, storage method (freezing or refrigeration), and blood components used (serum or plasma) were analyzed via ELISA, atomic force microscopy (AFM), dynamic light scattering (DLS) and Nanosight microscopy. Flow cytometry for exosomal alpha-2-Macroglobulin (α2M), a protein previously shown to be a promising blood-based AD biomarker, was performed on frozen serum from aged controls, patients with mild cognitive impairment (MCI) and patients with AD.

Summary of Results: ELISA, AFM, DLS and Nanosight analysis all demonstrated exosomes were isolated. Storing serum but not plasma at -80°C significantly reduced exosome yield (p<0.02). Flow cytometry demonstrated an increase of exosome-derived α2M in AD compared to controls.

Conclusions: Plasma is a superior source of blood exosomes compared to serum since freezing serum, but not plasma, causes a significant reduction in exosome yield. Blood exosomes are indeed a source of potential AD biomarkers. More α2M was detected in AD blood exosomes compared to controls. Utilizing exosomal α2M instead of free serum or plasma α2M could improve its diagnostic specificity and sensitivity.

123
COMPLEMENT-MEDIATED DEGENERATION OF MICROVASCULAR SMOOTH MUSCLE CELLS IN CEREBRAL AMYLOID ANGIOPATHY

Milosavljevic ER. Loma Linda University School of Medicine, Loma Linda, CA.

Purpose of Study: Alzheimer’s disease (AD) is the most pervasive neurodegenerative disease that will affect an estimated 42.3 million people worldwide by the year 2020. One of the most distinctive, pathological features of AD includes the accumulation of fibrillar amyloid-β (Aβ) protein in the brain parenchyma. In more than 75% of patients with AD, Aβ accumulates in the microvasculature of the brain, which is specifically known as cerebral amyloid angiopathy (CAA). As previous research indicates, depositions of Aβ in the microvasculature leads to complement binding and initiation of the cytolytic antineuronal cascade resulting to lysis of vascular smooth muscle cells. The objective of this study is to test for the presence of late complement activation, in the form of cytolytic membrane attack complex (MAC), with the addition of Aβ on cultured vascular smooth muscle cells (VSMCs) harvested from brain tissue biopsies taken during epilepsy resection.

Methods Used: Experiments were performed using cultured vascular smooth muscle cells (VSMCs) harvested in epileptic resections from Dr. H. Vinters at UCLA neuropathology department. Cells were maintained at standard conditions (5% CO2, 37°C) in DMEM media with 10% Fetal Bovine Serum (FBS). Bachem Aβ proteins h-1149 were used along with an Aβ scramble h-2972. Both were transformed from their monomer to fibrillized form with incubation for 5 days at 37°C. EVOS microscopy analysis was used to visualize cell viability of VSMCs treated with media only; cobra venom factor (CVF), a potent activator of the complement cascade, and high and low concentration of Aβ.

Summary of Results: Results from EVOS microscopy analysis indicate decreased number of viable cells in the presence of complement-intact human serum activated in the presence of Abeta. Also, Quidel ELISA experiments show that MAC is activated by Abeta in a concentration- and time-dependent manner.

Conclusions: Understanding the mechanism of degeneration of smooth muscle cells in CAA, which increases blood vessel fragility thereby giving rise to microbleeds and hemorrhagic strokes leading to cognitive decline, provides opportunities for new therapeutic approaches to halt this degenerative process.

124
WIRELESS TECHNOLOGY TO ASSESS NEUROMOTOR FUNCTION DURING SUBSTANCE USE

Arnell MJ1, Park E3, Lee SS1, Li C1, Getachew R2, Lu DC2, 1 David Geffen School of Medicine at UCLA, Los Angeles, CA; 2 David Geffen School of Medicine at UCLA, Los Angeles, CA and 3University of California Los Angeles, Los Angeles, CA.

Purpose of Study: Current tools for assessment of motor function lack objective and consistent quantitative measures. This study attempted to bridge this gap by providing sensitive, non-invasive, digital tools for assessing upper and lower extremity motor function. The tools used include a handgrip device for grip strength and accuracy, tablet PC for hand dexterity, music glove for manual speed and accuracy, and gait device for speed, balance, and coordination. These wireless devices are currently used to measure motor improvement in patients who undergo surgical intervention for spinal cord injury. The primary aim of this study was to expand the scope of use of these technologies to assess motor performance of healthy participants before and after consumption of caffeine or alcohol to determine hazards of using these substances in the workplace.

Methods Used: 60 healthy participants between the ages of 21 and 75 were randomized to three groups receiving caffeine, alcohol, and no substance intervention. Each group of participants was tested with the devices, received their respective intervention, and was retested with the same devices. The first group was given a 200 mg caffeine pill. The second group consumed 1.5 oz increments of 40% ABV spirit according to a modified version of the Widmark formula to achieve a target blood alcohol content of .08%, the US legal limit BAC for operation of a motor vehicle. Participants were tested for blood alcohol content by a Department of Transportation-approved breathalyzer.

Summary of Results: Preliminary analysis of six participants showed that performance on the devices improved slightly in individuals just over the legal limit BAC. However, this improvement is not statistically significant and will require further testing.

Conclusions: The motor assessment devices did not sensitively determine motor impairment in individuals who were over the legal limit for driving.
125

BOTULINUM TOXIN FOR THE TREATMENT OF NEUROPATHIC PAIN: A REVIEW

Ghosh N. School of Medicine, University of California, Irvine, Irvine, CA.

Purpose of Study: Neuropathic pain is a widespread chronic disorder, affecting millions of people in the United States. There are several guidelines in place for the treatment of neuropathic pain, involving the use of anti-depressants, gabapentinoids, topical anesthetics, opioids and non-steroidal anti-inflammatory drugs (NSAID). However, these therapies come with significant adverse side effects. Thus, extensive research has been done to find a therapy with a higher benefit-risk ratio, and Botulinum toxin has been suggested as an alternative treatment. Botulinum toxin (BoNT), a toxin created by Clostridium botulinum, has been used extensively for its muscle-paralyzing effects. The neurotoxin blocks the transmission of Acetylcholine (ACH) at the neuromuscular junction, thus preventing muscle contraction. It was believed that BoNT could be used to treat pain resulting from excessive muscle contraction, thus inviting trials to test its efficacy in treating different kinds of pain. This review will discuss neuropathic pain, its commonly accepted treatments and then summarize the current literature involving the use of BoNT as a therapy for neuropathic pain.

Methods Used: We conducted a thorough literature review of Pubmed publications and Cochrane summaries discussing neuropathic pain mechanism, its current treatments, as well as the use of Botulinum toxin for its treatment. Each article was evaluated based on sample size and population, study design and relevant findings.

Summary of Results: Several preclinical and clinical trials have shown that the BoNT injection offers neuropathic pain relief prior to the relaxation of surrounding muscles. This pain relief lasted anywhere from days to months with a single injection. Adverse side effects were usually limited to the injection site.

Conclusions: Botulinum toxin appears to be beneficial for the treatment of neuropathic pain. The pain relief felt prior to muscle relaxation suggests that besides the well-known mechanism of blocking ACh transmission, BoNT also has anti-nociceptive properties. Despite having a boxed warning for the rare risk of mortality with inappropriate administration, it generally has a favorable side effect profile. Further clinical trials should be conducted in order to become an approved treatment for neuropathic pain.

126

EXAMINING THE BEHAVIORAL EFFECTS OF AGING ON FACE AND VOICE PROCESSING

Liu RR1, Pancaroglu R2,3, Barton JF2,3. 1University of British Columbia, Vancouver, BC, Canada; 2University of British Columbia, Vancouver, BC, Canada and 3University of British Columbia, Vancouver, BC, Canada.

Purpose of Study: Age-related effects are evident in many sensory modalities, which could lead to effects on behaviour. Face and voice processing plays a large role in social interactions and recognition of people. While numerous studies has examined how face processing changes with age, few studies have examined voice processing, as humans age. We conclude that social cues to the identity of people are more reliably identified from visual perception of faces than from auditory perception of voices as humans age.

127

CEREBELLAR NORDRENERGIC INNERVATION IS FUNDAMENTAL FOR THE ONSET OF PARKINSON DISEASE RELATED TREMOR - STUDY IN THE RESERPINED-RAT MODEL

Pomykala KL2,3, Bolzoni F3,4, Ratka M2, Asan E4, Volkmann J2, Ip C2, Biella G2, Cavallari P2, Isaia IU,2. 1David Geffen School of Medicine at UCLA, Los Angeles, CA; 2University of Würzburg, Würzburg, Germany; 3Università degli Studi di Milano, Milano, Italy; 4University of Würzburg, Würzburg, Germany and 5Istituto di Bioimmagini e Fisiologia Molecolare, Seregny, Italy.

Purpose of Study: Despite its clinical importance, the etiology of tremor in Parkinson disease (PD) is unknown. Preliminary evidence suggests the presence of an independent oscillating tremor-related network involving the cerebellum-thalamo-cortical pathway. We evaluated the effect of a neurotoxin (DSP-4) that lesions noradrenergic (NA) terminals arising selectively from the locus coeruleus (LC) in the reserpinized-rat model of PD.

Methods Used: Eight male rats (200-220g) received 50mg/kg DSP-4 i.p. and 2 weeks later 10mg/kg reserpine (DR group). A group of 7 rats received reserpine only (R group). Tremor, rigidity, hypokinesia, postural flexion, and postural immobility were scored (0=none, 1=modest, 2=severe) at 0, 20, 40, 60, 80, 120 and 180 minutes following reserpine injection. Number of LC-NA axon terminals was counted on tyrosine hydroxylase fluorenscently stained slides.

Summary of Results: DSP-4 induced a severe NA innervation loss of the cerebellum (DR: 0.024±0.01; R: 0.27±0.04 axons/mm2, p<0.001). Tremor was greatly reduced in DR vs. R rats (peak score at 40min: 0.5±0.8 vs. 1.57±0.5 respectively, p<0.01) and four DR rats (50%) did not show any tremor. Besides tremor, reserpine-induced bradykinesia signs were sustained for the duration of animal observations (score ≥1) and did not differ between the two groups.

Conclusions: Noradrenergic innervation of the cerebellum is fundamental for the onset of tremor in the reserpinized model of PD.

128

REPURPOSING ANTIANGIOGENESIS DRUGS TO PREVENT HYPOXIC CEREBRAL INJURY

Tarshis S Irwin D. University of Colorado School of Medicine, Colorado Springs, CO.

Purpose of Study: Understanding the destruction processes of an oxygen starved brain can provide insight to unknown brain function under metabolic stress, hypoxic vascular injury in the blood brain barrier, and potential treatments for a wide range of diseases especially those including high ICP. A great mechanism for studying the hypoxic brain is high altitude, with its worst outcome (HACE) serving as our model. HACE is a deadly and unpredictable brain disease for which there is still no effective prevention. A new prophylactic treatment for high altitude cerebral edema (HACE) needs to be developed, without the inefficacy of acetazolamide and the dangerous side effects of dexamethasone. Rather than treating the resulting symptom (drastic cerebral edema) with a nonspecific anti-inflammatory, HACE should be prevented by blocking the disease pathway further upstream its vascular edema pathway. I hope to repurpose an
already existing anti-angiogenic drug to prevent the onset of HACE. This approach will also better reveal the mechanisms of HACE onset, a pathway still not well understood.

Already existing anti-angiogenic drugs, currently used for tumor growth delay and wet macular degeneration should be tested for efficacy in HACE prevention. Although these drugs are meant for angiogenesis inhibition, some will most likely prevent vascular permeability as well, since vascular leakiness must precede angiogenesis for new vessel formation to be possible. These chemicals are selective, meaning fewer unwanted side-effects or toxicity, and reversible, suggesting safer effects. Most importantly, all these potential drugs are cell permeable; the chemicals can pass directly through the endothelial cells, astrocyte endfeet, and tight junctions that comprise the blood brain barrier. This means that they can be administered intravenously or after some modification, orally, and no injection directly into the brain (unrealistic for future transition to human patients) will be necessary.

Methods Used: We exposed 25 rats to hypoxic conditions treated with anti-angiogenesis drugs or antioxidants (to test if another pathway, reactive oxygen species, were instead the main cause of HACE) and 5 to control conditions. Their brains were analyzed for leak and inflammation utilizing the Evans Blue protocol.

Summary of Results: (pending statistical analysis 10-3-2013)

Conclusions: (analysis 10-3)

129

BASAL GANGLIA CHANGES IN PRIMARY FOCAL DYSTONIA CORRELATE WITH INCREASED DEPRESSION AND ANXIETY SYMPTOMS

Tran R1, Shelton E2, Berman B3, 1University of Colorado School of Medicine, Aurora, CO and 2University of Colorado, Aurora, CO.

Purpose of Study: Primary focal dystonia (PFD) is a chronic neurological disorder with abnormal and sustained muscle contractions. PFD is associated with increased risk of anxiety and depression, but the pathophysiology of these non-motor symptoms is unknown. In this study we compared functional connectivity (FC) maps of PFD patients to healthy controls (HC) to examine differences in basal ganglia (BG) circuits involved in motor and non-motor functioning. We then tested for relationships between FC changes and clinical assessments of symptoms.

Methods Used: FC maps of 12 PFD patients and 19 HC were assessed with resting state functional MRI scans. Motor and limbic symptoms were assessed with different scales (e.g., the Beck Depression Inventory for depression). We applied seed-based analysis to examine FC of four BG networks using the dorsal caudate putamen, ventral rostral putamen, inferior ventral striatum, and dorsal caudate, which serve as nodes in motor, motivation, behavior, and cognitive circuits, respectively. Using a two-sample t-test we identified clusters in which PFD patients had significant differences in FC compared to HC. We then correlated FC within these clusters in PFD patients with clinical measures.

Summary of Results: Compared to HC, PFD patients demonstrated FC changes in all four BG circuits with altered connectivity found to involve the thalamus, insula, and cerebellum. In PFD patients, changes in FC of the motor BG circuit were correlated with motor symptoms (r = +0.69, p<0.02), depressive symptoms (r=0.72, p<0.01), and anxiety symptoms (r=0.74, p<0.01); changes in FC of the motivation BG circuit were correlated with anxiety symptoms (r=0.73, p<0.01); and changes in FC of the cognitive BG circuit were correlated with anxiety symptoms (r=0.60, p<0.05). There were no significant correlations between FC changes of the behavioral BG circuit and symptoms.

Conclusions: PFD patients showed changes during rest in FC of motor and non-motor BG circuits, with some changes correlating with levels of motor symptoms, anxiety, and depression. These findings suggest that FC changes with BG circuits may underlie both motor and non-motor symptoms in PFD and that circuit-based therapies for PFD may be needed to better treat symptoms and improve the lives of patients.

130

A HYBRID METHOD FOR BRAIN TUMOR SEGMENTATION

Yang H1, Wang Y1, Zhao L2, Liu Y1, Tang S1, 1Beijing Institute of Technology, Beijing, China and 2Liaoning University of Technology, Jinzhou, China.

Purpose of Study: Locating the brain tumors is very important for surgery to design operation plan and perform the operation. The brain tumor segmentation is a key step to locate the tumor. In this letter, a hybrid method for brain tumor segmentation is developed.

Methods Used: In the proposed method, firstly the edge-detected filter is used to remove the noise in the MR image and the skull is removed by a free software BET. Then, a modified Chan-Vese-based model has been proposed to segment brain tumors since the original Chan-Vese model is not suitable for the tumor segmentation. Both global intensity and local gradient properties are used for brain tumor segmentation. The geodesic length is used to constrain the local gradient. The flowchart of the proposed method is shown in the Fig.1.

Summary of Results: To validate the proposed method, the images used in this study are obtained from the Surgical Planning Laboratory (SPL) of the Harvard Medical School & NSG Brain Tumor Database. The Jaccard, Dice similarity coefficient, false positive ratio, false negative ratio, sensitivity, and specificity are used to evaluate the tumor segmentation accuracy Table 1 shows the values of quantitative assessments. The results indicate a higher segmentation quality for the tumors.

Conclusions: In this paper, we propose a modified Chan-Vese model for brain tumor segmentation. The performance is very well. Acknowledgments: This work was supported by the National Basic Research Program of China (2010CB732505), National Science Foundation Program of China (61272360), project of Ministry of Education of Liaoning (L20122230).

131

PATTERN OF BRAIN INJURY PREDICTS LONG TERM EPILEPSY FOLLOWING NEONATAL ENCEPHALOPATHY

Xu QH1, Chau V2, Miller S3, Poskitt K2, 1University of British Columbia, Vancouver, BC, Canada; 2University of British Columbia, Vancouver, BC, Canada and 3University of Toronto, Toronto, ON, Canada.

Purpose of Study: Hypoxic-ischemic encephalopathy (HIE) is a major cause of neonatal seizures and long-term epilepsy. The objectives were to access the association between the patterns of brain injury and development of epilepsy.

Methods Used: The retrospective study included term with HIE (197) between 2004-2012 at BC Children’s Hospital. The standardized MR imaging was done between 3 & 5 days of life. The predominant pattern was classified as: Normal, Watershed, Basal Ganglia (BG), Total, Focal-Multifocal. Specific attention was directed to lesions in the hippocampus, motor cortex and occipital cortex. Fisher exact test and Kruskal-Wallis analysis of variance
were used for categorical and continuous variables respectively. Logistic regression was performed to examine the relationships between specific brain injury pattern and epilepsy.

**Summary of Results:** Of the 197, 132 (67%) had long-term follow-up. Epilepsy was found in 18 kids who were sicker at birth and more disabled (P<0.001). A significantly higher proportion with BG or Total patterns developed epilepsy (P<0.001). Injury in the motor cortex, hippocampus and occipital cortex (P<0.01) was strongly associated with epilepsy. In a logistic regression model adjusting for the patterns of injury, all 3 structures persisted as risk factors. However, when all added to the model at the same time, only the motor cortex remained as an independent risk factor for epilepsy.

**Conclusions:** In newborns with HIE, motor cortex injury is the best predictor of long term epilepsy, independent of the predominant pattern of HIE.

---

**134**

**PRE-LUNG TRANSPLANT FRAILTY IS COMMON, AND IS ASSOCIATED WITH POOR HEALTH-RELATED QUALITY OF LIFE**

Dean M1, Blanc P1, Katz P1, Hays S1, Leard L1, Golden J1, Kukreja J2, Singer J1. 1UCSF, San Francisco, CA and 2UC San Francisco, San Francisco, CA.

**Purpose of Study:** Improved health related quality of life (HRQL) in a primary clinical goal of lung transplant (LT). HRQL determinants in LT remain poorly defined, limiting our ability to design interventions to improve this outcome. Frailty is a geriatric phenotype predictive of poor HRQL and adverse clinical outcomes in various medical and surgical populations. We hypothesized frailty might be associated with HRQL in LT candidates, even after accounting for other measures of lung disease severity.

**Methods Used:** Subjects considered for LT from 2012-2013 completed the EuroQol-5D (EQ5D) and Fried Frailty measure (FFM). Frailty was defined as the presence of ≥3 of the following: unintentional weight loss >4.5kg, low measured walk speed, self-reported low physical activity level, self-reported exhaustion, and low measured grip strength. HRQL was quantified by the EQ5D health utility instrument (range: -0.11 to 1.0; higher scores denote better health). Consistent with established cut-points for the EQ5D, the minimal clinically important difference (MCID) was defined as 0.06 units or more (i.e., better HRQL reflected in a Δ in EQ5D≥+0.06). We calculated Spearman correlations between FFM and: EQ5D, %FVC, 6MWD, and age. We tested the association between frailty and EQ5D using multivariate linear regression, controlling for age, 6MWD, lung disease diagnosis, and %FVC.

**Summary of Results:** The 85 subjects had a mean age of 58.6±9.6 years; 40% were female. Of the 85, 24 (28%) were frail. Frailty correlated with EQ5D (ρ= -0.43; p<0.0001) and, to a lesser extent, with 6MWD (ρ=-0.23; p<0.05) but not with %FVC or age (both p>0.4). Frail subjects scored 0.22 points lower on EQ5D than non-frail subjects after controlling for covariates (95% CI: -0.33 to -0.12; p<0.001).

**Conclusions:** We found that frailty is occasionally diagnosed only after lung explant and that HP can recur post-LT. Notably, 1 and 3-year survival after LT for HP compares favorably to the national estimates for LT for all causes (86% and 64%, 2012 data). Outcomes after LT for HP do not differ markedly by sex.
135 LUNG TRANSPLANT IMPROVES HEALTH RELATED QUALITY OF LIFE AT ONE YEAR AFTER TRANSPLANT
Richardson C1, Blanc P1, Hays S1, Leard L1, Golden J1, Kukreja J2, Singer J1.
1UCSF, San Francisco, CA and 2UCSF, San Francisco, CA.
Purpose of Study: Health Related Quality of Life (HRQL) is a key measure of lung transplant (LT) efficacy. Since the 2005 overhaul of organ allocation (Lung Allocation System [LAS]), however, no US study has evaluated the impact of LT on HRQL. The medical acuity of patients undergoing LT has increased dramatically under the LAS, potentially limiting the generalizability of pre-LAS estimates of HRQL to patients considering LT today. Thus, we aimed to study the impact of LT on HRQL in the LAS era.
Methods Used: We performed an interim analysis of a prospective cohort study of subjects undergoing LT between 2010-12 at UCSF. Subjects completed structured surveys pre- and 1-year post-LT. Generic-HRQL was quantified with the Short Form-12 Component Summary scale (SF12 PCS; range 0-100; normative population mean 50±10; high scores denote better HRQL). Respiratory-specific HRQL was quantified with the revised Airways Questionnaire-20 (AQ20R; range 0-20; low scores denote better HRQL). Changes from before to after LT were tested with paired t-tests; effect sizes were also calculated. An 8-point change in SF12 PCS and ½ standard deviation (SD) change in AQ20R were defined as clinically meaningful based on standard criteria. For all analyses, subjects who died prior to one-year were assigned the worst possible scores (e.g. 0 and 20, respectively).
Summary of Results: The 73 subjects included in this analysis were 52±13 years; 58% female. HRQL was markedly impaired before LT (SF12 19.0±8.2; AQ20R 13.2±4.7). Even after accounting for the five subjects who died, subjects reported a greater than two SD improvement in HRQL 1-year after LT (SF12 40.8±16.4; AQ20R 5.2±5.6; both p<.001). Effect sizes for change were large for both generic-(d=2.7) and respiratory-specific HRQL (d=1.7). At 1-year, 58 (79%) reported improvements in generic-HRQL and 62 (85%) reported improvements in respiratory-specific HRQL that exceeded the clinically meaningful threshold.
Conclusions: Lung transplant provides substantial and significant improvements in generic and respiratory-specific HRQL. This study provides contemporary data-based estimates of the impact of LT on HRQL in the LAS era, which may be important for patients and clinicians considering LT today.

136 IDENTIFYING AND VALIDATING NOVEL HEALTH-RELATED QUALITY OF LIFE DOMAINS IN LUNG TRANSPLANT
Purpose of Study: Health-related quality of life (HRQL) is a primary indicator of lung transplant (LT) efficacy. However, the content validity of existing HRQL instruments has not been established in LT. Qualitative methods are generally considered necessary for HRQL instrument development, including assessing content validity. To address this need, we undertook a qualitative study to identify important HRQL domains in LT.
Methods Used: We conducted one-on-one semi-structured interviews with LT recipients 3-36 months post-LT (n=8) and providers (n=9), which included LT physicians, nurse coordinators, pharmacists, and social workers. Consistent with principles of qualitative methods, sample size was determined by saturation (i.e., the point at which no new information was identified). Interviews aimed to identify HRQL domains relevant and specific to LT recipients. Initial interview questions and probes were informed by the 8 general health domains defined in the Medical Outcomes Survey Short Form-36 (SF36) supplemented by review of the LT literature and discussion with LT experts. Interviews were transcribed verbatim and coded for themes. Interviews were iteratively modified to refine probes, as appropriate, throughout the process.
Summary of Results: Respondents confirmed the importance of all SF36 domains. We also identified 10 new and distinct domains relevant and important to LT recipients and care providers. These included: general quality of life; health distress/health outlook; psychological status (i.e., depression, cognitive functioning, anxiety); fatigue/weakness; resistance to illness; intimacy; ability to relate to others; symptoms (i.e., gastrointestinal, neurological, pulmonary, sleep, body image, side effects of medications); treatment burden (i.e., time spent, difficulty, impact on daily life); and financial burden/stress to caregivers.
Conclusions: We identified novel health domains important in defining HRQL in LT that can be used to augment those assessed by the SF36. This study lays the groundwork for development of a LT-specific HRQL instrument. Such an instrument may provide a more comprehensive measure of transplant efficacy and also identify areas for potential intervention to improve HRQL.

137 ANALYZING THE OUTCOMES OF SURGICAL APPROACHES FOR SINONASAL AND ANTERIOR SKULL BASE TUMORS
Kumar A Hwang P. Stanford University School of Medicine, Palo Alto, CA.
Purpose of Study: To examine and compare the treatment of traditional anterior craniofacial resection (ACFR) and exclusive endonasal approach (EEA) in the management of sinonasal malignancies and anterior skull base tumors.
Methods Used: The medical records of all patients undergoing surgical treatment for sinonasal and anterior skull base malignancies at Stanford Hospitals between 1997 and 2013 were analyzed using the Stanford Cancer Center Research Database (SCCRD) database. Comparison of treatment outcomes including disease-free survival and recurrence rates was performed.
Summary of Results: 117 patients satisfied the inclusion criteria for this study. 33 patients had undergone ACFR, 70 patients EEA, and 14 a combined ACFR + EEA approach. The median disease-free-survival for 50% of ACFR patients was 6.50 (+/- 2.14) years, and the median disease-free-survival for 50% of EEA patients was 5.00 (+/- 0.93) years. 8 (24%) of the ACFR patients had recurrence, 11 (16%) of the EEA patients had recurrence, and 1 (7%) of the ACFR + EEA patients had recurrence. The Cox regression suggests that the differences in recurrence rates for ACFR, EEA, and ACFR + EEA patients are not statistically significant (p=0.0878).
Conclusions: The differences in recurrence rates for ACFR, EEA, and ACFR + EEA patients are not statistically significant, but the longitudinal survival patterns for the three cohorts and the differing pattern of survival for ACFR and EEA patients suggest clinically significance.

138 A COMPARISON OF SURGICAL OUTCOMES BETWEEN IN-HOURS AND AFTER-HOURS TRACHEOESOPHAGEAL FISTULA REPAIRS
Yeung A1,2, Butterworth S1,2. 1University of British Columbia, Vancouver, BC, Canada and 2BC Children’s Hospital, Vancouver, BC, Canada.
Purpose of Study: Patients with non-emergent surgical operations have been found to have worse outcomes when the surgery is performed after-hours. The aim of the study was to investigate the surgical outcomes between in-hours and after-hours repairs of tracheoesophageal fistulas (TEFs) in a paediatric population.
Methods Used: We retrospectively reviewed all cases of surgical TEF repairs (n=32) at British Columbia Children’s Hospital between 2005 and 2010. The patient characteristics and surgical outcomes between the in-hours (n=25) and after-hours (n=7) groups were compared.
Summary of Results: The after-hours group experienced significantly more post-operative leaks than the in-hours group (p<0.05). There were no...
significant differences in the incidence of intraoperative complications, postoperative strictures, postoperative TEF recurrences, or mortality between the two groups. Patient characteristics (age and bodyweight at operation, skin-to-skin operative time, incidence of congenital heart disease, incidence of intraoperative desaturations, intraoperative blood loss, total ventilation time, and length of postoperative hospital stay) were also not significantly different between the in-hours and after-hours groups.

**Conclusions:** Paediatric patients with TEF repairs performed after-hours appear to be at a greater risk of developing postoperative leaks. Factors such as surgeon fatigue and inadequate OR staffing levels may play a role in this increase in postoperative complications. The results from these data will be able to inform refinements to the surgical prioritization system, allocation of resources and ultimately, improvements in the care of children with acute surgical needs.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>In-hours (n = 25)</th>
<th>After-hours (n = 7)</th>
<th>P value (Yates Correction)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoperative complications</td>
<td>Present 0% (n = 0)</td>
<td>14.29% (n = 1)</td>
<td>0.489</td>
</tr>
<tr>
<td></td>
<td>Absent 100% (n = 25)</td>
<td>85.71% (n = 6)</td>
<td></td>
</tr>
<tr>
<td>Postoperative leak</td>
<td>Present 4% (n = 1)</td>
<td>42.86% (n = 3)</td>
<td>0.056</td>
</tr>
<tr>
<td></td>
<td>Absent 96% (n = 24)</td>
<td>57.14% (n = 4)</td>
<td></td>
</tr>
<tr>
<td>Postoperative stricture</td>
<td>Present 40% (n = 10)</td>
<td>57.14% (n = 2)</td>
<td>0.706</td>
</tr>
<tr>
<td></td>
<td>Absent 60% (n = 15)</td>
<td>42.86% (n = 3)</td>
<td></td>
</tr>
<tr>
<td>Postoperative recurrence</td>
<td>Present 8% (n = 2)</td>
<td>0% (n = 0)</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Absent 92% (n = 23)</td>
<td>100% (n = 7)</td>
<td></td>
</tr>
</tbody>
</table>

### OUTCOMES OF SCLEROTHERAPY FOR THE TREATMENT OF VENOUS VASCULAR MALFORMATIONS

**Gorman J 1, Bucevska M 2, Amega J 2,3, Courtemanche D 2,3. 1University of British Columbia, Vancouver, BC, Canada; 2University of British Columbia, Vancouver, BC, Canada and 3British Columbia Children’s Hospital, Vancouver, BC, Canada.**

**Purpose of Study:** Venous vascular malformations (VMs) are the second most common vascular anomaly, with a prevalence of approximately 1.5%. VMs are congenital, low-flow lesions which grow in proportion to the patient and do not spontaneously involute. The natural history of these lesions is degenerative. The preferred treatment of VMs is sclerotherapy, commonly utilizing sclerosing agents such as doxorubicin or ethanol. This study reviews the outcomes and complications of sclerotherapy for the treatment of VMs in patients managed by the Vascular Anomalies Clinic at BC Children’s Hospital.

**Methods Used:** A 10 year retrospective chart review with minimum 2 year follow-up was conducted for patients with VMs who presented to the Vascular Anomalies Clinic at the British Columbia Children’s Hospital (BCCH) since May 1, 2001. Data collected included demographic data, VM characteristics, sclerotherapy treatment details, outcomes, re-expansion rates, and follow-up course.

**Summary of Results:** Of the 65 separate lesions examined in this study, the most common location of the VM was the head and neck (48%) and the most common presenting complaint was swelling or the presence of a mass (85%). VMs were categorized as either complex or simple based on the extent and anatomic location of the lesion; complex VMs were treated with fluoroscopic guidance and simple VMs were treated as minor surgery. The complication rates for the treatment of complex and simple VMs were 29% and 9%, respectively. The majority of complications were minor and transient for both complex (75%) and simple (100%) VMs.

**Conclusions:** This study demonstrated that both simple and complex VMs were successfully treated with sclerotherapy at BCCH. Sclerotherapy is a relatively safe procedure, where complications tend to be minor and transient. Furthermore, patients with simple VMs can attain the benefits of sclerotherapy as minor surgery while avoiding the anesthetic and radiation dose typically associated with treatment in the interventional radiology suite.

### LUMBAR MICRODISKECTOMY: RETROSPECTIVE CASE SERIES AND PREDICTIVE MODELING OF PATIENT OUTCOMES

Lu D, McArthur D, Holly L, Lu DC. David Geffen School of Medicine at UCLA, Los Angeles, CA.

**Purpose of Study:** Microdiscectomy has emerged as an alternative to open discectomy for the management of sciatic pain and sensorimotor deficit. Our objective was to evaluate patient outcomes following lumbar microdiscectomy, identify perioperative risk factors, and construct a predictive model for success or failure of surgery.

**Methods Used:** Medical records were reviewed for lumbar microdiscectomy cases performed between 6/1/11 and 6/1/13. Patients were scored by an independent investigator preoperatively and at latest follow-up according to Odom’s criteria. Data analysis and predictive modeling were performed using R statistical software. Outcome distributions were compared for each risk factor by Kruskal-Wallis rank sum test. Best-fitting predictive models were assessed for factor interaction and prognostic significance.

**Summary of Results:** Of 102 patients, 81 (79%) showed excellent or good surgical outcomes. No difference in outcomes was found for sex (p=0.1), age (p=0.59), neurosurgeon (p=0.77), presence of chronic pain (p=0.56), failed prior epidural steroid injection (p=0.37), duration of symptoms (p=0.49), acute etiology (p=0.47), smoking or illicit drug use (p=0.08), or BMI (p=0.56). Length of follow-up was negatively correlated with successful outcome (p=0.02). Statistical models incorporating length of follow-up and BMI were most predictive of surgical outcome (AICc=97.9).

**Conclusions:** Outcomes in our patient population are consistent with case series reported in the literature. No surveyed risk factor differentiated between patients with successful or failed spinal surgery. Perioperative parameters affecting lumbar microdiscectomy remain elusive and require further investigation.

**Patient outcomes based on Odom's criteria.**

<table>
<thead>
<tr>
<th>Odom's criteria</th>
<th>Outcome description</th>
<th>Patient count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>All preoperative symptoms relieved, abnormal findings improved</td>
<td>46</td>
</tr>
<tr>
<td>Good</td>
<td>Minimal persistence of preoperative symptoms, abnormal findings unchanged or improved</td>
<td>35</td>
</tr>
<tr>
<td>Fair</td>
<td>Definite relief of some preoperative symptoms, other symptoms unchanged or slightly improved</td>
<td>14</td>
</tr>
<tr>
<td>Poor</td>
<td>Symptoms and signs unchanged or exacerbated</td>
<td>7</td>
</tr>
</tbody>
</table>

Relative strength of predictive models.

<table>
<thead>
<tr>
<th>Model</th>
<th>Sex</th>
<th>Age</th>
<th>S urgeon</th>
<th>Chronic pain</th>
<th>Failed injection</th>
<th>Duration</th>
<th>Acute etiology</th>
<th>Smoking</th>
<th>BMI</th>
<th>EBL</th>
<th>LOP</th>
<th>AICc</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>97.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>98.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>99.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>99.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>99.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### REVITALIZATION OF BONE ALLOGRAFT WITH HUMAN INDUCED PLURIPOTENT STEM CELLS

Davis B, Saugue M, Baldini T, Bilousova G, Payne K. University of Colorado School of Medicine, Aurora, CO.

**Purpose of Study:** The aim of this study was to determine whether human induced pluripotent stem cells (iPSCs) could adhere, remain viable, and undergo osteogenic differentiation on a human cancellous bone allograft.
Methods Used: Human fibroblasts were reprogrammed to iPSCs and differentiated towards the mesenchymal lineage (referred to as mesenchymal progenitors or iPSC-MPs). iPSC-MPs were evaluated for mesenchymal markers CD90, CD73 and CD105 by flow cytometry. Bone marrow-derived mesenchymal stem cells (BM-MSC) were the positive control. Osteogenic differentiation potential in monolayer culture was evaluated by stimulating iPSC-MPs with either complete culture medium (CCM) or osteogenic medium (OSM). After 4 weeks, calcium deposition was evaluated by Alizarin Red stain. iPSC-MPs were seeded onto 4.8mm x 4.8mm decellularized cylindrical cancellous bone cores obtained from female cadaveric humeral head. Scaffolds were seeded with 1.2 x 10^6 cells and cultured in OSM or CCM. An unseeded group was cultured in OSM. Viability and attachment was evaluated using the LIVE/DEAD assay at 3 hours, 3 days, and 28 days. Histological samples were obtained after 28 days, decalcified, paraffin embedded and stained with Hematoxylin and Eosin (H&E).

Summary of Results: During mesenchymal induction, iPSCs began to display a fibroblast-like morphology usually seen with MSCs. iPSC-MPs also expressed mesenchymal cell surface markers CD90, CD73 and CD105. iPSC-MPs cultured in OSM in monolayer stained positive for Alizarin Red indicative of osteogenic differentiation. The LIVE/DEAD assay revealed that cells attached and were viable up to 28 days regardless if they were in CCM or OSM. These live cells were mainly seen around the outside edge of the construct. H&E staining showed variability in the porosity of the bone allografts and indicated that cells were present at 28 days. The resulting tissue appeared denser in the scaffolds cultured in OSM.

Conclusions: Human iPSCs were able to attach and remain viable on a human bone allograft, suggesting that they have potential to revitalize tissue. The lack of cells within the center of the scaffold suggests that future experiments may require a perfusion system. The greater tissue formation in the bone scaffold seeded with iPSCs and cultured in OSM suggests that iPSCs can be stimulated to form matrix within a bone allograft.

142 FACTORS AFFECTING USABILITY OF TECHNOLOGY IN THE OR: THE K-MOUSE USBILITY TEST
Phang M1, Bucev ska M2, Courtemanche D2,3. 1University of British Columbia, Vancouver, BC, Canada; 2University of British Columbia, Vancouver, BC, Canada and 3BC Children’s Hospital, Vancouver, BC, Canada.

Purpose of Study: With increasing use of picture archiving and communications systems (PACS) to review imaging in the operating room (OR), much effort has been put into the development of novel human-computer interfaces (HCIs) that allow surgeons to review imaging within a sterile field. K-Mouse is an HCI that allows surgeons to navigate PACS intraoperatively by moving their hands and performing gestures in front of a Microsoft Kinect infrared depth-sensing camera. By comparing the K-Mouse against a mouse-and-keyboard interface in simulated OR scenarios, this study aims to identify factors specific to an OR setting that determine the usability of HCIs.

Methods Used: Surgeons, surgical fellows, and surgical residents were asked to complete a series of tests using both a mouse/keyboard and the K-Mouse. Two sets of tests were devised: a general set designed to establish basic usability metrics, and a set designed to simulate typical intraoperative tasks using Phillips iSite PACS. Data was collected on time elapsed, tracking accuracy, and hesitancy. Participants were interviewed after completion of the tests.

Summary of Results: Eight participants completed the test procedure. In general usability tests, subjects took 5 to 8 times longer to complete straight-line movements using the K-Mouse, and 1.5 times longer to complete organic movements. Singular actions such as clicking and scrolling took approximately 2 times longer. Completion of simulated intraoperative tasks on iSite took 3 to 5 times longer. Participants expressed more frustration completing tasks using iSite compared to the general tests.

Conclusions: This study suggests that several barriers prevent the K-Mouse from being used in its current form, including fatigue, unreliable hand-to-screen tracking, and poorly-adapted user interfaces. However, with further development, intraoperative use of the K-Mouse or a similar system seems feasible, and participants stated they could see using a more refined system in the future. Furthermore, this study provided insight into factors that determine the usability of an HCI in the OR. Future HCIs for use in the OR must be developed with the ergonomic constraints of the OR in mind, and software must be designed to accommodate the nature of non-traditional HCIs.

143 ROTATOR CUFF MUSCLE MAPPING: DEPTHS OF SUPRASPINATUS AND INFRASPINATUS MUSCLES RELATIVE TO SKIN
McKnight R, Sato E, Ward SR. University Of California San Diego School Of Medicine, San Diego, CA.

Purpose of Study: Two-photon microscopy has recently been adapted to measure muscle sarcomere lengths through a 20 gauge needle. This technology shows promise for less-invasively measuring sarcomere lengths in deep muscles over time in cases of pathology and recovery. However, this technique requires a precise understanding of muscle geometry relative to superficial landmarks because it is not conducive to ultrasound (US)-guided needle placement. We are interested in the supraspinatus (SS) and infraspinatus (IS) muscles because they are frequently injured and undergo dramatic atrophic changes in cases of chronic tendon disease.

Methods Used: This study used US to image the scapula of men and women aged 22-55, without pathology, to determine the depth of the SS and IS muscles relative to skin at various regions of the scapula.

Summary of Results: At 1.9cm from the scapular spine, the 95% confidence intervals (CI) for the mid-belly depth (MBD) of SS relative to skin is shown to be -2.84+.23cm for males and -2.31+.24cm for females. Male SS MBD correlated with scapular spine length, but not significantly (r2=0.53, p=.162), while female SS MBD did not correlate with any measured variables. At this time, IS MBD differed significantly between genders (p=.008), while IS MBD did not. Results show the 95% CI for the MBD of IS relative to skin to be -2.45+.33cm for males and -2.04+.41cm for females. Female IS MBD significantly correlated with BMI (r2=.978, p=.001).

Conclusions: The results indicate that SS MBD differs significantly between genders, while IS MBD does not. In females, IS MBD correlates with BMI. The MBD 95% CI for the SS and IS muscles will allow researchers who utilize two-photon microscopy to create appropriate length needles for both genders and BMI may be a useful predictor of appropriate needle length in females. A future study will compare the differences between IS and SS MBD in patients with a history of rotator cuff tears.
Methods Used: Various epithelial grafting methods have been developed and expanded throughout the years. Epithelial grafts differ from split- and full-thickness skin grafts in that only the epithelial skin layer is removed. We present our experience using a new epithelial harvesting system to produce epithelial grafts. These grafts differ were placed on 4 patients (2 males and 2 females; mean age 50), whose comorbidities included diabetes, tobacco use, peripheral vascular disease, and obesity. All donor sites (right thigh) were cleaned using alcohol before harvesting grafts. After 45 minutes of harvesting procedure, epithelial grafts were removed using a film dressing and transferred to recipient sites, which included a secondary burn to the right breast, right scalp melanoma excision site, chronic foot wound, and wound created after removal of a sacral tattoo. In 3 patients, a guaze bolster followed by an occlusive dressing was used to cover the recipient site. In 1 patient, a reticulated open-cell foam was used as a bolster followed by an occlusive dressing to cover the recipient site. Film dressings were removed 3-5 days post grafting. Follow up occurred between 2-3 months.

Summary of Results: Three out of four patients had complete graft take; one patient had partial graft take. All donor sites healed completely without scarring.

Conclusions: In these 4 patients, epithelial grafting proved to be effective for use on various wound types and as an alternative for recipient sites in need of epithelial coverage. CelluTomeTM Epidermal Harvesting System, V.A.C.® GranuFoam™ Dressing (KCI USA, Inc., San Antonio, TX); Tegaderm Film (3M TM, Minneapolis, MN)

DESCEMET’S STRIPPING AUTOMATED ENDOTHELIAL KERATOPLASTY RESULTS OF VISUAL RECOVERY, ENDOTHELIAL CELL LOSS, AND EARLY COMPLICATIONS OF A SINGLE SURGEON USING THE TERRY TECHNIQUE

Truong A1, Lee J2, Cuzzo L2, Shamie N2. 1University of California, Irvine School of Medicine; Irvine, CA and 2Keck School of Medicine, University of Southern California, Los Angeles, CA.

Purpose of Study: To evaluate rates of visual recovery, endothelial cell loss, and early complications at 6 months after Descemet’s Stripping Automated Endothelial Keratoplasty (DSAEK) of a single surgeon using the Terry underfold technique and compare reproducibility to prior published results on the same technique.

Methods Used: Retrospective chart review of consecutive patients undergoing DSAEK for endothelial failure by a single surgeon at an academic tertiary referral center using the Terry 40/60 underfolding technique. Outcome measures included best corrected visual acuity and microscropy average endothelial cell loss at 6 months, early post-operative complications, and rate of late endothelial failure. Early post-operative complications included rate of graft dislocation, graft rejection, primary graft failure, and intrascleral pressure spike.

Summary of Results: Ninety-four consecutive eyes from eighty-four patients were enrolled in the study. Forty-eight eyes (51%) had either fuch peripheral vascular disease, and obesity. All donor sites (right thigh) were cleaned using alcohol before harvesting grafts. After 45 minutes of harvesting procedure, epithelial grafts were removed using a film dressing and transferred to recipient sites, which included a secondary burn to the right breast, right scalp melanoma excision site, chronic foot wound, and wound created after removal of a sacral tattoo. In 3 patients, a guaze bolster followed by an occlusive dressing was used to cover the recipient site. In 1 patient, a reticulated open-cell foam was used as a bolster followed by an occlusive dressing to cover the recipient site. Film dressings were removed 3-5 days post grafting. Follow up occurred between 2-3 months.

Summary of Results: Three out of four patients had complete graft take; one patient had partial graft take. All donor sites healed completely without scarring.

Conclusions: In these 4 patients, epithelial grafting proved to be effective for use on various wound types and as an alternative for recipient sites in need of epithelial coverage. CelluTomeTM Epidermal Harvesting System, V.A.C.® GranuFoam™ Dressing (KCI USA, Inc., San Antonio, TX); Tegaderm Film (3M TM, Minneapolis, MN)

DESCEMET’S STRIPPING AUTOMATED ENDOTHELIAL KERATOPLASTY RESULTS OF VISUAL RECOVERY, ENDOTHELIAL CELL LOSS, AND EARLY COMPLICATIONS OF A SINGLE SURGEON USING THE TERRY TECHNIQUE

Truong A1, Lee J2, Cuzzo L2, Shamie N2. 1University of California, Irvine School of Medicine; Irvine, CA and 2Keck School of Medicine, University of Southern California, Los Angeles, CA.

Purpose of Study: To evaluate rates of visual recovery, endothelial cell loss, and early complications at 6 months after Descemet’s Stripping Automated Endothelial Keratoplasty (DSAEK) of a single surgeon using the Terry underfold technique and compare reproducibility to prior published results on the same technique.

Methods Used: Retrospective chart review of consecutive patients undergoing DSAEK for endothelial failure by a single surgeon at an academic tertiary referral center using the Terry 40/60 underfolding technique. Outcome measures included best corrected visual acuity and microscropy average endothelial cell loss at 6 months, early post-operative complications, and rate of late endothelial failure. Early post-operative complications included rate of graft dislocation, graft rejection, primary graft failure, and intrascleral pressure spike.

Summary of Results: Ninety-four consecutive eyes from eighty-four patients were enrolled in the study. Forty-eight eyes (51%) had either fuch peripheral vascular disease, and obesity. All donor sites (right thigh) were cleaned using alcohol before harvesting grafts. After 45 minutes of harvesting procedure, epithelial grafts were removed using a film dressing and transferred to recipient sites, which included a secondary burn to the right breast, right scalp melanoma excision site, chronic foot wound, and wound created after removal of a sacral tattoo. In 3 patients, a guaze bolster followed by an occlusive dressing was used to cover the recipient site. In 1 patient, a reticulated open-cell foam was used as a bolster followed by an occlusive dressing to cover the recipient site. Film dressings were removed 3-5 days post grafting. Follow up occurred between 2-3 months.

Summary of Results: Three out of four patients had complete graft take; one patient had partial graft take. All donor sites healed completely without scarring.

Conclusions: In these 4 patients, epithelial grafting proved to be effective for use on various wound types and as an alternative for recipient sites in need of epithelial coverage. CelluTomeTM Epidermal Harvesting System, V.A.C.® GranuFoam™ Dressing (KCI USA, Inc., San Antonio, TX); Tegaderm Film (3M TM, Minneapolis, MN)
based on WHO criteria 3) repeat surgery for follow-up histopathology. Fisher exact test with non-Gaussian distribution was used for statistical analysis.

Summary of Results: 351 patients were included in the study. The average age at primary resection was 51 years (range: 5-80). 325 patients (92.6%) received radiotherapy and 314 patients (89.5%) had additional chemotherapy. The median length of survival from the time of initial GBM resection was about 20 months. A significantly greater number of GBM patients receiving bevacizumab developed SGS (15.4%) versus the no bevacizumab group (0.6%), p<0.0001, with a relative risk of 25.6%. Based on this study, there was no statistically significant difference in survival times for GBM patients treated with bevacizumab, compared to those who did not receive bevacizumab.

Conclusions: Our results suggest that bevacizumab is correlated with an increased incidence of SGS in GBM patients compared to those who did not receive bevacizumab. This increase in SGS may suggest that bevacizumab plays an important role in the pathogenesis of secondary gliosarcoma.

| TABLE 1. SGS development in Bevacizumab and No-bevacizumab cohorts |
|-----------------|-----------------|-----------------|
| Bevacizumab     | No Bevacizumab  | Total           |
| SGS             | 6               | 2               | 8               |
| No SGS          | 33              | 310             | 343             |
| Total           | 39              | 312             | 351             |

148

COMMUNITY-PARTNERED COLLABORATION TO BUILD AN INTEGRATED PALLIATIVE CARE CLINIC: THE VIEW FROM UROLOGY

Ballon-Landa E1,2, Bergman J2,3,4, Lorenz KA3,4, Saucedo F5, Saigal C2,3,4, Bennett CP2,3, Litwin MS2,3, UC Irvine School of Medicine, Irvine, CA; 2David Geffen School of Medicine at UCLA, Los Angeles, CA; 3VA Greater Los Angeles Healthcare System, Los Angeles, CA; 4RAND Corporation, Santa Monica, CA; 5UCLA Fielding School of Public Health, Los Angeles, CA and 3David Geffen School of Medicine at UCLA, Los Angeles, CA

Purpose of Study: Clinicians’ failure to adequately address end-of-life issues has led to high cost and low quality. Urologists develop close, longitudinal relationships with their patients with cancer. We partnered with patients, families, and palliative care clinicians to develop an integrated urology-palliative care clinic for patients with metastatic cancer. We qualitatively assessed urologists’ satisfaction with our multidisciplinary clinic model.

Methods Used: We conducted semi-structured interviews with 18 clinicians who practiced in the Greater Los Angeles VA clinic. Open-ended questions allowed participants to express themselves freely, revealing insights into feasibility, quality of care, and the role of the multidisciplinary clinic. We analyzed transcripts using a multistage, cutting-and-sorting technique in an inductive approach based on grounded theory analysis. Finally, we administered a 5-point validated 13-item physician job satisfaction survey of clinicians’ perspectives.

Summary of Results: Clinicians found that referring a patient to palliative care in the urology clinic was feasible and appropriate. Patients were receptive to supportive care, and physicians agreed that quality of care was improved following the intervention. None reported that the referral was overly time-intensive, nor that it disrupted clinic time as patients were happier and better attuned to their needs. Clinicians suggested that further improvement could be achieved with closer integration, and acknowledged that the infrastructure of the VA system (integrated care, EMR, lack of payment incentives, veteran benefits) facilitated such a model. Physicians expressed no overt dissatisfaction (1 or 2), and on average were at least somewhat satisfied, with mean responses 24 for 8 of 13 survey items.

Conclusions: Clinician satisfaction with a multidisciplinary palliative care/urology clinic for patients with advanced cancer is high. Avenues to further refine this model should be pursued.

149

DOES SYSTEMIC ILLNESS IMPACT PAIN THRESHOLDS IN CHILDREN UNDERGOING APPENDECTOMY?

Davis P1, Daum C1, Romanu R1, Stedk R1, Hassanian M1, Tagge E2, Hanna A1, Applegate R3, 1Loma Linda University School of Medicine, Loma Linda, CA; 2Loma Linda University School of Medicine, Loma Linda, CA

Purpose of Study: Children with appendicitis may be operated during the same admission as diagnosis (acute) or be treated with antibiotics, discharged and scheduled for appendectomy at a later time (interval). We hypothesize inflammation may alter pain sensitivity, which may impact comfort of the patient, analgesic requirements and postoperative length of stay. This study compares perioperative outcomes in children undergoing acute or interval laparoscopic appendectomy.

Methods Used: Patients operated between 1999 and 2013 were identified in a surgical database. Medical records of 180 subjects 15 years who underwent appendectomy for diagnosed appendicitis were reviewed. Data extraction included demographics, pain scores from nursing notes using either the pain visual-analogue (0 to 10) or FLACC scales; perioperative pain medication; surgical findings; and hospital length of stay.

Summary of Results: Acute had more inflammation, received more postoperative analgesic and had longer hospital length of stay (Table). Further analysis revealed patients with intraoperative findings consistent with acute inflammation had higher postop opioid requirement regardless of surgery timing suggesting greater inflammation may result in higher analgesic requirements after surgery. Further research is needed to clarify the optimal timing of laparoscopic appendectomy.

150

IMPACT OF PORT-LESS NEEDLESCOPY INSTRUMENTS ON COSMESIS IN THE PORCINE MODEL

Vasantachart J1, Martin J1, Maldonado J1, Lee M2, Yeo A1, Aisyof M2, Engrebretsen S1, Olgin G2, Lightfoot M2, Li R2, Hill ME3, Baldwin D2, 1Loma Linda University, Loma Linda, CA; 2Loma Linda University, Loma Linda, CA; 3Loma Linda University, Loma Linda, CA

Purpose of Study: Cosmesis is a critical measure for any surgical procedure. Port-less approaches have been gaining popularity due to lower cost and decreased risks associated with port placement and removal. This study compared cosmesis in the porcine model with and without a port.

Methods Used: A total of 12 pigs were used in this study. All procedures were performed under general anesthesia and aseptic technique. Two laparoscopic surgeons performed all procedures. One surgeon performed laparoscopic appendectomy with a port, while the other performed laparoscopic appendectomy without a port. The pigs were divided into two groups: port-less and port. The cosmesis was assessed by an independent observer who was blinded to the procedure. The cosmesis score was based on the amount of tissue discoloration, swelling, and suturing. The mean values were compared using a t-test.

Summary of Results: The results showed that the mean cosmesis score was significantly lower in the port-less group compared to the port group. The mean cosmesis score for the port-less group was 2.5, while the mean cosmesis score for the port group was 3.8. The difference was statistically significant (p<0.05). This study demonstrated that port-less laparoscopic appendectomy results in better cosmesis compared to traditional laparoscopic appendectomy with a port.

Conclusions: Port-less laparoscopic appendectomy results in better cosmesis compared to traditional laparoscopic appendectomy with a port. This study highlights the potential benefits of port-less laparoscopic procedures in reducing cosmesis and improving patient satisfaction.
Purpose of Study: Minimally invasive surgical techniques reduce scarring compared with traditional open surgery. However, these procedures may be technically cumbersome when trying to maintain single-site or natural orifice access. To simplify these procedures, surgeons may consider employing additional needlescopic ports and instruments. This study evaluates the cosmesis of portals needlescopic instruments compared to instruments with ports in a porcine model.

Methods Used: This was a prospective, randomized, single-blinded study. Two female farm pigs underwent a survival surgery in which a grid was tattooed on the pigs’ abdomens and randomized to 2.75 mm trocars, 2.75 mm portalless surgical tools and control sites which remained uninstrumented. A 2.25 mm surgical tool was placed into each trocar, and all tools were moved in a predefined series of motions for 3 hours to simulate typical intraoperative forces. Postoperative cosmesis was evaluated 4 weeks later by a blinded academic plastic surgeon during a nonsurvival procedure. The scars were measured, and the presence or absence of scars was assessed from a distance of 5 feet. Additionally, each scar was rated using the Vancouver Scar Scale (VSS) without restrictions.

Summary of Results: A total of 80 ports, 80 portless instruments and 12 controls were used. The port and portless sites both resulted in minimal scarring with no statistical difference between techniques. The average scar size of the port and portless sites were 3x2 mm with no significant difference in lengths (p=0.714) or widths (p=0.891). Only 31.3% (25/80) of the port incision sites and 27.5% (22/80) of the portless incision sites were identified from 5 feet. There was no difference in VSS score for port and portless sites (0.79 and 0.75 respectively, p=0.853).

Conclusions: Scarring was minimal and equivalent between port and portalless surgical sites with the same external diameter. This will potentially eliminate the need of an extra needlescopic port in laparoscopic surgery. Further human studies are needed to confirm these findings.

152

CERCAL WIRE: PRIMARY FIXATION METHOD FOR LONG SPIRAL FRACTURES IN LONG BONE

Epperly S, Burke C, Dajnowicz W, Basmajan H, Inceoglu S, Botimer G. Loma Linda University, Loma Linda, CA.

Purpose of Study: Compression plates are used in cases in which closed intramedullary nailing is contraindicated, i.e., patients with periarticular fractures. Compression plates provide desirable results but are costly. There is also a risk of weakening the bone and causing fatigue fractures once the plate is removed, a risk that is not present using cerclage wire fixation. Our objective is to test whether cerclage wire is a viable option for primary fixation in long spiral fractures, as it would be an inexpensive alternative to plating.

Methods Used: Preparation: Sixteen sheep femurs were used for this study. In each specimen, we made a 1 cm slit at a 40° angle with the longitudinal axis and cut through full cortical thickness using a Dremel power tool with a 0.040” thick wheel. The ends of the femur were embedded in Cerrobend. The femur was mounted to the universal biaxial materials testing machine (ElectroPuls E10000, Instron, Canton, MA). 500 N of compression was applied and the femur was torqued at 0.1%. This yielded a fracture length of 3.32 (3.00-3.78) diameters on average. Fixation: Eleven femurs were fixed with 3 double-banded 18-gauge cerclage wires that were placed equidistantly along the fracture. 5 femurs were fixed using a 10-hole locking plate, which was applied to the lateral cortex with a near-near, far-far screw orientation with four bicortical screws after initial reduction with a 3.5mm cortical screw. Testing: Each specimen was positioned on the Instron machine at a 15° anterior angle and a 7.8o varus angle. Cyclic loading was applied at 10 Hz starting from 700 N and increasing 100 N every 10,000 cycles with a standard deviation of ±100 N. Only 31.3% (25/80) of the port incision sites and 27.5% (22/80) of the portless incision sites were identified from 5 feet. There was no difference in VSS score for port and portless sites (0.79 and 0.75 respectively, p=0.853).

Conclusions: Scarring was minimal and equivalent between port and portalless surgical sites with the same external diameter. This will potentially eliminate the need of an extra needlescopic port in laparoscopic surgery. Further human studies are needed to confirm these findings.

151

CERCLAGE WIRE: PRIMARY FIXATION METHOD FOR LONG SPIRAL FRACTURES IN LONG BONE

Epperly S, Burke C, Dajnowicz W, Basmajan H, Inceoglu S, Botimer G. Loma Linda University, Loma Linda, CA.

Purpose of Study: Compression plates are used in cases in which closed intramedullary nailing is contraindicated, i.e., patients with periarticular fractures. Compression plates provide desirable results but are costly. There is also a risk of weakening the bone and causing fatigue fractures once the plate is removed, a risk that is not present using cerclage wire fixation. Our objective is to test whether cerclage wire is a viable option for primary fixation in long spiral fractures, as it would be an inexpensive alternative to plating.

Methods Used: Preparation: Sixteen sheep femurs were used for this study. In each specimen, we made a 1 cm slit at a 40° angle with the longitudinal axis and cut through full cortical thickness using a Dremel power tool with a 0.040” thick wheel. The ends of the femur were embedded in Cerrobend. The femur was mounted to the universal biaxial materials testing machine (ElectroPuls E10000, Instron, Canton, MA). 500 N of compression was applied and the femur was torqued at 0.1%. This yielded a fracture length of 3.32 (3.00-3.78) diameters on average. Fixation: Eleven femurs were fixed with 3 double-banded 18-gauge cerclage wires that were placed equidistantly along the fracture. 5 femurs were fixed using a 10-hole locking plate, which was applied to the lateral cortex with a near-near, far-far screw orientation with four bicortical screws after initial reduction with a 3.5mm cortical screw. Testing: Each specimen was positioned on the Instron machine at a 15° anterior angle and a 7.8o varus angle. Cyclic loading was applied at 10 Hz starting from 700 N and increasing 100 N every 10,000 cycles with a standard deviation of ±100 N. Only 31.3% (25/80) of the port incision sites and 27.5% (22/80) of the portless incision sites were identified from 5 feet. There was no difference in VSS score for port and portless sites (0.79 and 0.75 respectively, p=0.853).

Conclusions: Scarring was minimal and equivalent between port and portalless surgical sites with the same external diameter. This will potentially eliminate the need of an extra needlescopic port in laparoscopic surgery. Further human studies are needed to confirm these findings.

152

COMPARISON OF LARYNGOSCOPES FOR ENDOTRACHEAL INTUBATION BY TRAINEES IN CHILDREN UNDER 2

Daum C, Vadi M, Ghazal E, Applegate R. Loma Linda University, Loma Linda, CA.

Purpose of Study: This study compares intubating times between the Storz DCI, GlideScope® and direct laryngoscopy in children <2 years old. Study aim: determine differences in time to intubate a difficult airway when used by trainees.

Methods Used: Patients <2 years scheduled for surgery and endotracheal intubation were randomly assigned to intubation by GlideScope® video laryngoscope (G), Storz DCI® video laryngoscope, or standard laryngoscope (DL) after standardization of anatomic projection. Manual inline neck stabilization simulated difficult airway such as after trauma. Patients with known difficult intubation, elevated intracranial pressure, or increased aspiration risk were excluded. Laryngoscopists were anesthesiology trainees (clinical anesthesia year 2 or above) who had completed ≥1 month of pediatric anesthesiology rotation. Basic proficiency with each laryngoscope was shown by performing ≥3 consecutive intubations in <30 sec each on an infant airway manikin prior to study participation. Total time to successful intubation, number of intubation attempts, and best glottic view were recorded. An intergroup time difference ≥10 sec was considered clinically significant.

Summary of Results: Analysis of data from 93 intubations is shown in the Table.

Conclusions: Intubation was longer with S than DL. Grade 1 view was less likely but success on 1st attempt more likely in DL. We found no other significant intergroup differences. Two conclusions can be drawn: 1) There may be a clinically significant difference in TTSI when trainees use these laryngoscopes. The technique that should be utilized in a difficult airway should be what the anesthesiologist is most comfortable with. 2) Manikin intubation times are not necessarily indicative of the TTSI in this infant population. Trainees also need clinical experience to develop expertise with a laryngoscopy technique.
153

SPY IMAGING USE IN POST-MASTECTOMY BREAST RECONSTRUCTION PATIENTS: PREVENTATIVE OR CONSERVATIVE?

Lewis P, Mattison G, Kim H, Gupta S. Loma Linda University, Loma Linda, CA.

Purpose of Study: SPY imaging utilizes fluorescent dye to intra-operatively assess perfusion and viability of tissue. This study compared the surgeon’s assessment of flap viability with that of the SPY imaging perfusion during breast cancer post-mastectomy reconstruction.

Methods Used: The intra-operative difference between the plastic surgeon’s assessment of skin viability and the SPY image was analyzed in 16 breasts after mastectomy. The surgeon marked the area of the skin flap to excise, then SPY imaging was performed. The skin flap was resected prior to prosthesis placement according to the plastic surgeon’s assessment.

Summary of Results: A total of 16 breasts were analyzed. There was one incidence of necrosis requiring surgical debridement along with tissue expander removal and replacement. In one case, SPY imaging indicated a greater area of viability than the surgeon’s assessment. For the remaining breasts, resecting the area of diminished perfusion as indicated by the SPY would have resulted in a larger area of resection (p=0.038). Three of the 15 cases were nipple-sparing mastectomies. None of the nipples were well-perfused by SPY imaging, but no post-op necrosis occurred.

Conclusions: In this study, SPY was found to be conservative in its estimation of viability and could result in a more aggressive resection than the area deemed viable by the human eye. However, it is possible that the case of necrosis might have been prevented following the SPY imaging guidance for tissue viability. Overall, SPY imaging has the potential to be a valuable tool in assisting in the evaluation of skin flap viability following a mastectomy. Further analysis may reveal an explanation for the false negatives obtained in this study. Anything from excessive retraction and implant size to vasoactive medications and surgical experience can affect the image obtained. SPY imaging has a great deal of potential as a complementary tool to be integrated with the experienced surgeon’s analysis during post-mastectomy breast reconstruction.

154

LASER-GUIDED PERCUTANEOUS ACCESS—A NOVEL TECHNIQUE EVALUATED IN A BENCHTOP MODEL

Martin J1,2, Lee M1,2, Vassantachart J1,2, Maldonado J1,2, Yeo A1,2, Olgin G2, Lightfoot M2, Li R2, Engbretsen S2, Smith JC2, Baldwin D2, Loma Linda University, Loma Linda, CA and 2Loma Linda University School of Medicine, Loma Linda, CA.

Purpose of Study: The most commonly employed technique for percutaneous renal access utilizes continuous fluoroscopy, which accounts for a substantial percentage of procedural radiation exposure. In an attempt to minimize radiation dose, we have developed a novel laser-DARRT (Direct Access Radiation Technique). The purpose of this study is to compare the novel laser-DARRT technique to the conventional technique using a benchtop kidney model.

Methods Used: In the laser-DARRT, fluoroscopy was used only for selecting the skin site above the calyx. Utilizing laser alignment, the needle was inserted through the kidney parenchyma into the collecting system and depth was then confirmed using a pulse of fluoroscopy. This technique was then compared to the conventional technique, which utilizes continuous fluoroscopy for direct visualization in a randomized-controlled trial using a benchtop kidney model. Twenty subjects of varying experience with percutaneous access obtained entry into the upper, middle, or lower pole. Endpoints measured included insertion time, number of puncture attempts, number of course corrections, fluoroscopy time, and subjective procedural difficulty (1-10). Paired samples and the Wilcoxon Signed Rank Tests were used for statistical analysis with alpha set to 0.05.

Summary of Results: A total of 120 attempts were recorded by the 20 subjects (60 conventional and 60 laser-guided). Using the laser-DARRT technique, fluoroscopy time used to obtain caliceal access was significantly reduced in all three groups (6.69 vs. 20.22 sec, p<0.001; 6.55 vs. 13.93 sec, p<0.001; 7.90 vs. 18.51 sec, p<0.001). The subjects also rated the Laser DARRT technique easier to use (2.56 vs. 4.89, p<0.001). No statistical difference was seen between the techniques in regard to insertion time, puncture attempts, or course corrections.

Conclusions: This benchtop study demonstrates that the novel laser DARRT reduced fluoroscopy time by 63%. Therefore, we feel that this technique is a promising new option for percutaneous renal access. These results have implications in terms of routine endourological and radiological practice as well as future research in decreasing ionizing radiation exposure.

155

ORAL VERSUS INTRAVENOUS ACETAMINOPHEN FOR PRIMARY PEDRIATRIC CLEFT PALATE REPAIR: A RANDOMIZED CONTROLLED TRIAL

Davis P1, Ratsiu J1, Nour C1, Martin M2, Ray A2, Applegate R1, Loma Linda University School of Medicine, Loma Linda, CA and 2Loma Linda University School of Medicine, Loma Linda, CA.

Purpose of Study: Acetaminophen given to adults decreases postoperative analgesic requirements. This study investigates if oral and intravenous acetaminophen are effective anagesics for primary cleft palate repair in children as measured by opioid sparing effects.

Methods Used: IRB approved, double blind, randomized controlled trial registered in ClinicalTrials.gov (NCT01500109). Children <2 were randomized after written informed consent to: IV Acetaminophen/oral placebo; oral acetaminophen/IV placebo; or oral/IV placebo. Dosing was: IV Acetaminophen 12.5 mg/kg/dose; PO acetaminophen 15mg/kg/dose. Study agents were prepared by the pharmacy to blind patients, parents and hospital staff. All patients received PO midazolam 0.5 mg/kg preoperatively. Intraoperative management included dexamethasone 0.5mg/kg IV and local field block by the surgeon. Intraoperative and recovery room analgesics were given as determined by blinded anesthesiota team (fentanyl standardized based on patient weight). Postoperative rescue analgesic was morphine 50 mcg/kg/dose; placebos were provided to match calculated volume and color of study drugs. Primary outcome measure was 24-hour opioid as morphine equivalents, mcg/kg. Secondary outcome measures include age-appropriate pain scale.

Summary of Results: Placebo required more analgesics to attain similar postoperative pain scores than IV, while oral was not significantly different from IV (Table). Placebo required at least one more dose of rescue analgesic during the postoperative ward stay (N = 38, p = 0.01).

Conclusions: Our results suggest IV acetaminophen decreases postoperative analgesic requirement in these children. We were not able to demonstrate a difference between oral and IV administration in this interim analysis. Further research is needed to determine if patients experience fewer opioid associated side effects.

<table>
<thead>
<tr>
<th>Gender #</th>
<th>F: M</th>
<th>Placebo N = 14</th>
<th>Oral N = 10</th>
<th>IV N = 14</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age months median: 25 to 75% range</td>
<td>8.68 to 11.00</td>
<td>10.60 to 15.85</td>
<td>7.56 to 11.32</td>
<td>0.74</td>
<td></td>
</tr>
<tr>
<td>Weight kg median: 25 to 75% range</td>
<td>8.57 to 9.71</td>
<td>9.46 to 11.22</td>
<td>8.37 to 9.0</td>
<td>0.99</td>
<td></td>
</tr>
<tr>
<td>Parental satisfaction scores median 25 to 75% range</td>
<td>17.15 to 18.5</td>
<td>16.10 to 19.0</td>
<td>18.16 to 19.3</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>Morphine equivalents in 24 hours mcg/kg mean; 95% CI</td>
<td>122.2 (103.3 to 144.3)</td>
<td>81.6 (55.5 to 107.7)</td>
<td>70.74 (87.0 to 97.2)</td>
<td>0.005</td>
<td></td>
</tr>
</tbody>
</table>

IV needed less analgesic than placebo (p=0.05, Student’s t-test comparison of means) over the 24-hour study period, while oral did not reach significance (p=0.05). IV was less than placebo and oral during surgery (p=0.05), and both oral and IV were lower than placebo during the postoperative period (p=0.01).
A RETROSPECTIVE ANALYSIS OF THE ROLE OF PERIOPERATIVE PATIENT TEMPERATURE IN LOWER EXTREMITY FREE FLAP RECONSTRUCTION

Bowman S, Lewis P, Vogel, J S. Gupta. Loma Linda University School of Medicine, Redlands, CA.

Purpose of Study: To retrospectively examine perioperative conditions, postop outcomes and complications following lower extremity free flap reconstruction. Perioperative management, including core temperature control, is a vital aspect of all surgical procedures. Surgery increases risk for hypothermia, cited as core temperature ≤36°C, due to surgical exposure and anesthesia-related thermal effects. This may lead to infection, impaired wound healing, increased blood loss, cardiac morbidity, longer hospital stay and increased cost. Intraoperative hyperthermia, core temp >37.5°C, may also increase patient risk. Perioperative normothermia has shown to reduce recovery times and postcomplications. Free flap reconstruction patients are often victims of acute trauma with associated comorbidities increasing risk of postcomplications. This emphasizes the influence of optimizing temperatures to minimize postcomplications such as recipient site infection.

Methods Used: We analyzed patient medical records of lower extremity free flap reconstruction from June 2001-June 2012 for demographics, indication, recipient/donor site, flap type, comorbidities, intraoperative blood loss, core temperatures, and complications within one month. Statistical analysis utilized t-test for comparison of means.

Summary of Results: 64 patients underwent lower extremity free flaps. Tavg, Tmax and Tmin were 36.3°, 37.0°, and 35.7°C, respectively. Overall flap failure rate was 7.8%(5/64). Vascular thrombosis occurred in 3.1%(2/64) of cases and was identified in 10.5%(2/19) of patients requiring re-operation. Infection accounted for 26.3%(5/19) of re-operations, occurring in 5/64(7.8%) patients with lower mean core temperatures(Tavg=36.06°C,p=0.26). Infection risk increased for patients with Tmax below the median value(relative risk 1.5,p=0.053).

Conclusions: The importance of optimizing intraoperative core temp during free flap reconstruction cannot be understated and is worth investigating to potentially reduce patient complications. In this preliminary study, we found that patients with postop infections had lower mean core temperatures in the perioperative period and those with a Tmax below the median had an increased risk of infection. Further data collection should yield more significant results and confirm this hypothesis.

WAFMR, WSCI, WAP, WSPR, WSMRF

Student Subspecialty Award Poster Session

6:00 PM
Thursday, January 23, 2014

157

SKELETAL MUSCLE SPASTICITY RESULTS FROM SATELLITE CELL DEFICIENCY

Lyubasyuk V1, McKay B2, Dayanidhi S1, Chambers H2, Lieber RL1.
1UCSD, La Jolla, CA; 2Rady’s Children Hospital, San Diego, CA and 3McMaster University, Hamilton, ON, Canada.

Purpose of Study: Muscle contracture is a cause of major disability in cerebral palsy patients. There is limited knowledge about the cellular changes in muscles that underlie contracture. A recent flow cytometry study demonstrated decreased numbers of satellite cells per myofibers in cerebral palsy muscle (5.3±2.3%) compared to normal (12.8±2.8%). Satellite cells are myogenic stem cells that are responsible for myofiber growth, homeostasis and repair. Their absence may compromise muscle’s ability to restore damaged myofibers or generate new myofibers after cell division. The use of flow cytometry in human muscle is uncommon, thus the focus of this study was to quantify satellite cells in spastic and normal muscle using traditional immunohistochemistry, which is the golden standard for enumeration.

Methods Used: Semitendinosus muscle biopsies from pediatric patients were used (n=11). Muscle cross-sections of 10 μm were prepared with cryosection with OCT as the embedding media. Pax7/laminin/Dapi co-immunofluorescent stain was performed. Satellite cells were quantified at 40X.

Summary of Results: The satellite cell was defined based on its location between the basal lamina (demarcated by laminin) and sarcolemma, and co-localization of Pax7 stain with Dapi. The number of satellite cells/100 myofibers was reduced by 70% (p<0.000001) in children with CP (2.89±0.39) compared to control (8.77±0.79).

Conclusions: Quantification of satellite cells in situ demonstrated drastically decreased satellite cell number in spastic muscle compared to normal. This is important because the number of satellite cells is supposed to increase after muscle injury. Abnormally small numbers of satellite cells in cerebral muscle might be responsible for its limited ability to regenerate and grow. This limitation in longitudinal growth may be responsible for contractures that children with cerebral palsy develop. This possible novel mechanism opens new opportunities for the development of novel cerebral palsy treatments.

THINNING OF THE LEFT ROSTRAL ANTERIOR CINGULATE AND LEFT MEDIAL ORBITOFRONTAL CORTICES IN ADOLESCENT FEMALES WITH ANTISOCIAL SUBSTANCE DEPENDENCE

Boulos P1, Dahvani M2, Sakai J3. 1University of Colorado School of Medicine, Aurora, CO and 2University of Colorado School of Medicine, Aurora, CO.

Purpose of Study: Some individuals have onset of substance use disorders early in adolescence, develop multiple substance use disorder diagnoses, and have severe persistent courses. Youths in this population are likely to have a number of precursors, associated cognitive deficits, and characteristic co-morbidities such as conduct disorder. We have previously termed this Antisocial Substance Dependence. Although such youths exhibit more impulsivity, risk-taking, and problems of inhibition, relatively little is known about brain differences seen in such youths. This is especially true among adolescent females.

Methods Used: We recruited 22 patients from a university-based treatment program for youths with serious substance and conduct problems and 21 community controls, all female and aged 14-19 years. We obtained T1 structural brain images using a General Electric 3T MRI scanner and assessed for group differences in cortical thickness across the entire brain using FreeSurfer’s QDEC program and for three regions-of-interest bilaterally (total of 6 comparisons). These regions of interest were defined by the Desikan’s atlas, chosen based on a priori predictions from the literature, and included: 1) medial orbitofrontal cortex; 2) rostral anterior cingulate cortex; 3) middle frontal gyrus. Age and IQ were entered as nuisance factors for all analyses.

Summary of Results: Using a vertex-level threshold of p < 0.005 and Monte Carlo Simulation-determined cluster threshold we demonstrated on whole-brain analyses that one region, including the left rostral anterior cingulate cortex and extending into the left medial orbitofrontal region (355.84 mm² in size) was significantly thinner in patients. Region-of-interest analyses showed no significant difference in any of the 6 regions.

Conclusions: Adolescent females with Antisocial Substance Dependence have significantly thinner left rostral anterior cingulate and left medial orbitofrontal cortices. These regions have been hypothesized to be associated with poor behavioral control in past studies.

© 2013 The American Federation for Medical Research

191
VENTRICULAR ASSIST COMPLICATIONS ON THE WAITING LIST AND POST-HEART TRANSPLANT OUTCOMES

Siu M, Yu Z, Lioy F, Hamilton M, Kobashigawa J. Cedars-Sinai Medical Center, Los Angeles, CA.

Purpose of Study: Mechanical circulatory support devices have complications unique to this class of devices. Currently, patients awaiting heart transplant on Ventricular Assist Device (VADs) and listed as status 1B are allowed 30 days of status 1A. However, if these patients develop complications while on the heart transplant waitlist, then they are elevated to status 1A listing. This study is being performed to determine the incidence of complications in VAD patients and to assess whether they have compromised outcomes after heart transplantation compared to non-complicated VAD patients on the waiting list.

Methods Used: Between 2007 and 2012 we evaluated 72 patients awaiting heart transplant who were on VAD support pre-transplant. All patients were assessed for complications while on the waitlist as defined by the new “Guidance Regarding Adult Heart Status 1A(b) Device-Related Complications”. Patients were then divided into those that developed VAD complications while on the waitlist and those who did not. Post-transplant outcomes up to 3 years, including actuarial survival, freedom from cardiac allograft vasculopathy (CAV) and freedom from non-fatal major adverse cardiac events (NF-MACE), were assessed.

Summary of Results: 15 patients developed complications while awaiting heart transplant. Complicated VAD patients had comparable 3 year post-transplant outcomes with non-complicated VAD patients. 1 year freedom from any rejection, cellular rejection and antibody-mediated rejection were also the same between the two groups. Complicated VAD patients had numerically lower freedom from re-hospitalization 1 year post-transplant. (See Table).

Conclusions: VAD patients who developed complications while on the heart transplant waitlist appear to have comparable post-transplant outcomes. This supports upgrading these patients to status 1A listing pre-transplant as they have acceptable post-transplant outcomes.

<table>
<thead>
<tr>
<th>Complicated VAD (n=15)</th>
<th>Non-Complicated VAD (n=57)</th>
<th>log-rank p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 Year Actuarial Survival</td>
<td>93.3%</td>
<td>84.2%</td>
</tr>
<tr>
<td>3 Year Freedom from CAV</td>
<td>86.7%</td>
<td>87.7%</td>
</tr>
<tr>
<td>3 Year Freedom from NF-MACE</td>
<td>93.3%</td>
<td>93.0%</td>
</tr>
<tr>
<td>1 Year Freedom from Any Rejection</td>
<td>93.3%</td>
<td>87.7%</td>
</tr>
<tr>
<td>1 Year Freedom from Rehospitalization</td>
<td>66.7%</td>
<td>80.7%</td>
</tr>
</tbody>
</table>

Session: STUDENT SUBSPECIALTY AWARD POSTER SESSION

160

CONGREGATION-BASED INTERVENTION IN RESOURCE LIMITED SETTINGS: IMPLEMENTATION CHALLENGES & LESSONS LEARNED

Akondeng C1, Ezeanolue EE2, Ogidi A3, Osaji A4, Obiefune M5, Ehiri J3, 1University of Nevada Las Vegas, Las Vegas, NV, 2University of Nevada School of medicine, Las Vegas, NV, 3University of Arizona, Tucson, AZ and 4PeTR-GS, Enugu, Nigeria.

Purpose of Study: The Healthy Beginning Initiative (HBI) is a congregation-based approach to implement evidence-based interventions for Prevention of Mother-to-Child HIV Transmission (PMTCT) at the community level. We report challenges and lessons learned in implementing this initiative in southeast Nigeria with the hope that the experience would help to inform programs in other resource limited settings.

Methods Used: Focus group sessions and questionnaire survey of 15 HBI program staff. We assessed challenges related to: 1) Recruitment [study site selection; Church recruitment; Church randomization; Staff recruitment and training]; 2) Intervention [Participant enrollment, completion of pre-natal survey, laboratory testing]; and 3) Retention [post-partum follow-up, completion of post-partum survey, and potential linkage to care]. Programs using HBI model to promote birth outcomes through screening and linkage to care should first establish a model site to train CHAs before activating several implementation sites.

161

CHARACTERIZATION OF PRDM15 EXPRESSION DURING RETINAL DEVELOPMENT

Adewumi J1,2, Brezzinski F3, Park K2, 1University of Colorado School of Medicine, Aurora, CO and 2University of Colorado School of Medicine, Aurora, CO.

Purpose of Study: Diseases that result in retinal neuronal cell death cause vision loss in millions of people. This vision loss is permanent and irreversible in these patients because retinal neurons are incapable of regenerating. One promising approach is to use stem cells to create and transplant new neurons, thereby replacing the lost cells in patients. To accomplish this, a thorough understanding of the mechanisms that govern retinal neuronal development is required. Here, we investigated the role of a poorly understood transcription factor, Prdm15, in retinal development.

Methods Used: We spatially and temporally characterized Prdm15 expression in the murine retina using RT-PCR and immunohistochemical approaches. Mouse retinas were examined from embryonic (E) day 13.5 to mature adult stages. To determine which cell types express Prdm15, retinal sections were co-immunostained with multiple cell type-specific markers.

Summary of Results: Using RT-PCR, we determined that Prdm15 is expressed both during embryonic retinal development and in the mature adult retina. To assay the spatial expression pattern, we then immunostained retinal sections with anti-Prdm15 antibodies. Early in retinal development (E13.5) Prdm15 expression was sparse. Prdm15 progressively marked a larger fraction of the retina such that the entire adult neural retina was Prdm15 labeled. During embryogenesis, Prdm15+ cells co-labeled with early neuronal-specific markers, but not with proliferative progenitor cell markers.

Conclusions: We observed that Prdm15 expression onset correlated closely with the decision of proliferative progenitor cells to permanently exit the cell cycle and differentiate as retinal neurons. These data suggest that Prdm15 may control cell cycle exit in the retina. Gain- and loss-of-function studies are underway to test this possibility.

162

ROLE OF ADIPOSE TISSUE HYPOXIA IN INSULIN RESISTANCE

Bredbeck B1, Lawler H1, Erickson C3, Rassoul N1,2, 1University of Colorado, Aurora, CO and 2Denver VA, Denver, CO.

Purpose of Study: We hypothesized that improved angiogenesis in expanding fat results in decreased adipose tissue hypoxia and protection from insulin resistance. Adipose tissue oxygenation (AT pO2) and markers of angiogenesis and inflammation were investigated in obese insulin sensitive (OBIS) compared to obese insulin resistant (OBIR) and lean subjects.

Methods Used: Non-diabetic, sedentary subjects were enrolled in this study. OBIS subjects were characterized by BMI 30-40 kg/m2, absence of metabolic syndrome criteria and insulin sensitivity (SI) values above 2.7x10^-4 mI/μU/mL. SI was calculated using insulin modified frequently sampled intravenous glucose tolerance test. Total body fat was quantified by dual energy X ray absorptiometry. Partial pressure of oxygen in subcutaneous adipose tissue (SAT) was measured in vivo. Plasma angiogenesis factors were measured using ELISA. The expression of candidate genes involved in angiogenesis and inflammation were measured in SAT using SYBR qPCR.

192 © 2013 The American Federation for Medical Research
Summary of Results: Obese group (n=12) had a BMI of 34.1±1.3 while lean group (n=4) had a BMI of 22.9±1.0 (p<0.01 v. obese). OBIS (n=6) and OBIR groups were similar in age, BMI and body fat but different in SI. The mean SI was 4.4±0.8, 3.5±0.3, and 1.8±0.2 in the lean, OBIS, and OBIR groups, respectively (p<0.001, OBIS v. OBIR). ATPo2 was increased in lean as compared to obese subjects (53 ± 1.9 v. 37.7±2.9 mm/Hg, p<0.001). Obese subjects had increased gene expression of CD68 and decreased VEGF-A by 31% and -192% respectively (p<0.05 vs lean); but mRNA levels of HIF1a, FGF2, HGF, ANGPTL2 and endothelin were similar among groups. However, OBIS subjects had increased plasma levels of ANGPTL2 (335.0±40.7 v. 159.5±33.5 pg/ml, p=0.008 v. OBIR), and HGF (37.2±3.87 v. 25.7±1.2 pg/ml, p=0.05 v. lean). Plasma VEGF-A and FGF2 levels were similar among groups and EGF and endothelin were undetectable in circulation. ATPo2 correlated with mRNA levels of VEGF-A and negatively with BMI (r=0.7, -0.8 respectively, p<0.05) but it did not correlate with SI.

Conclusions: We confirmed that obesity was associated with adipose tissue hypoxia and inflammation; yet there was no distinction in ATPo2 between the OBIS and OBIR groups. Our data suggest that adipose tissue hypoxia is simply a consequence of fat expansion and not related to insulin resistance.

163
INFLAMMATORY COLITIS, LYMPHATIC INSUFFICIENCY, AND PROGRESSION TO COLORECTAL CANCER IN AN EXPERIMENTAL MOUSE MODEL


Purpose of Study: Inflammatory bowel disease (IBD) is a well-recognized risk factor for colorectal cancer (CRC) [15-20% lifetime risk in ulcerative colitis (UC)]. The lymphatic system has been implicated in both IBD pathophysiology and CRC growth/spread. Previously, we showed in acute dextran sulfate sodium (DSS) colitis, lymphatic deficient mice [knockout of angiopeptin-2 (Ang2)] exhibited reduced lymphangiogenesis and downregulated inflammatory markers. This study extends these observations to chronic UC and examines progression to CRC.

Methods Used: C57B6 adult mice (Ang2 +/−,+/−, +/+ (Regeneron)) were divided into 4 groups. Group 1 - single 4 or 12 mg/kg IP dose of procarcinogen azoxymethane (AOM) and 14 days later, 1-1/2% DSS in drinking water for 7 days then 14 days off DSS (cycle repeated 1-2X -clinical severity score). Controls included AOM alone (Group 2), DSS cycles without AOM (Group 3), or untreated (Group 4). Clinical severity scores (changes in body weight, energy, stool consistency, occult blood) were followed. At sacrifice, colon length was measured and tissue sampled in 4 segments from proximal to distal colorectum and assessed by inflammatory index, tumor burden, and histologic features.

Summary of Results: Groups 1 and 3 showed similar clinical severity and mortality and reduced survival (46.5% c.f. 90%) in Ang2−/− whereas Groups 2 (4mg/kg AOM) and 4 were unaffected. Group 2 exhibited rapid 100% mortality at 12 mg/kg AOM but 0% at 4mg/kg. Group 1 had 91% non-invasive CRC incidence in the distal segment. Ang2−/− were not protected from CRC, and clinical severity tended to be worse. Tumor burden in +/− mice (13.5% of distal colon surface) was significantly higher than +/+ (4.6%, p=0.008) and +/+ (5.5%, p=0.007) (n.s. +/− vs +/+).

Conclusions: This refined mouse model of UC progression to CRC is rapid, reproducible, and well-tolerated with high CRC incidence demonstrating that even subacute UC in the presence of a low-dose procarcinogen tolerated by the normal colon is a CRC forerunner. Further, lymphatic deficiency, defective lymphangiogenesis, and impaired lymphatic-generated inflammation do not protect against either the UC clinical severity or its progression to non-invasive CRC.

164
MULTIPLE CHOICE AND IMAGE MAPPED ONLINE MODULES FOR TEACHING THORACIC RADIOLOGIC ANATOMY

Sue M,1 Brown K2, Gu Z3, Krause S4, 1DGSOM at UCLA, Los Angeles, CA; 2DGSOM at UCLA, Los Angeles, CA; 3DGSOM at UCLA, Los Angeles, CA; and 4DGSOM at UCLA, Los Angeles, CA.

Purpose of Study: This study aims to determine the efficacy of teaching thoracic radiologic anatomy using Perceptual and Adaptive Learning Modules (PALMs) in multiple-choice (MCQ) and image-mapped (IM) formats.

Methods Used: Repeated exposures to different images with the same underlying pattern increase the speed and accuracy of pattern recognition. Thoracic radiologic anatomy PALMs utilize this principle by presenting learners with a sequence of images, categorized by structure, and asking them to identify specific anatomic structures. PALMs adapt to a learner’s ability by sequentially presenting the structures to be identified based on the learner’s previous accuracy and response time (RT) for each structure, and by removing learned structures as the module progresses. In MCQ PALMs, learners identify a structure from a list of 5 choices. IM PALMs ask the learner to click on the location of a given structure. After each trial, both formats provide feedback to the learner on accuracy and RT as well as the correct identity or location of the structure.

Both IM and MCQ PALMs were developed for PA and lateral chest X-rays and thoracic CT scans with and without contrast. We compared efficacy of the PALMs in enhancing performance of Year 2, 3 and 4 medical students based on pre- and post-tests. A Year 2 focus group was also used to compare the two formats and provide feedback about the PALMs.

Summary of Results: The use of either PALM format significantly and dramatically improved knowledge of thoracic anatomy with minimal time investment. Some modules showed significant differences in RTs and accuracies between MCQ and IM PALMs, but no systematic trends were observed.

Conclusions: Students found both types of PALMs useful but preferred the IM to MCQ versions.

165
ANALYZING THE CLINICAL INDICATIONS WHEN TESTING FOR LYNNCH SYNDROME USING NEXT GENERATION SEQUENCING

Perez M, Gallego C, Bennett R, Jarvik G. University of Washington, Seattle, WA.

Purpose of Study: Massive parallel sequencing (MPS) allows physicians to screen multiple genes at once to look for pathogenic variants in a patient’s genome. The Coloseq panel consists of 13 genes associated with colorectal polyps and malignancy including Lynch Syndrome (LS), an inherited susceptibility to cancer of the digestive tract and endometrium. Current guidelines recommend using age, family history, and histologic tests to screen for LS before proceeding to genetic testing. The Amsterdam II Criteria and Bethesda Guidelines have been used to help identify people and families at risk of LS. The study analyzes the efficacy of established guidelines when determining who should receive genetic testing using Coloseq.

Methods Used: A chart review was performed on patients (n=101) who had Coloseq performed at the University of Washington. An abstraction form was used to collect personal information, family history, and lab results. Patients were excluded if they had Coloseq performed but results were not available.

Summary of Results: A total of 30 patients for whom the Coloseq test was performed had a variant returned. Of these, 9 variants were pathogenic, 5 likely pathogenic, and 16 were variants of unknown significance (VUS). Of the 39 patients who fit Bethesda Guidelines and/or Amsterdam II Criteria, 8 (20.5%) were found to have a pathogenic or likely pathogenic variant. Four of these 8 were in LS genes. For subjects that did not meet Amsterdam II or Bethesda criteria the rate of identification of pathogenic or likely pathogenic mutations was 6/62 (9.7%); 3 of the 6 were in LS genes. Of the 9 patients who showed loss of protein expression from a LS gene by sequencing tests, 4 had a pathogenic or likely pathogenic variant.

Conclusions: The sensitivity of the Coloseq panel depended on clinical indication. Although patients meeting Amsterdam II and Bethesda Guidelines had a higher positive test rate, these guidelines lacked the sensitivity to identify all patients with pathogenic or likely pathogenic variants in LS genes. The extended panel improved yield vs. LS genes alone. With 16 of the 30 returned variants being VUS, emphasis would be needed for shared pathogenicity information and for patient follow up when additional information is obtained.
INTERIM RESULTS: AN INNOVATIVE COMBINATION OF EXCIMER LASER, CLOBETASOL SPRAY, AND CALCITRIOL OINTMENT FOR THE TREATMENT OF PSORIASIS


Purpose of Study: Psoriasis is a chronic inflammatory dermatosis that is estimated to affect 2-3% of the US population. The therapeutic approach may be determined based on the distribution of psoriasis such that localized disease is managed with topical agents and targeted UV therapy, while biological agents are usually reserved for generalized disease. The excimer laser is a targeted treatment modality indicated for localized psoriasis that allows selective irradiation of affected skin, resulting in less photodamage compared to traditional whole body phototherapy. The use of laser in combination with topical therapy has never been studied in generalized psoriasis.

In this study, we aim to improve the excimer laser efficacy with clobetasol spray and calcitriol ointment for the treatment of generalized psoriasis.

Methods Used: Patients with plaque psoriasis involving 10-30% body surface area were recruited for this 12-week study. All patients underwent twice weekly treatments with the XTRAC® Velocity 308nm excimer laser until week 6 and thereafter as needed if ≥75% improvement in Psoriasis Area Severity Index (PASI). The 12-week study period is divided into three 4-week treatment periods in which the patients supplemented laser treatment with twice daily dosing of topical agents, including clobetasol spray (weeks 1-4), calcitriol ointment (weeks 5-8), or both clobetasol and calcitriol (weeks 9-12). The primary endpoint was the percentage of patients achieving ≥75% reduction in PASI (PASI-75) at week 12.

Summary of Results: To date, a total of 21 patients have completed the protocol. At week 12, 76% of patients (16/21) achieved PASI-75 with an average of 15 laser treatments. The treatments were well tolerated with the most commonly reported side effects of pruritis, burning, and superficial blistering.

Conclusions: This is the first ever study investigating the treatment of generalized psoriasis with excimer laser in combination with clobetasol and calcitriol. At week 12, 76% of patients achieved PASI-75, which is superior to the efficacy of biologic medications without the internal risks of systemic therapy. While the excimer laser is usually reserved for localized psoriasis, the results of this study demonstrate its utility in generalized psoriasis when supplemented with topical therapy.

COMBINATORIAL ANTIGEN RECOGNITION BY ENGINEERED T CELLS

Salter AL, Liu L, Riddell SR. 1University of Washington, Seattle, WA 2Fred Hutchinson Cancer Research Center, Seattle, WA and 3University of Washington, Seattle, WA.

Purpose of Study: Adoptive transfer of gene-modified T cells expressing a synthetic chimeric antigen receptor (CAR) is emerging as an effective cancer therapy. CARs consist of a recognition domain fused to transmembrane, costimulatory, and activation domains, and redirect T cell specificity to a tumor cell surface molecule. However, single wholly restricted tumor antigens are rare in solid tumors, and on-target, off-tumor toxicity is observed with CARs for molecules co-expressed on some normal cells. To mitigate toxicity, we constructed a CAR library that provides activation and costimulatory signals on separate vectors to require simultaneous recognition of two antigens.

Methods Used: CAR lentiviral vectors were constructed by linking coding sequences for recognition, transmembrane, costimulatory and/or activation domains, in a single reading frame. Human CD8+ T cells were transduced with CARs encoding recognition and costimulatory domains for CD19, ROR1 and/or EGFR, and dual expressing cells were purified by cell sorting. Target cells expressing one or more of the CD19, ROR1, and/or EGFR target molecules were analyzed for recognition by CAR-modified T cells using cytotoxicity, cytokine release, and proliferation assays.

Summary of Results: We assembled a library of seventeen CAR vectors that linked activation or costimulatory domains to distinct recognition domains specific for tumor antigens such as EGFR, CD19, or ROR1. Human CD8+ T cells transduced with an activating and costimulatory CAR recognizing 2 different antigens could be isolated and propagated for analysis. Transduced CD8+ T cells mediate more efficient recognition of target cells expressing both antigens than targets expressing only one antigen.

Conclusions: Delivering activating and costimulatory signals in trans is an attractive strategy to impose selectivity for tumor cell recognition because T cell proliferation and cytokotoxicity should be limited to cells simultaneously expressing both cell surface antigens. Our CAR library offers a novel way to target two tumor antigens using gene-modified T cells and may reduce toxicity when one antigen is expressed on normal host tissue.

HEALTH-FAIR IDENTIFICATION OF SUBJECTS AT RISK FOR FUTURE RHEUMATOID ARTHRITIS


Purpose of Study: It is established there is a ‘preclinical’ period of rheumatoid arthritis (RA) when biomarkers including rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibodies (CCP) are abnormal while joint exam is negative for synovitis. RF and CCP abnormalities are also highly predictive of future RA, although most data regarding prediction are derived from retrospective studies and little is known from prospective community-based studies. Therefore, in a community health fair we identified and followed subjects with elevated biomarkers but absent clinical RA to evaluate rates and predictive factors for development of future RA.

Methods Used: Volunteers were tested for serum CCP3 (INOVA) at a Colorado health fair from 2008-2012. Subjects with CCP3 positivity without RA by physical examination were invited for biannual follow-up that included assessment of demographic factors, environmental exposures, joint symptoms and findings assessed by a trained study physician or nurse, and testing of CCP3 and CCP3.1 (INOVA), CCP2 (Axis-Shield), RF isoforms IgG/IgA (INOVA), C-reactive protein (CRP), and the shared epitope (SE).

Summary of Results: 7178 volunteers were initially evaluated, and 158 (2%) were CCP3+ without RA development as CCP3 >3x normal plus positivity for any RF assay at any level (OR 5.5, 95% CI 1.2-25.3; sensitivity 39%; specificity 90%; positive predictive value 70%). Age, sex, smoking, family history of RA, baseline joint symptoms or examination tenderness, CRP and SE were not associated with development of future RA. Predictive factors for development of future RA included CCP3 positivity, age (OR 2.8), baseline RF positivity (OR 2.7), and CCP3 positivity present at the baseline health fair (OR 40.3).

Conclusions: A health fair evaluation is able to identify subjects at-risk for future RA. CCP3 >3x normal and RF positivity were most strongly associated with development of RA. These findings may be used to develop methods to identify subjects for studies of preclinical RA, and RA prevention.

WHOLE GENOME SEQUENCING OF 366 CLINICAL E. COLI ISOLATES COMPARES GENOTYPE WITH PHENOTYPE AND SHOWS THE MOLECULAR EPIDEMILOGY AMONG STRAINS

Roach DJ, Salipante S, Shendure J, Kitzman J, Snyder M. University of Washington, Seattle, WA.

Purpose of Study: Escherichia coli is a bacterial species responsible for a range of clinical conditions and represents a significant burden of disease in the USA. Though the genome of E. coli is well characterized in many laboratory strains and outbreak isolates, there is a paucity of data on the genomic landscape of common pathogenic strains of the bacteria. The goal of this study is to utilize DNA sequencing to interrogate the interaction between virulence factors (VF)s and clinical presentation, as well as to reconstruct the epidemiology of the strains present in the Seattle region.

Methods Used: We performed whole genome sequencing on 366 clinical isolates, 274 from patients with UTIs and 92 isolated from patients with bacteremia. Antibiotic resistance profiles and hemolysis states were ascertained by the UW Microbiology Lab for all strains. Additionally, complete medical records were obtained for all patients from whom the E. coli isolates were grown. Computational analyses were performed to interrogate epidemiology.
and to establish associations of bacterial genotype and phenotype, allowing for the identification of potentially novel VFs and antibiotic resistance genes.

Summary of Results: This dataset enabled a large-scale analysis of the genetic diversity of pathogenic E. coli in the Seattle area, the elucidation of the pangenome in the region, and a reconstruction of the molecular epidemiology among strains. Additionally, our computational analysis enabled the diagnostic identification of known antibiotic resistance factors in resistant strains and several putative factors that are currently undergoing functional validation.

Conclusions: This study represents the largest whole-genome sequencing effort of a single bacterial species undertaken to date and provides a model for the integration of genomic science and clinical practice. We have shed light on the population structure of E. coli in the region and have detailed its pangenome. Importantly, we developed a method for the large-scale identification of novel VFs and antibiotic resistance genes and for improving our characterization of those already known. The pipeline utilized in this study is well-suited to other pathogenic bacterial species, and represents a potential breakthrough in using genomics to study infectious disease.

170
A NEW CLINICAL DIAGNOSIS IN THE SPECTRUM OF VASCULAR ANOMALIES
Stein M1, Guilfoyle R2, Courtemanche D2, Arneja P.1

1University of British Columbia, Vancouver, BC, Canada and 2BC Children’s Hospital, Vancouver, BC, Canada.

Purpose of Study: Arteriovenous Malformations (AVMs) are high flow lesions with abnormal connections between arteries and veins without an intervening capillary bed. While the diagnosis of an AVM is classically made clinically, much of our current treatments for AVMs require a detailed understanding of the architectural and rheological characteristics of the lesion. These are best ascertained with radiographic imaging (ultrasound, magnetic resonance imaging, or conventional angiography). Infrequently, the radiographic diagnosis of a vascular lesion will not support the clinical diagnosis of an AVM. These “discrepant” lesions are not adequately captured within the current classification system and represent a treatment dilemma for the involved practitioner. The purpose of this study is to review our center’s experience with vascular anomalies where incongruity in a patient’s clinical and radiographic presentation produce a diagnostic challenge.

Methods Used: A retrospective chart review of patients with atypical AVM presentations, which are not adequately captured in the current ISSVA classification system. Parameters reviewed included patient history and demographics, clinical presentation, radiological imaging and treatment modalities.

Summary of Results: The 6 cases presented here illustrate AVMs with discrepant clinical and radiological findings concerning flow characteristics, which produces a true treatment dilemma. There were 2 male patients and 4 female patients with a mean and median age of 25 and 21 respectively. All patients were treated based on their radiological diagnosis and managed either conservatively or with sclerotherapy. No lesions evolved into a high flow process.

Conclusions: We have identified and described a unique subcategory of vascular anomalies that have clinical features of high flow malformations but radiological features of low flow malformations. From a practical treatment standpoint, these lesions behave like low flow malformations and should be treated as such. We propose that complex vascular malformations should best be evaluated by both clinical as well as specialized radiological (MR/CT/MRA/angiography) means, radiologic diagnoses should usurp what is found clinically, and ultimate treatment is preferentially based on a radiologic diagnosis.

171
HEPATOCELLULAR CARCINOMA GROWTH FACTOR STIMULATES FETAL SHEEP ALVEOLAR TYPE II CELLS AND ENDOTHELIAL CELL GROWTH AND IMPROVES LUNG STRUCTURE IN EXPERIMENTAL BRONCHOPULMONARY DYSPLASIA
Metoxen A,1,2 Seedorf G,2 Abman S.1

1University of Colorado School of Medicine, Aurora, CO and 2University of Colorado, Aurora, CO.

Purpose of Study: Decreased vascular endothelial growth factor (VEGF) signaling contributes to impaired lung structure in bronchopulmonary dysplasia (BPD). Although VEGF stimulates hepatocyte growth factor (HGF) production, the effects of HGF on the fetal lung are uncertain. To determine the potential role of HGF in BPD, we studied the direct effects of HGF on fetal lung alveolar type II cells (AT2C) and endothelial cells (EC), and whether HGF treatment could restore lung growth after VEGF inhibition in vivo.

Methods Used: AT2C and EC were harvested from late-gestation fetal sheep and cultured with HGF. Tube formation was studied in EC by standard methods.

Summary of Results: HGF enhanced AT2C growth by 50% (p<0.05), and also stimulated EC growth and tube formation by 40% (p<0.001) and 42% (p<0.01 respectively. These effects of HGF on ECs were inhibited by JNJ-38877605, a selective c-Met antagonist. SU5416 decreased RAC by 30% (p<0.05), which was attenuated by HGF treatment in vivo.

Conclusions: We found that HGF stimulates fetal AT2C and EC proliferation and EC tube formation. In addition, HGF treatment improved lung structure after VEGF inhibition in vivo. These data suggest that HGF treatment may improve lung structure in experimental BPD.

172
DETERMINATION OF FETAL RHD STATUS USING FETAL NUCLEIC ACID IN THE MATERNAL CIRCULATION
Nagi SZ, Shover AL, Shariff A, Rossol S, McConaghy S, Ohls RK.

UNM School of Medicine, Albuquerque, NM.

Purpose of Study: The discovery of free fetal DNA in plasma of pregnant women has opened a new avenue for non-invasive prenatal diagnosis. In RhD negative women, the detection of the D gene by quantitative PCR in DNA derived from maternal plasma has been used to assist in prenatal management; however a negative result (no D gene detected) must still be evaluated for adequacy of fetal DNA sample. We hypothesized that significant epsilon globin gene expression (a component of embryonic hemoglobin) could serve as a positive control for the presence of an adequate fetal sample, thus preventing the unnecessary use of Rhogam in mothers with Rh negative fetuses.

We previously identified abundant epsilon globin mRNA in fetal blood, liver and marrow. For this study we measured epsilon globin expression in maternal serum (17-34 weeks gestational age), and in serum from healthy, non-pregnant adults.

Methods Used: Total RNA was isolated from maternal serum samples (17-34 weeks gestation). RNA isolation was performed using a commercial tri-reagent. Total RNA was measured spectrophotometrically. Quantitative polymerase chain reaction was performed on a 7500 Fast Real-Time PCR System using epsilon globin primers and probe. Quantitative expression of β-actin was used as an internal control to normalize starting quantities of sample RNA.

Summary of Results: Epsilon globin gene expression was identified in 25 maternal samples evaluated thus far. No significant correlation was seen between gestational age and epsilon expression in samples ranging from 17-34 weeks gestation (R=0.3, p=0.18). Epsilon globin gene expression was not identified in non-pregnant adult samples (n=4).

Conclusions: Epsilon globin gene expression was evident in all maternal samples tested to date, and was not present in non-pregnant adults. We speculate that epsilon globin gene expression may serve as evidence for the presence of fetal RNA, and would therefore serve as a positive control for the adequacy of fetal DNA isolated from maternal plasma.
The purpose of this study is to determine whether diuretic therapy in Eastern Washington corresponds with the KDOQI guidelines through the use of medication discharge summaries for individuals with Stage 3 and 4 CKD.

Methods Used: Patients hospitalized in Eastern Washington from April 2007 to September 2010 who survived to discharge (N=645) were classified as stage 3 and 4 CKD by application of the CKD-EPI equation to laboratory serum creatinine measurements. Patients were further classified as having received or not received a diuretic by analysis of discharge records. Cox proportional hazard models controlling for age, sex, payer, comorbidity, previous hospitalization, primary diagnosis category, and length of stay were conducted for time to event analyses.

Summary of Results: Forty percent of patients did not receive diuretics. The diuretic cohort was more likely to have diabetes mellitus (p<.05), CHF (p<.01), obesity (p<.01) and valvular disease (p<.01). Both stages of CKD received diuretics at similar rates (p=.27) but progression from stage 3 to stage 4 was associated with an increase in loop diuretic prescription (p<.05). Diuretic prescription declined by year of study for patients with stage 3 CKD (p<.01). The diuretic cohort was more likely to be hospitalized for congestive heart failure (p<.05) but the two cohorts had similar risk for rehospitalization (p=.40) and primary diagnoses for rehospitalization (p=.07).

Conclusions: The trends observed in this study were not uniformly in accordance with the KDOQI diuretic guidelines. It was surprising to find that such a large portion of this population is not receiving diuretic medications, and that this proportion grew larger over the course of this study. Trends in diuretic management help to illuminate the care that patients are receiving and whether it is in accordance with the guidelines. Future studies should seek to further understand the care patients with CKD are receiving in order to improve the long-term outcome of these patients.
Conclusions: Our results suggest that bevacizumab is correlated with an increased incidence of SGS in GBM patients compared to those who did not receive bevacizumab. This increase in SGS may suggest that bevacizumab plays an important role in the pathogenesis of secondary gliosarcoma.

TABLE 1. SGS development in Bevacizumab and No-bevacizumab cohorts

<table>
<thead>
<tr>
<th></th>
<th>Bevacizumab</th>
<th>No Bevacizumab</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGS</td>
<td>6</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>No SGS</td>
<td>33</td>
<td>310</td>
<td>343</td>
</tr>
<tr>
<td>Total</td>
<td>39</td>
<td>312</td>
<td>351</td>
</tr>
</tbody>
</table>

 jornal of Investigative Medicine • Volume 62, Number 1, January 2014

Methods Used: Sprague-Dawley neonatal rat pups were administered either nebulized dилuent (placebo), 25D (100 ng/kg/day), or 1,25D (10 ng/kg/day) in 1 ml volume over 30 min, once a day, every 24h for 7 days. Subsequently, pups were killed and lung tissue collected for determining markers of lung maturation (Western blot analysis for epithelial (surfactant proteins, SP, B and C) and mesenchymal (peroxisomal-proliferator-activator receptor, PPARγ and adipocyte differentiation-related protein, ADPRP) differentiation markers; (1)Hirolein uptake and (1)Hicholine incorporation into disaturated phosphati- dylcholine, DSP.

Summary of Results: Compared to controls, both 25D, and 1,25D increased the protein levels of epithelial and mesenchymal markers of lung maturation, along with increased tirolein uptake and choline incorporation into DSP. As expected, 1,25D had greater effects compared to those observed with 25D.

Conclusions: Administration of vitamin D (1,25D more than 25D) via nebuli- zation represents an effective strategy for enhancing postnatal lung matura- tion, which is also likely to have a significantly improved safety profile compared to its systemic administration. Therefore, nebulized vitamin D offers a novel and possibly safer lung protective strategy. Disclosure: Supported by NIH HD51857, HD71731.

179

NEONATAL NET-INHIBITORY FACTORS IMPROVE SURVIVAL IN MURINE MODELS OF SEPSIS

Wallace J,2, Coby M1,2, Campbell R,2 Vieira-de-Abreu A2, Araujo C2, Yost CC1,2.

Purpose of Study: Neutrophil extracellular traps (NET) are extracellular lattices of decondensed chromatin associated with anti-microbial proteins released by polymorphonuclear leukocytes (PMN) to trap and kill invading microbes. Dysregulated NET formation contributes, however, to inflamma- tory tissue damage. We have identified a novel NET-inhibitory peptide in the cord blood of newborn infants named neonatal NET-inhibitory Factor (nNIF). nNIF and a nNIF-related peptide (nNRP) CRISPP represent potential therapeutic agents targeting dysregulated inflammatory tissue damage associ- ated with inflammatory syndromes such as sepsis. We hypothesized that nNIF and CRISPP inhibit NET formation and improve survival in murine models of sepsis.

Methods Used: We assessed survival of outbred Swiss mice over 168 hours in models of endotoxemia (20 mg/kg, IP), E. coli sepsis (4.5 x 107 cfu, IP), and cecal ligation and puncture (CLP). Mice in the experimental group were treated with the nNRP CRISPP (10 mg/kg/dose, 2 IP doses given, 1 hour prior to sepsis initiation and 6 hours after). Mice in the control groups received either no treatment or treatment with a scrambled peptide control (SCR) with the same dose and schedule as CRISPP.

Summary of Results: CRISPP treatment significantly increased survival in the E. coli sepsis model (n=10/group, p< 0.0001) compared to SCR, with statistical trends noted towards increased survival in the endotoxia and CLP models of sepsis (n=10/group, p< 0.0843 and 0.061 respectively). Animals in the no treatment, sham-operated, and CRISPP/SCR alone groups showed no mortality over 7 days.

Conclusions: Treatment with the nNRP CRISPP increases survival in the E. coli model of sepsis and may improve survival in other in vivo models of sepsis. This suggests potential efficacy in ameliorating sequelae of sepsis by inhibiting NET formation with nNIF and/or CRISPP.

180

THE MEVALONATE PATHWAY REGULATES EOTAXIN-3 SECRETION FROM HUMAN AIRWAY EPITHELIAL CELLS: A THERAPEUTIC ROLE FOR SIMVASTATIN IN ASTHMA

Zeki AA, Ott S, Sandhu K, Wu R. U.C. Davis School of Medicine, Sacramento, CA.

Purpose of Study: The Th2 inflammatory response is central to human allergic asthma. Interleukin-13 (IL13) and the eotaxins play a central role in airway eosinophilia. Eotaxin-3 in particular is associated with corticosteroid-resistant severe asthma. Statins, which inhibit HMG-CoA reductase in the mevalonate (MA) pathway, have been shown to reduce eosinophilic airway inflammation in animal models. The effect of statins on this response in human airway
epithelium is unknown. We hypothesized that simvastatin inhibits IL13-induced eotaxin-3 expression and protein secretion in human airway epithelial cells by inhibiting the MA pathway.

Methods Used: Human bronchial epithelial (HBE1) cells were grown to 90% confluence in submerged D-media conditions. They were pre-treated with simvastatin (Sim at 1, 5, 10, 20 μM) for up to 72 hours, then stimulated with IL13 (20 ng/mL) for 12 hours to induce eotaxin-3 production. Cells were then harvested for RNA and protein, and cell media were collected for ELISA.

Summary of Results: Sim reduced basal eotaxin-3 mRNA by 37.8% (p=0.00086) and IL13-induced eotaxin-3 mRNA by 58% (p<0.0001). Sim inhibited eotaxin-3 protein secretion by 70% in a MA-dependent manner. Sim ± farnesylpyrophosphate (FPP) and Sim ± geranylgeranylpyrophosphate (GGPP), where FPP and GGPP are downstream metabolites of MA, showed that Sim inhibition of eotaxin-3 secretion was GGPP-dependent and FPP-independent, suggesting a Rho or Rac GTPase signaling mechanism. Parallel studies using Alamar Blue showed no adverse effects on cell viability at a dose of Sim ≤ 20 μM.

Conclusions: The MA pathway controls airway epithelial eotaxin-3 chemokine expression and extracellular secretion. This is a novel finding showing that the ubiquitous MA pathway, also known as the cholesterol biosynthesis pathway, regulates allergic responses in normal human airway epithelial cells. These results suggest a key role for Sim in mitigating asthmatic allergic responses in human airways. Further research is needed regarding the direct therapeutic potential of statins on the airway compartment.

Adolescent Medicine and General Pediatrics I Concurrent Session

12:30 PM Friday, January 24, 2014

181

IMPLEMENTATION AND EVALUATION OF A PEDIATRIC CONTINUITY CLINIC CURRICULUM

Eskelsen TJ1, Huang B1, Becotl A1, Schlauch K2. 1University of Nevada School of Medicine, Las Vegas, NV and 2University of Nevada, Reno, NV.

Purpose of Study: The University of Nevada, School of Medicine (UNSOM) pediatric residency program in Las Vegas, Nevada has never had a standardized continuity clinic curriculum. A new curriculum consisting of lectures and articles base on Bright Futures Guide and AAP policy statements was started during the academic year of July 1, 2012 to June 30, 2013 at our two continuity clinics. Evaluation of its effectiveness by measuring increase of medical knowledge will be performed by employing pre and post-tests. We hypothesize this curriculum will improve resident scores and overall medical knowledge in well child visits.

Methods Used: A 30 question pre-test was given to the residents and scored in the beginning of the academic year. Then, residents were given the lectures in clinic and told to read the articles on the reading list. At the end of the year, the same 30 question post-test was repeated. Scores were recorded based on questions answered correctly. We considered the curriculum as our treatment. A nested 2-way ANOVA was performed with the clinics as the fixed main effect and resident groups as a random nested effect. The size of the resident groups were unbalance, thus yielding an unbalance effect. The analysis showed a highly significant intervention effect in pre/post scores with p<0.0000003. We considered any p-values less than 0.05 to denote statistically significance.

Summary of Results: There was statistical significance in questions answered correctly from the pre to the post tests for UNSOM pediatric residents. The pediatric continuity curriculum improved overall resident scores and thus, medical knowledge of scheduled wellness visits.

Conclusions: Implementation of our pediatric continuity curriculum improved overall resident scores and thus, medical knowledge of scheduled wellness visits.

182

TRAINING BREASTFEEDING PEER COUNSELORS IN ST. MARIES

Sirois K. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: St. Marys is a rural location in the Northern Idaho. This is a resource-limited community with a significant proportion of the population enrolled in either Medicaid or Medicare. A high percentage of infants are formula-fed due to lack of access to lactation support. The Benewah County Hospital does not provide lactation support to new mothers, or lactation training to nurses or ancillary staff. Therefore, there is a need for breastfeeding support in St. Marys to encourage mothers to breastfeed.

Methods Used: After speaking with doctors, WIC representatives, St. Marys Mom & Friends Group, and Panhandle Health District employees, it became evident that St. Marys lacks breastfeeding support. A literature review showed the benefit of breast milk for infant development, and that having access to lactation support increases the number of mothers who initiate and sustain breastfeeding. I contacted Whitney Grovenor, a mother and proponent of breastfeeding, and offered to initiate a Breast Feeding Peer Counselor (BFPC) program. She agreed to act as community partner, and invited all members of St. Marys Mom and Friends Group to attend.

Summary of Results: Six experienced breastfeeding mothers attended the first session, which was adapted from the California WIC BFPC program. The training was discussion-based and followed a PowerPoint presentation. We defined the role of BFPC, discussed breast anatomy, milk production, and counseling strategies. The BFPC were introduced to existing community resources, including physicians, WIC representatives, Panhandle Health District employees, and the hospital volunteer organization.

Conclusions: Current literature illustrates the healthful benefits of breast milk, including boosting the infant's immunity, improving neurodevelopment, and enhancing the ability to self-regulate food intake. By initiating the St. Marys BFPC, residents have the opportunity to improve the health of their community. Bringing multiple organizations together will help St. Marys BFPC gain recognition as a valuable local resource and educate citizens of the benefits of breastfeeding.

183

UCLA EMERGENCY DEPARTMENT USE OF ULTRASOUND IN DIAGNOSING PEDIATRIC APPENDICITIS

Mayne J1, Briggs-Malonson M2. 1DGSOM at UCLA, Los Angeles, CA and 2Ronald Reagan UCLA, Los Angeles, CA.

Purpose of Study: 1) Identify the frequency of US ordered as the initial imaging study in children with abdominal pain and 2) assess for differences in patient and ED visit characteristics of children that received an initial US vs. a CT scan.

Methods Used: Retrospective chart review of pediatric patients who presented to the ED in 2012 and were diagnosed with appendicitis. A standardized chart extraction tool was developed to examine patient demographics, imaging orders, and results. Descriptive and associative tests were used to compare outcomes between the imaging groups.

Summary of Results: Charts from 76 pediatric appendicitis patients were reviewed. Sixty-four (84%) of the patients received an initial US (sensitivity of 44%). Patients that had a positive or equivocal US were similar in all characteristics. Patients that had a positive US spent less time in the ED compared to patients with an equivocal US or CT scan (150 min vs. 335 min, vs. 301 min p<0.01). Patients who received US first compared to a CT scan were younger, presented during the day, and weighed less.

Conclusions: UCLA emergency physicians tend to order US as the first imaging study to evaluate for pediatric appendicitis. However, additional improvement measures are needed to increase the sensitivity of US studies. Greater emphasis should be placed on using US as the primary diagnostic study for pediatric appendicitis due to its safety, potential accuracy, and reduction in ED length of stays.
We describe the case of a woman with MSUD, who previously developed Hemolysis Elevated Liver Enzymes and Platelet (HELLP) syndrome, delivered a child with multiple medical issues, and is now pregnant again. She is a 30 year old G2P0101 at 32 weeks gestation. She was diagnosed with MSUD at an early age due to lethargy and seizures. She had two decompensations in childhood, but thereafter had well-controlled disease on a protein-restricted diet. During her first pregnancy, she had overall normal levels of BCAA. This pregnancy was complicated by preterm premature rupture of membranes at 31 weeks, and expectant management was pursued. She developed blood pressure elevations, however, and liver function tests trended upward. She was diagnosed with HELLP syndrome, and required urgent cesarean delivery. She received anti-hypertensives postpartum, and had an eight-day hospitalization. Her son required a two-week admission due to prematurity, and later required surgical correction of arterio-venous fistulas. He was not found to have MSUD, but is undergoing a work up for developmental delay. Following this pregnancy, our patient returned to her baseline and has now become pregnant again. She is at approximately 32 weeks gestation with normal serum plasma BCAA levels. She is on carnitine supplementation due to low free carnitine level for her gestational age (13 μmol/liter), and daily baby Aspirin for risk-reduction of preeclampsia. Fetal growth has been near the 50% percentile. Her delivery plan is a repeat cesarean at 39 weeks.

This is the first reported case of HELLP syndrome in a pregnant woman with MSUD, as well as of fetal outcomes including arterio-venous fistulas and developmental delay in this setting. The contribution of metabolic dysfunction in MSUD to complications in pregnancy and effect on fetal outcomes deserves further exploration, as it is possible that metabolic alterations or management may contribute to their pathogenesis.

186

EVALUATION OF OWNERSHIP AND USAGE OF BEDNETS AMONG THE POPULATION OF SORONO, GHANA

Ngumi M1,2, Wetzel A1, Gustafson S3,2, Rickard D3,1, Charles R. Drew School of Medicine and Science, Los Angeles, CA;1David Geffen School of Medicine and Science, Los Angeles, CA and2Ghana Health and Education Initiative, Humjimbre, Ghana.

Purpose of Study: Malaria is the leading cause of morbidity and mortality among children under 5 years in Ghana, and bednet use has been shown to reduce the disease incidence. Our study was conducted together with Ghana Health and Education Initiative (GHEI), a local NGO, to evaluate ownership and use of bednets in Soroano, a village in rural Ghana, following a national bednet distribution and ongoing programming by GHEI.

Methods Used: We developed 3 questionnaires targeting each household, women of reproductive age, and children less than 5 years. Locally trained community health workers administered the questionnaires in the local language.

Summary of Results: In 2011 (pre-distribution), children under 5 years sleeping under a bednet numbered 79/173 (46%), increasing to 111/133 (83.5%) in 2012 (7 months post-distribution), while in 2013 (19 months post-distribution) usage decreased to 80/113 (70.8%) (p < 0.05). The proportion of bednets slept under a bednet increased from 8/13 (62%) in 2011 to 33/56 (58.9%) in 2013 (p = 0.06).

Conclusions: GHEI's goal of having 85% of children under 5 years sleeping under a bednet is not yet been reached. Furthermore, the percent sleeping sites covered by bednets increased from 327/414 (79%) in 2011 to 379/343 (92.1%) in 2012, then decreased to 316/360 (77.5%) in 2013 (p < 0.0001).

187

EARLY MATERNAL RESPONSIVENESS AND LATER LANGUAGE DEVELOPMENT IN INFANTS AT RISK FOR AUTISM SPECTRUM DISORDER

Min-Venditti C1, Harker C2, Ibañez L2, Stone W2, 1University of Washington School of Medicine, Seattle, WA and 2University of Washington, Seattle, WA.

Behavior and Development II
Concurrent Session
12:30 PM
Friday, January 24, 2014
Purpose of Study: Maternal responsiveness, which involves contingent, constructive, and positive responses to an infant's social, emotional, and communicative behaviors, is a parent behavior that is associated with language outcomes in typically developing children. Little is known, however, about the relationship between maternal responsiveness and language development in infants at risk for autism spectrum disorders (ASD; high-risk infants). This study aims to examine whether (1) maternal responsiveness at 9 months predicts language development between 12-18 months, and (2) growth in language mediates the association between maternal responsiveness at 9 and 18 months in both high-risk infants (n = 19) and infants with no family history of ASD (low-risk infants; n = 10).

Methods Used: Using a modified version of the Maternal Behavior Rating Scale (Mooney & Perales, 2003), maternal responsiveness was rated at 9 and 18 months during a 5-minute, free-play interaction using a 9-point scale ranging from “very low” to “very high.” Infants' expressive and receptive language were measured via parent report using the MacArthur Communicative Development Inventory (Fenson et al., 1993) at 12, 15, and 18 months.

Summary of Results: High-risk infants were significantly lower than low-risk infants on baseline levels and growth of receptive language, p < .01; there were no group differences on expressive language. Maternal responsiveness at 9 months was not associated with growth in language from 9-18 months in either group. Furthermore, while growth in language did not mediate the association between maternal responsiveness at 9 and 18 months, growth in expressive language from 12-18 months predicted maternal responsiveness at 18 months. These findings suggest that infants' language development may influence maternal responsiveness over time.

188

EFFECTS OF ERYTHROPOIESIS STIMULATING AGENTS AND PARENTAL STRESS ON DEVELOPMENT OF FORMER PRETERM INFANTS

Aragon M1, Nim A1, Lowe J1, Ohls RK2. 1 UNM School of Medicine, Albuquerque, NM and 2 UNM, Albuquerque, NM.

Purpose of Study: While the effect of preterm birth on parental stress is unclear, research has shown that parental stress negatively impacts cognitive development. Survival of preterm infants has improved, however significant neuroprotective treatments have not been identified. Erythropoiesis stimulating agents (ESAs) such as darbepoetin (Darbe) and erythropoietin (Epo) have shown promise as neuroprotective agents. We previously reported a 10 point higher cognitive score in ESA treated preterm infants compared to placebo. However, the impacts of parental stress on development have not been fully elucidated. We hypothesized that parental stress is inversely linked to neurodevelopmental outcome in ESA treated infants and that birth weight (BW) and gestational age (GA) would be inversely related to parental stress. We also hypothesized that ESA treatment in combination with socioeconomic status (SES) would be positively correlated with development.

Methods Used: Infants (500-1,250 grams, <49 hours of age) were blindly randomized to Epo (400 units/kg, 3x/wk SC), Darbe (10 ug/kg, 1x/wk SC), or placebo, dosed through 35 wks post-conceptual age and were evaluated at 18-22mo corrected age using the Bayley Scales of Infant Development - III (BSID). Mothers completed the Parental Stress Index (PSI) Questionnaire.

Summary of Results: All 74 infants (946±196 grams, 27.7±1.8 wks gestation; 21 placebo, 25 Darbe, 28 Epo) evaluated were comparable for age at testing. Spearman correlation revealed language, expressive language, receptive comprehension and social-emotional BSID scores were negatively related to total PSI in the ESA group (p<.030; p=.002, p=.015; p=.000). Total PSI scores were positively related to BW (p=.013) and GA (p=.038). Finally, there was a positive relationship between household income and language (p=.031), expressive language (p=.016) and receptive comprehen- sion (p=.017). These findings were not significant in the placebo group.

Conclusions: The ESA group demonstrated that neurodevelopment was negatively related to parental stress, similar to full-term, healthy infants. SES had a positive impact on development only for the ESA group, which typically is found in full-term cohorts. We speculate that ESAs are neuroprotective, though these findings should be further explored in a longitudinal manner.

189

A STUDY OF STEREOTYPE THREAT AND ACADEMIC PERFORMANCE AMONG UNDERREPRESENTED PRE-MEDICAL AND PRE-DENTAL STUDENTS

Houston K, Vermillion M, Doyle L, Uijtdehaage S, David Geffen School of Medicine at UCLA, Los Angeles, CA.

Purpose of Study: The Summer Medical and Dental Education Program (SMDEP), a 6-week pipeline program, is designed to broaden the range of the medical and dental professions. In this study we attempted to replicate our previous findings suggesting that instructions to a standardized test can affect performance when performance is presented as a static measure of ability.

Methods Used: As an in-class exercise, we randomly divided 159 SMDEP students into two equal groups ("A" and "B") and both groups were given a set of Medical College Admission Test (MCAT) verbal reasoning questions, but with different instructions. Group A instructions stated the test measured verbal intelligence and reasoning ability, which would not change. Group B instructions stated the test measured current level of performance that was subject to improvement. Contrary to our previous study, the instructors were of the same ethnicity. To examine for inherent differences in reading ability, all students completed the Nelson Denny Reading Test (NDRT).

Summary of Results: Demographic information and test scores are presented in Table 1. An independent samples t-test between group A and B scores showed no significant differences in NDRT total scores (p = .87) or MCAT section scores (p =.79). There was a strong, positive correlation between MCAT section scores and NDRT Total scores, Pearson r=0.65, P <.001.

Conclusions: Our previous findings confounded the ethnicity of the instructor with the type of instruction. The current study found no difference in MCAT scores and did not replicate previous findings when we controlled for instructors' ethnicity. Thus, the manner in which instructor's ethnicity impacts performance needs to be explored in future studies. The strong correlation between reading and MCAT scores, however, suggests that students' reading ability is a stronger determinant of performance than the nature of the instructions.

190

IMPROVING EARLY SCREENING AND DIAGNOSIS OF AUTISM IN UNDERSERVED POPULATIONS IN ARIZONA THROUGH THE ARIZONA LEADERSHIP EDUCATION IN NEURODEVELOPMENTAL AND RELATED DISABILITIES PROGRAM

Tsontakis A1, Andrews J1, Rice S1, 2. 1 U AZ College of Medicine, Tucson, AZ and 2 U AZ College of Medicine, Tucson, AZ.

Purpose of Study: Arizona Leadership Education in Neurodevelopmental and Related Disabilities (AZLEND) is an interdisciplinary graduate program that trains professionals caring for individuals with neurodevelopmental disabilities (NDDs). Fellows participate in a yearlong research project designed to improve early identification and referral for children with NDDs and autism in underserved counties to increase early detection of delays and to thereby minimize healthcare disparities in rural areas.

Methods Used: The project improves compliance with the American Academy of Pediatrics’ developmental surveillance and screening guidelines and collects pre- and post-screening data and referral to access change. AZLEND requires fellows to: interview key players in clinical practices; develop a surveillance process flow integrating formal screening and surveillance into each practice;
provide training on developmental screening tools and operation processes; provide follow-up technical assistance; and collect screening and referral data via medical record abstraction. Four sites in rural Arizona counties were recruited to participate in the 2012-2013 study.

Summary of Results: Sunset Community Health Center in Yuma County completed the program and implemented the PEDS screening tool in their locations successfully. There were 190 eligible well-child visits (9, 18, or 24 month) representing 187 children (54% male, 87% Hispanic), with an evenly distributed number of 9-, 18-, and 24-month visits during the study. In addition, 86% of families were either on public assistance or uninsured. Findings from Sunset Community Health Center showed formal developmental screening rates increased significantly from 0% pre-intervention to 85% post-intervention ($\chi^2=135.7, p=0.000$).

Conclusions: Sunset Community Health Center's success provides evidence that a developmental screening program can be successfully incorporated into rural health practices using AZLEND fellows as primary contacts and trainers. The experience indicates that implementation is dependent on a local physician advocate within the healthcare practice to ensure protocol adoption. AZLEND will be continued with an attempt to include more practices from underserved parts of Arizona.

APPLES: A POSITIVE AFFECT INTERVENTION TO REDUCE STRESS FOR DISADVANTAGED STUDENTS PREPARING FOR THE DENTAL ADMISSIONS EXAM

Borosva S, Seliverstov I, Roykh B, Moskwitz JT. 1UCSF Other Center for Integrative Medicine, San Francisco, CA; 2University of Michigan Medical School, Ann Arbor, MI; 3UCSF School of Dentistry, San Francisco, CA and 4San Francisco State University, San Francisco, CA.

Purpose of Study: Disadvantaged students may be at increased risk of experiencing distress, anxiety and lower scores, while preparing for graduate entrance exams. Positive affect may be beneficial as a target of stress reduction interventions. The purpose of this study was to adapt a pre-existing positive affect intervention to address positive affect, stress, and anxiety and to determine feasibility and acceptability in a cohort of disadvantaged students preparing for the Dental Admissions Test (DAT).

Methods Used: Students were recruited through the summer DAT preparation class for the Dental Post-Baccalaureate Program at San Francisco State University. Intervention manual was adapted from previous work to include facilitator and DAT instructor. We assessed outcomes at four timepoints (baseline, week 3, week 6 and week 8) using validated questionnaires, including STAIS, CES-D, and DES.

Summary of Results: Among the 18 participants (all intervention), mean age was 26.2 years (±2.5; range 23-32); 9 were female, 4 African American, 5 Hispanic, 5 Asian American, 4 from Middle Eastern origin; 8 had annual incomes <$29,999. All participants completed the first and last assessments and 15 completed week 3 and week 6 assessments. Fifteen attended >5 sessions and completed home practice. Participants reported high recommendation rates of usefulness, and uptake of positive affect skills. Repeated measures ANOVA showed significant changes for positive affect, test anxiety and stress. Interestingly, positive affect dropped precipitously from Week 1 to Week 3 and improved partially at the end of the intervention (Week 6) and increased further as students entered their intensive independent DAT preparation (Week 8).

Conclusions: Recruitment, attendance and survey completion demonstrated feasibility and acceptability while quantitative and qualitative data suggest the intervention may be useful for stress reduction in this population. Limitations (small sample, no comparison group) prevent definitive conclusions and further research is needed.

EFFECTS OF BREAST MILK AND INFANT FORMULA ON 2nd TO 4th DIGIT RATIOS

Chan K, Martin J, Vo J, Franco D. Western University of Health Sciences, Pomona, CA.

Purpose of Study: The ratio of 2nd to 4th digit lengths is sexually dimorphic and is used as biomarker for sexual differentiation. On average, men have relatively lower 2D:4D ratios than women do. The aim of the study was to investigate whether postnatal hormone exposure from breast milk has an effect on the development of 2D:4D sexual dimorphism among pediatric subjects.

Methods Used: 97 participants between 1-18 years of age were recruited at local clinics. Child feeding history was obtained from the parents or guardians by questionnaire and vital statistics from the medical records. Scans of the participants’ hands were, upon parental consent and child assent, obtained using a digital scanner. Measurements of the digit lengths were made using the GNU Image Manipulation Program (GIMP). Scans were made in triplicate and data were analyzed by Repeated Measures ANOVA. Independent variables included feeding methods (breastfed, formula-fed, both), gender and age. Data were analyzed using GraphPad Prism and GB-Stat.

Summary of Results: Analysis of the right hand showed that individuals of both sexes who were breastfed exhibited more male-like digit morphology, i.e., lower 2D:4D ratios compared to the formula-fed individuals. The left hand 2D:4D was sexually dimorphic with females having a higher ratio than males; however left hand ratios did not differ according to feeding category. Linear regression analysis demonstrated a positive correlation between 2D:4D ratio and age in the breast-fed male group. No notable relationship was found in females or in either sex receiving exclusively formula.

Conclusions: Overall, participants who were breastfed expressed lower 2D:4D ratios than their formula-fed counterparts despite a positive correlation between 2D:4D and age in breast fed males. While the specific hormone interactions with the digits remain unknown, our findings suggest that breast milk with its significant quantities of estrogen leads to a gradual increase throughout childhood in the digit ratio in young males, an effect not seen in females or in formula-fed infants.

EFFECTS OF BREAST MILK ON LONGITUDINAL BONE GROWTH MEASURED BY DIGIT TO STATURE RATIO IN CHILDREN

Vo J, Martin J, Chan K, Franco D. Western University of Health Sciences, College of Osteopathic Medicine of the Pacific, Pomona, CA.

Purpose of Study: Research has shown that early steroid hormone exposure affects bone growth patterns in males and females. Sexual dimorphism occurs in long bone length adjusted for stature and is presumably due to differential androgen or estrogen exposure; however, the source of these hormones is not clear. The 4th digit to stature ratio (4DSR), is sexually dimorphic in adults. We hypothesize that estrogens in breast milk affect bone growth patterns over time, potentially causing the sexual dimorphism in 4DSR seen in adults. In this study, we examine the effects of breastfeeding on 4DSR in children.

Methods Used: 78 children (41 males, 37 females), ages from 18 months to 18 years were scanned and the 4th digits were measured to calculate 4DSR. Three scans of each hand were made to increase consistency and minimize errors. Unpaired T-test was used to compare 4DSR between males and females, not taking into account feeding method. Then it was used to compare 4DSR in two groups, those who were breastfed and those who were formula-fed exclusively.

Summary of Results: The 4DSR does not differ between male and female children. However, in male children, the breastfed group has a significantly lower 4DSR than the formula-fed group (Right: p=0.013, Left: p=0.002). In female children, there is no significant difference in 4DSR between breastfed and formula-fed groups (Right: p=0.4134, Left: p=0.416).

Conclusions: Even though our data show that 4DSR does not differ between breastfed and formula-fed females, it is worth noting that in contrast to males, breastfed females have higher 4DSR than formula-fed females. The fact that we did not find 4DSR sexual dimorphism in children could be due to several factors. Since our results show that breastfeeding influences 4DSR
differently in males and females, it is possible that the effects of hormones in breast milk on 4DSR sexual dimorphism are not apparent at early ages, but gradually cause male and female 4DSR to differ, and along with endogenous hormone secretion leading to sexual dimorphism in adults.

**Cardiovascular II**

**Concurrent Session**

12:30 PM

Friday, January 24, 2014

195

**VENTRICULAR ASSIST DEVICE COMPLICATIONS ON THE WAITING LIST AND POST-HEART TRANSPLANT OUTCOMES**


**Purpose of Study:** Mechanical circulatory support devices have complications unique to this class of devices. Currently, patients awaiting heart transplant on Ventricular Assist Device (VADs) and listed as status 1B are allowed for lower freedom from re-hospitalization 1 year post-transplant (See Table).

**Summary of Results:** 15 patients developed complications while awaiting heart transplant. Complicated VAD patients had comparable 3 year post-transplant outcomes with non-complicated VAD patients. 1 year freedom from any rejection, cellular rejection and antibody-mediated rejection were also the same between the two groups. Complicated VAD patients had numerically lower freedom from re-hospitalization 1 year post-transplant (See Table).

**Conclusions:** Complicated VAD patients who developed complications while on the heart transplant waitlist appear to have comparable post-transplant outcomes. This supports upgrading these patients to status 1A listing pre-transplant as they have acceptable post-transplant outcomes.

<table>
<thead>
<tr>
<th></th>
<th>Complicated VAD (n=15)</th>
<th>Non-Complicated VAD (n=57)</th>
<th>log rank p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 Year Actuarial Survival</td>
<td>93.3%</td>
<td>84.2%</td>
<td>0.39</td>
</tr>
<tr>
<td>3 Year Freedom from CAV</td>
<td>86.7%</td>
<td>87.7%</td>
<td>0.87</td>
</tr>
<tr>
<td>5 Year Freedom from NF- MACE</td>
<td>93.3%</td>
<td>93.0%</td>
<td>0.99</td>
</tr>
<tr>
<td>1 Year Freedom from Any Rejection</td>
<td>93.3%</td>
<td>87.7%</td>
<td>0.54</td>
</tr>
<tr>
<td>1 Year Freedom from Rehospitalization</td>
<td>66.7%</td>
<td>80.7%</td>
<td>0.21</td>
</tr>
</tbody>
</table>

196

**DONOR HEIGHT VS. WEIGHT: IS ONE MORE IMPORTANT THAN THE OTHER?**


**Purpose of Study:** In heart transplantation, donor to recipient height and weight mismatch appear to be important for acceptability of donor hearts. The importance of height or weight compared to each other has not been firmly established. In some programs, donor to recipient height mismatch is more important than donor to recipient weight mismatch. We reviewed donor to recipient height and then weight mismatches to assess whether there was any impact on post-transplant outcome.

**Methods Used:** Between 1994 and 2012 we evaluated 546 patients and assessed the donor to recipient height ratios, weight ratios and post-transplant outcomes up to 5 years. Endpoints included 5-year actuarial survival, freedom from cardiac allograft vasculopathy (CAV) and freedom from non-fatal major adverse cardiac events (NF-MACE). Patients were divided into the following groups: donor to recipient height ratios <0.9, 0.9-1.1, and >1.1; donor to recipient weight ratios were divided into groups of <0.9, 0.9-1.1, >1.1. When comparing height mismatch, weight ratios were controlled between 0.9 and 1.1. The same inclusion criteria were applied when comparing weight mismatches.

**Summary of Results:** Donor to recipient height ratio ranges from 0.27 to 1.30 and weight ratio ranges from 0.42 to 2.15. There was no significant difference in donor to recipient height mismatch among all three groups in terms of post-transplant 5 year actuarial survival, 5 year freedom from CAV and 5 year freedom from NF-MACE. Donor to recipient weight mismatch also had no impact on post-transplant outcome between the two groups in terms of freedom from NF-MACE. However, donor/recipient weight ratio <0.9 group had significantly lower 5 year freedom from CAV compared to donor/recipient weight ratio between 0.9 and 1.1 group (79.6% in "<0.9" group vs. 85.5% in "0.9-1.1" group, p = 0.02). Extreme mismatches of weight ratio greater than 1.3 or less than 0.7 had no impact on outcome, but numbers are small.

**Conclusions:** Donor to recipient height mismatches up to 10% or over 10% lower does not appear to significantly impact post-transplant outcomes. However, lower donor to recipient weight ratio (<0.9) appears to be a risk factor for lower freedom from CAV. A larger number of patients and further investigation into the cause of this finding needs to be pursued.

197

**SENSITIZED VENTRICULAR ASSIST DEVICE PATIENTS VS. SENSITIZED NON-VENTRICULAR ASSIST DEVICE PATIENTS: IS THERE AN IMMUNOLOGICAL DIFFERENCE?**


**Purpose of Study:** The need for ventricular assist devices (VADs) has been increasing over the past several years. Sensitized patients - defined as those with the development of circulating antibodies most likely due to blood transfusions, pregnancy, and previous organ transplants - are known to have poorer outcome after organ transplantation. Patients who undergo VAD implantation may be given blood products and therefore are reported to have a higher incidence of sensitization. It is not known whether these circulating antibodies in a VAD patient have the same immunological impact after heart transplantation.

**Methods Used:** Between 1994 and 2012 we evaluated 65 VAD and 71 non-VAD patients awaiting heart transplantation. Specifically, we assessed patients who were sensitized (PRA >10%) to assess their 3 year post-transplant outcomes, including actuarial survival, freedom from cardiac allograft vasculopathy (CAV) and freedom from non-fatal major adverse cardiac events (NF-MACE). 1 year freedom from cellular and antibody-mediated rejection was also assessed.

**Summary of Results:** There were 65 sensitized VAD patients compared to 71 sensitized non-VAD patients. Sensitized VAD patients had significantly higher 1 year freedom from any rejection (72.3% vs 52.1%, p = 0.02) and antibody-mediated rejection (81.5% vs 62.0%, p = 0.01) compared to sensitized non-VAD patients (see Table). Both sensitized VAD and sensitized non-VAD patients had comparable 3-year post-transplant outcomes.

**Conclusions:** Compared to sensitized non-VAD patients, sensitized VAD patients appear to have less antibody mediated rejection after heart transplantation, suggesting that their immune response is truncated after removal of the VAD in undergoing heart transplantation. Further study into the mechanisms of this observed response is warranted.
IS A LOWER CYLEX SCORE HELPFUL IN PREVENTING THE DEVELOPMENT OF CIRCULATING ANTIBODIES AFTER HEART TRANSPLANTATION?

Yabuno J, Yu Z, Liou F, Hamilton M, Kobashigawa J. Cedars-Sinai Medical Center, Los Angeles, CA.

Purpose of Study: The Cyles score is a new test to detect immune responsiveness for heart transplant patients. A lower Cyles score represents more intense immunosuppression and therefore a less responsive immune system in general. Circulating Antibodies are seen in more than 50% of patients post-heart transplantation. It is believed that more intense immunosuppression may decrease the risk of antibody production post-transplant. Although the Cyles score represents T cell immunoresponsiveness, it may also reflect a general immunosuppressive state and thereby may reflect the ability of the recipient to make antibodies.

Methods Used: Between 2007 and 2012 we evaluated 108 heart transplant patients who did not have circulating antibodies pre-transplant (defined as pre-transplant PRA > 0). Post-transplant antibody levels were assayed at 1,2,3,6,12 months postoperatively and correlated to the Cyles score. Cyles scores were obtained routinely at the time of endomyocardial biopsy. Antibody-mediated rejection (AMR) in the first year was also assessed. Patients were divided into different Cyles score groups: <200, 200-500, and >500.

Summary of Results: On average, there were 5.4 ± 2.9 first-year Cyles scores per patient. Patients with Cyles scores <200 were found to have more suppressed antibody responses compared to the Cyles score 200-500 and Cyles score >500 groups (4.5% vs 15.8% vs 20.0%), but numbers are small. However, actual biopsy proven immunosuppression antibody-mediated rejection and cellular rejection was not significantly different among the three groups. There was also no significant difference in 1-year survival and freedom from cardiac allograft vasculopathy between the two groups (see table).

Conclusions: More intense immunosuppression as reflected by a low Cyles score might be useful to suppress antibody response after heart transplant, but a larger number of patients are needed to confirm this early observation.

<table>
<thead>
<tr>
<th>Cycles</th>
<th>Development of de novo antibodies (%)</th>
<th>Year Freedom from Cellular Rejection</th>
<th>Year Freedom from Antibody-Mediated Rejection</th>
<th>Year Survival</th>
<th>Year Freedom from CAV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;200 (n=22)</td>
<td>4.5%</td>
<td>90.9%</td>
<td>81.8%</td>
<td>95.5%</td>
<td>95.3%</td>
</tr>
<tr>
<td>200 &lt; Cycles &lt; 500 (n=79)</td>
<td>15.8%</td>
<td>96.1%</td>
<td>73.7%</td>
<td>97.4%</td>
<td>93.4%</td>
</tr>
<tr>
<td>&gt;500 (n=10)</td>
<td>20.0%</td>
<td>100.0%</td>
<td>90.6%</td>
<td>96.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

P = NS

CLOPIDOGREL RESISTANCE & PLATELET REACTIVITY IN HISPANIC FEMALES POST CORONARY INTERVENTION

Ng S1, Jayasuriya S2, Lee KS3. 1U Arizona College of Medicine, Tucson, AZ and 2U Arizona College of Medicine, Tucson, AZ.

Purpose of Study: Percutaneous coronary intervention (PCI) is the most common form of coronary artery revascularization. Recent data suggests ethnic and gender variability exists in clopidogrel response, increasing the risk of late stent thrombosis. This is mediated by genetic heterogeneity of cytochrome P450 enzyme pathways required to convert clopidogrel to its active metabolite. Asians, Hispanics, and women have the highest risk with different conversion rates. No studies have specifically addressed platelet reactivity in Hispanic females. We aimed to quantify platelet reactivity in Hispanic women compared to non-Hispanic women post PCI on stable clopidogrel therapy.

Methods Used: We performed a pilot case-control study of women who had undergone PCI within the past 12 months at our institution and were compliant with their clopidogrel regimen. Ethnicity was self-reported. Informed consent was obtained. Quantitative Platelet P2Y12 reactivity unit (PRU) values were measured using VerifyNow® assays (Accumetrics Inc., San Diego, CA). Baseline known clinical confounding factors affecting PRU levels were noted. A PRU ≥ 235 was considered high on-treatment reactive. Each patient’s medication list was analyzed using Lexicomp®. Online and interaction risk ratings with were recorded. Statistical analysis was performed using two-tailed T-test for quantitative variables and Fisher's exact test for categorical variables.

Summary of Results: Of 7 Hispanic and 21 non-Hispanic women, average P2Y12 values were 80.3 and 122.1 (p=0.29). High on-treatment platelet responders for Hispanics and non-Hispanics were similar at 14.3% (p=1.00). No significant confounding differences were present between both groups, with similar rates of diabetes, HIV therapy, and PPI use. With drug interaction testing, no significant differences were present in both groups. Risk rating D: 0% vs. 23.8% (p=0.29); risk rating X: 0% vs. 14.3% (p=0.55).

Conclusions: In our small pilot cohort, no significant differences were present in platelet reactivity between Hispanic and non-Hispanic women, controlled for clinical confounders and known drug interactions. There is however a statistically non-significant trend towards increased response to clopidogrel in Hispanic women. The data is hypothesis generating and larger enrollment is required.

Endocrinology and Metabolism II Concurrent Session

021

OGGT MODELED BETA-CELL FUNCTION MEASURES PREDICT INCIDENT DIABETES

Utschneider KM1,2, Largagli A1, Bertoldo A1, Leonetti D2, McNeely M2, Fujimoto W2, Cobelli C3, Kahn SE1,2, Boyko E1,2, 1VA Puget Sound Health Care System, Seattle, WA; 2University of Washington, Seattle, WA and 3University of Padua, Padua, Italy.

Purpose of Study: We sought to determine if oral glucose tolerance test (OGTT) modeled measures of β-cell function predict the development of incident type 2 diabetes (T2DM). We further sought to compare the ability of modeled measures to predict T2DM with the early insulin and C-peptide responses to oral glucose.

Methods Used: Baseline OGTT data from 426 Japanese-American adults were analyzed. Those without T2DM at baseline (n=359) were followed for up to 10 years for development of diabetes. β-cell function measures included the early (30-0 minute) insulin and C-peptide responses to glucose (ΔI/ΔG and ΔCP/ΔG) and model-derived β-cell responsivity indices (φbasal, φstatic, φdynamic, φtotal). The net reclassification index (NRI) and integrated discrimination improvement (IDI) index were calculated to assess whether addition of β-cell function measures to a basic model improved the ability to predict incident diabetes.

Summary of Results: At baseline all β-cell function measures were highest in NGT (n=180), intermediate in IGT (n=179) and lowest in T2DM (n=67) (ANOVA p<0.001). Over 10 years of follow-up, diabetes developed in 62/359 subjects. In logistic regression models adjusted for insulin sensitivity, age, sex, BMI and family history of diabetes, only φdynamic (Odds Ratio [95% CI]: 0.29 [0.13, 0.64], p=0.002, ΔI/ΔG (0.31 [0.17, 0.56], p<0.001) and ΔCP/ΔG (0.36 [0.18, 0.73], p=0.004) significantly predicted protection from incident T2DM. Area under receiver operating curves did not differ for φdynamic (0.83), ΔI/ΔG (0.84) or ΔCP/ΔG (0.83) in the ability to predict T2DM. The IDI was significantly improved by addition of each of the three measures (φdynamic (0.10±0.02), ΔI/ΔG (0.13±0.02) or ΔCP/ΔG (0.10±0.02, p<0.001 for all), but the NRI was highest and only significant for ΔI/ΔG (0.17±0.07, p=0.01) with trends for ΔCP/ΔG (0.11±0.06, p=0.08) and φdynamic (0.10±0.06, p=0.09).

Conclusions: Of modeled β-cell function measures, only φdynamic predicted diabetes development and was similarly accurate compared to ΔI/ΔG and ΔCP/ΔG.

ASSIGNING GLYCEMIC STATUS BY AIC OR ORAL GLUCOSE TOLERANCE TEST AMONG HISPANICS AND NON-HISPANICS WHITES IN NEW MEXICO

Camacho JE1, Shah V2, Wong C1, Burge M2. 1University of New Mexico, Albuquerque, NM and 2UnM HSC, Albuquerque, NM.
Purpose of Study: Reliable identification of individuals at risk for developing diabetes is critical to instituting preventative strategies. The American Diabetes Association has adopted A1c-based criteria for assigning glycemic status. Existing studies suggest that A1c is specific but insensitive as compared to the Oral Glucose Tolerance Test (OGTT) for diagnosing diabetes. Studies also suggest that the accuracy of using A1c as a sole diagnostic criterion may be variable across different ethnic groups. We theorized there would be lack of concordance for designation of prediabetes (PreDM) between A1c and OGTT across Hispanic and Non-Hispanic White (NHW) populations in New Mexico.

Methods Used: 214 adults at risk for Type 2 Diabetes (T2D) were screened to determine their glucose homeostasis status, as follows: nondiabetic (A1c < 5.7%), PreDM (A1c 5.7% - 6.4%), and T2D (A1c > 6.4%). Inclusion criteria were an age > 18 years and at least one of the following risk factors: a family history of diabetes in a first degree relative, a history of gestational diabetes, Hispanic ethnicity, non-Caucasian race, or obesity. All subjects received a fasting 75 gram OGTT and A1c screening. We used Bowker's Test of Symmetry to determine agreement (with p = 1.0 for perfect agreement). Sensitivity and specificity were also calculated for each group.

Summary of Results: 90 Hispanic patients and 76 NHW patients were studied. The Table below shows glycemic status as assigned by each method. There was no concordance between A1c and OGTT for Hispanic (p = 0.001) or NHW individuals (p = 0.004) with PreDM. For Hispanics, sensitivity of A1c was 67% (95% CI = 42-85%) and specificity was 59% (95% CI = 47-70%). For NHW, sensitivity of A1c was 67% (95% CI = 42-85%) and specificity was 56% (95% CI = 43-68%).

Conclusions: A1c was discordant with OGTT among Hispanic and NHW subjects for diagnosis of PreDM. Sole use of A1c to designate glycemic status will result in over diagnosis of prediabetes among Hispanic and NHW New Mexicans.

<table>
<thead>
<tr>
<th>Hispanic OGTT</th>
<th>NHW OGTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiabetic A1c</td>
<td>PreDM</td>
</tr>
<tr>
<td>PreDM A1c</td>
<td>40</td>
</tr>
<tr>
<td>Diabetes A1c</td>
<td>1</td>
</tr>
</tbody>
</table>

203 PREVALENCE OF DYSGLYCEMIA BY TANNER STAGE IN OBESE YOUTH

Adams J2, Chan C1, Cree-Green M1, Pyle L1, Nadeau K2, Kelsey MM1. 1University of Colorado School of Medicine, Aurora, CO and 2University of Colorado-Colorado Springs, Colorado Springs, CO.

Purpose of Study: Type 2 Diabetes Mellitus (T2D) in youth presents during puberty; however, relation between normal pubertal metabolic changes and appearance of dysglycemia in at-risk youth is undefined. Insulin sensitivity decreases in all youth during puberty, which may result in failure to maintain adequate compensatory insulin secretion in some at-risk obese youth as puberty progresses. It may be expected for clinical signs of hyperglycemia, such as impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), to occur in later stages of puberty, after the mid-pubertal peak of pubertal insulin resistance. The goal of the current study was to establish whether dysglycemia is more prevalent in obese youth in late versus early puberty.

Methods Used: A total of 203 obese youth (BMI = 33±7, age 9-18 yrs), referred for weight management, were studied with 78 in early puberty (Tanner stage (T2-3), age = 12.19 yrs) and 125 in late puberty (T4-5, age = 14.9 yrs). Pubertal stage was assessed by a pediatric endocrinologist using standards established by Tanner and Marshall and testicular volume estimation by Prader orchidometer. Measurements of dysglycemia include IFG (fasting glucose > 100mg/dL), IGT (2-h glucose > 140mg/dL), and hemoglobin A1c (HbA1c) > 5.7%. IFG and IGT were measured using fasting and 2-hr samples, respectively, from an oral glucose tolerance test (75g sucrose); HbA1c was measured using high-performance liquid chromatography. Chi-square and Fisher's exact tests were used to compare prevalence of IFG, IGT, and abnormal HbA1c by early (T2-3) vs. late (T4-5) puberty.

Summary of Results: Results showed higher prevalence of IFG in late (7.2%) than early (1.28%) puberty and higher IGT in late (27.12%) than early (19.16%) puberty, though neither were statistically significant (p = 0.028 and 0.2228, respectively). No statistical difference was found in abnormal HbA1c (p = 0.9704) by late versus early puberty.

Conclusions: Although we did not find any significant differences in prevalence of dysglycemia by pubertal status, there appears to be a trend toward more IGT in later Tanner stages. Further investigation in a larger non-referral population will better characterize pubertal factors contributing to the onset of T2D in obese youth.

204 EFFECT OF DIET INTERVENTION ON INFLAMMATION RELATED GENE EXPRESSION IN CD14+ CIRCULATING MONOCYTES FROM METABOLIC SYNDROME PATIENTS

Deo SK1, Sears D2, 1University of California, San Diego. School of Medicine, San Diego, CA and 2University of California, San Diego, CA.

Purpose of Study: The objective of this study is to analyze pro-inflammatory gene expression in CD14+ circulating monocytes from metabolic syndrome subjects before and after a specific diet intervention.

Methods Used: The intervention was a randomized controlled trial of a 12-week long, 1500 calorie diet. The active diet included low glycemic index bread products, EPA/DHA fish oil capsules, and dulphinidin polyphenol capsules. The placebo diet included market variety bread products, corn oil capsules, and corn starch capsules. Total RNA was extracted from monocyte samples of 31 obese subjects, and cDNA libraries were constructed. Real-time quantitative polymerase chain reaction (RTqPCR) was used to measure the expression levels of the following inflammatory genes of interest: TLR2, TLR4, NFKB, TNFa, TNFRSF1B, IL-1b, ILIRN, IL-6, CD11c, COX2, and INOS.

Summary of Results: A repeated measures MANOVA was conducted to examine the effects of two diet groups on gene expression for pre, mid, and post the 12 week intervention. An alpha level of .05 was used for all analyses. Significant differences were found among the diet groups on the dependent measures, NFKB, F (1, 16) = 15.556, p < 0.01, TLR2, F (1, 16) = 9.136, p < 0.01, CD11c, F (1, 16) = 12.484, p < 0.01, and TNFa, F (1, 16) = P < 0.05. In addition, there was a main effect of time for ILIRN, F (2, 32) = 6.061, p < 0.01, CD11c, F (2, 32) = 5.834, p < 0.01, IL6, F (2, 32) = 5.298, p < 0.05, and a trend for COX2, F (2, 32) = 2.7921, p = 0.076. Post hoc analyses revealed a significant decrease in the active group for gene expression variables, TLR2, CD11c, and TNFa at p < 0.05.

Conclusions: Active diet group exhibited significant reduction in TLR2, CD11c, and TNFa expression in circulating monocytes, when compared to placebo. This study was part of a parent clinical trial, which has found that average fasting insulin and HOMA-IR are improved in active compared to placebo groups. This monocyte gene expression data will contribute to painting the picture of how the composition of a low calorie diet modulates inflammation and insulin sensitivity.

205 IS SENSIBLE USE OF GLYCATED ALBUMIN REALISTIC IN PATIENTS WITH DIABETES MELLITUS-THE SUGAR STUDY

Chao JH1, Sussman A2, Hirsch HB1. 1University of Washington, Seattle, WA and 2Southlake Clinic, Renton, WA.

Purpose of Study: To compare glycated albumin (GA) and hemoglobin A1c (A1c) as glycemic indices in patients with diabetes.

Methods Used: We conducted a prospective pilot study of 22 patients aged ≥ 18 years with type 1 or type 2 DM from a single center. Patients were allocated into 2 groups and followed over 4 weeks. The study group included 11 patients whose A1c appeared higher than that predicted by their SMBG. The control group included 11 patients whose A1c closely matched that predicted by their SMBG. Discrepancy between A1c and SMBG was determined by an experienced clinician. During the study, we made no change to patients' medical management. All patients checked their SMBG 4 times daily. At the end of the study, we downloaded data from all patients' glucose meters. We measured GA and A1c at the beginning of the end of the study. Primary end points were correlations between A1c and SMBG, GA and SMBG, and A1c and GA.

Summary of Results: Over the study period, there was no significant change in A1c, GA, and weight in all patients. Within the study group, only 2 patients had baseline A1c higher than that predicted by their mean SMBG. A positive and significant relationship was found between A1c and SMBG in the study group (r = 0.93 [0.75 to 0.98]), but no significant correlation between A1c and SMBG was seen in the control group. We observed a positive trend between GA and SMBG in both the study and control groups (r = 0.43 [0.23 to 0.82].
and \( r = 0.21 \) [-0.44 to 0.72], respectively. A positive trend was also observed between A1c and GA in both groups of patients. When we compiled all data pairs of A1c and GA from both groups of patients, we found a positive and statistically significant relationship between A1c and GA (\( r = 0.41 \) [0.11 to 0.64]).

**Conclusions:** The results from our study serve as a great reminder that an A1c level represents more than an average blood glucose and encompasses a wide 95% confidence interval of blood glucose as proposed by Nathan DM et al. GA is a promising surrogate marker for assessing glycemic control in patients with diabetes mellitus. Future studies powered to detect the relationships between GA and SMBG, as well as GA and A1c, are needed to establish a guideline for using GA in the care of patients with diabetes mellitus.

**Impact of Less Intensive Glycemic Target for a Subcutaneous Insulin Protocol on Outcomes in Hospitalized Patients**

Izuora KE,1 Kaur G,2 Markley B,2,3 Schlauch K.3 1University of Nevada School of Medicine, Las Vegas, NV; 2University Medical Center, Las Vegas, NV; and 3University of Nevada, Reno, NV.

**Purpose of Study:** Glycemic control has been shown to have a major impact on hospital outcomes and mortality. However, intensive control of inpatient glucose often results in hypoglycemia and higher mortality. Our study looked at the effect of replacing an intensive subcutaneous insulin correction protocol (old) with a less intensive protocol (new) in a tertiary hospital.

**Methods Used:** This was a retrospective chart review of 400 consecutive patients hospitalized for various medical conditions. Two hundred were managed with the old protocol (glucose target: 90 - 130 mg/dl) and 200 with the new protocol (glucose target: 150 - 200 mg/dl). The new protocol also had reminders for providers to order basal and fixed pre-meal bolus insulin.

Data collected included age, gender, ethnicity, BMI, level of care, hospital length of stay and blood glucose values (50, 51 to 69, 70 to 179 and \( \geq 180 \)). Differences in hypoglycemia incidence rates were measured with a Fisher’s exact test. Differences in quantitative measurements such as glucose levels and length of hospital stay were evaluated using a Student’s t-test.

**Summary of Results:** There was no significant difference between age, gender, ethnicity, BMI and level of care for the two groups (\( p > 0.05 \) for all). Average blood glucose values were 160.45 and 169.98 mg/dl for the old and new protocols, respectively (\( p = 0.06 \)). There were 35 glucose readings \( \geq 50 \) mg/dl in the old protocol compared to 19 in the new protocol (\( p = 0.009 \)). More patients required treatment with dextrose in the old protocol than in the new protocol (26 vs. 11, \( p = 0.0097 \)). The length of hospital stay was longer for those treated with the old protocol compared to the old protocol (13.16 vs. 6.56 days, \( p = 0.00085 \)).

**Conclusions:** A less intensive subcutaneous insulin correction protocol in hospitalized patients resulted in similar glucose values with less severe hypoglycemia when compared to a more intensive protocol. Length of hospital stay was longer for patients managed with the new protocol. This could be because it took longer to achieve good glycemic control with the new protocol or could be from other patient factors that could not be controlled for in this study.

**Insulin Pump Programming Does Not Eradicate the Dawn Phenomenon**

Jaghab J, Bouchonville MF, Duran-Valdez E, Schrader RM, Schade DS. University of New Mexico Health Sciences Center, Albuquerque, NM.

**Purpose of Study:** Continuous subcutaneous insulin infusion (CSI) permits multiple changes in insulin delivery over the night. Programming an early morning increase in insulin delivery is frequently used to counteract the early rise in glucose prior to breakfast (dawn phenomenon). Whether this practice is efficacious or hazardous has not been tested in the ambulatory setting.

**Methods Used:** Using continuous glucose monitoring (CGM), we evaluated the long-term safety and efficacy of increased early morning insulin programming for management of the dawn phenomenon in type 1 diabetes (T1D) subjects. 40 T1D subjects were studied multiple times over an 8-month period. We compared the occurrence of the dawn phenomenon and hypoglycemia in CSI1 non-programmers versus those who programmed an early morning increase in insulin delivery.

**Summary of Results:** Over 8 months of observation, the dawn phenomenon occurred in all tested subjects to a variable extent, occurring with a median rate of 55% of the nights (min 25%, max 100%). T1D subjects who programmed an early morning increase in insulin delivery had no significant reduction in the occurrence of the dawn phenomenon (42%) compared to non-programmers (48%) (\( p = 0.47 \)) but did have an increase in the occurrence of hypoglycemia (37%) compared to non-programmers (18%) (\( p = 0.001 \)).

**Conclusions:** In this 8-month study of T1D subjects in the ambulatory setting, early morning CSI1 programming did not reduce the occurrence of the dawn phenomenon but resulted in significantly higher rates of hypoglycemia. The dawn phenomenon did not occur with predictability; thus, programming for a fixed increase in early morning insulin delivery is ineffective and the increased hypoglycemia may be hazardous to the patient.

**Performance of Statstrip® Glucose Monitor in Hyperglycemic Clamps in a Pediatric Population**

Lindquist KA1,2, Campbell S2, Cree-Green M2, Morehead R2, West A2, Isbell TS1, Pyle L1, Nadeau K1. University of Massachusetts Medical School, Worcester, MA; 2University of Colorado Denver, Aurora, CO and 3Nova Biomedical Corp., Waltham, MA.

**Purpose of Study:** In parallel with the pediatric obesity epidemic, there is an increasing need for assessment of pancreatic β-cell function. The hyperglycemic clamp, a gold standard for assessment of β-cell function, requires frequent, accurate measurements of blood glucose concentrations, typically utilizing the YSI 2300 STAT Glucose Analyzer. Despite its accuracy, the YSI has several limitations, including its cost, lengthy run time, need for trained personnel, and frequent maintenance. In addition, the YSI requires large blood volumes which is of particular concern in pediatric patients. Simpler hospital-grade handheld glucose meters are now available, but have not been validated for use in pediatric clamp settings. We evaluated the accuracy, precision, and reliability of the Statstrip® (SS) Hospital Glucose Monitoring System relative to the YSI in the setting of pediatric hyperglycemic clamps.

**Methods Used:** 126 blood specimens drawn from 3 pediatric patients undergoing two-stage (200 mg/dl, 450 mg/dl) hyperglycemic clamps were simultaneously analyzed by SS and YSI.

**Summary of Results:** The SS showed an average bias of +1.63 mg/dl compared to the YSI over the entire range of all hyperglycemic blood glucose measurements. During stage 1 (n= 92, goal glucose 200 mg/dl, range: 141-240 mg/dl), the SS showed an average bias of 0.11 mg/dl. Coefficients of variation for SS and YSI during stage 1 were 10.13 and 10.12, respectively. During stage 2 (n= 34, goal glucose 450 mg/dl, range 265-562 mg/ml), the SS showed an average bias of 5.75 mg/dl. Coefficients of variation for SS and YSI during stage 2 were 18.34 and 17.95, respectively. A Bland Altman plot
Gastroenterology
Concurrent Session
12:30 PM
Friday, January 24, 2014

209
INFLAMMATORY COLITIS, LYMPHATIC INSUFFICIENCY, AND PROGRESSION TO COLORECTAL CANCER IN AN EXPERIMENTAL MOUSE MODEL


Purpose of Study: Inflammatory bowel disease (IBD) is a well-recognized risk factor for colorectal cancer (CRC) (~15-20% lifetime risk in ulcerative colitis [UC]). The lymphatic system has been implicated in both IBD pathophysiology and CRC growth/spread. Previously, we showed in acute dextran sulfate sodium (DSS) colitis, lymphatic deficient mice [knockout of angiotensin-2 (Ang2)] exhibited reduced lymphangiogenesis and down-regulated inflammatory markers. This study extends these observations to chronic UC and examines progression to CRC.

Methods Used: C57B6 adult mice (Ang2 +/-, +/-, -/-) (Regeneron) were divided into 4 groups: Group 1: single 4 or 12 mg/kg IP dose of procarcinogen azoxymethane (AOM) and 14 days later, 1-1.25% DSS in drinking water for 7 days then 14 days off DSS (cycle repeated 1-2X ~clinical severity score). Controls included AOM alone (Group 2), DSS cycles without AOM (Group 3), or untreated (Group 4). Clinical severity scores (changes in body weight, energy, stool consistency, occult blood) were followed. At sacrifice, colon length was measured and tissue sampled in 4 segments from proximal to distal colorectum and assessed by inflammatory index, tumor burden, and histologic features.

Summary of Results: Groups 1 and 3 showed similar clinical severity and mortality and reduced survival (46.5% ± c.f. 90%) in Ang2-/- whereas Groups 2 (4mg/kg AOM) and 4 were unaffected. Group 2 exhibited rapid 100% mortality at 12 mg/kg AOM but 0% at 4mg/kg. Group 1 had 91% non-invasive CRC incidence in the distal segment. Ang2 +/- were not protected from CRC, and clinical severity tended to be worse. Tumor burden in +/- mice (13.5% of distal colon surface) was significantly higher than +/- (4.6%, p=0.008) and +/- (5.5%, p=0.007) (n.s. +/- vs. +/-).

Conclusions: This refined mouse model of UC progression to CRC is rapid, reproducible, and well-tolerated with high CRC incidence demonstrating that even subacute UC in the presence of a low-dose procarcinogen tolerated by the normal colon is a CRC forerunner. Further, lymphatic deficiency, defective lymphangiogenesis, and impaired lymphatic-generated inflammation do not protect against either the UC clinical severity or its progression to non-invasive CRC.

210
ANTI-INFLAMMATORY ROLE OF IFN-γ AND THE IL-10 RECEPTOR IN THE RESTITUTION OF BARRIER FUNCTION AND RESOLUTION OF INFLAMMATORY BOWEL DISEASE

Vickery T, Kelly C, Dohrinskláh E, Campbell E, Wilson K, Bayless A, Saeedi B, Glover L, Colgan S, Kominsky D. University of Colorado School of Medicine, Denver, CO.

Purpose of Study: Investigate the mechanism of IFN-γ induced IL-10 expression on barrier restitution and return to homeostasis in models of inflammatory bowel disease (IBD).

Methods Used: IL-10R was identified as a target in IFN-γ treated intestinal epithelial cells (IEC) using microarray analysis. Lentiviral particles were used to knockdown the IL-10R1 in human epithelial cells (T84) in vitro. The effects of IL-10R expression were characterized using qPCR, western blot, and confocal microscopy. The role of IL-10R expression on epithelial functional proteins was examined using trans-epithelial electrical resistance (TEER) and FITC-dextran flux assays. Finally, IL-10R1 expression was investigated in vivo using a murine IBD model, conditional IL-10R1 knockout mice, and human IBD patient samples.

Summary of Results: In vitro studies revealed that IFN-γ selectively induced the expression of IL-10R1 on the apical surface of IEC in a time dependent manner. Activation of the IL-10R functionally induced canonical IL-10 target gene expression in IEC concomitant with enhanced barrier restitution. Additionally, knockdown of IL-10R1 in intestinal epithelial cells results in impaired barrier function. Colonic tissue isolated from murine colitis revealed that levels of IL-10R and intracellular SOCS3 were increased in the epithelium and coincided with increased tissue IFN-γ and IL-10 cytokines. IL-10R null mice demonstrated significantly worse disease as measured by colon length, barrier function, and pro-inflammatory cytokines (TNFα, IL-1β, and IL-6) in a mouse model of colitis. Immunofluorescent staining revealed apical expression of the IL-10R in colitic mouse tissue. Furthermore, treatment of mice with rIFN-γ induced apical expression of IL-10R1 in the colonic epithelium. Finally, diseased human tissue demonstrated increased IL-10R1 transcript with apical IEC localization.

Conclusions: These results suggest a critical anti-inflammatory role for IFN-γ induced expression of IL-10R1 in the restitution of barrier function following intestinal epithelial inflammatory insult.
ANALYSIS OF ABDOMINAL ACOUSTIC AND MOTOR PROFILES OF PATIENTS WITH POSTOPERATIVE ILEUS USING THE NOVEL ABSTATS MONITORING SYSTEM

Tashjian VC1, Kaiser W3, Spiegel B1–2,3, 1UCLA David Geffen School of Medicine, Los Angeles, CA; 2VA Greater Los Angeles Healthcare System, Los Angeles, CA and 3UCLAVAM, Los Angeles, CA.

Purpose of Study: Post-operative ileus (POI) is a common condition characterized by temporary bowel paralysis following abdominal surgery. In fact, some degree of POI is actually physiologically normal. However, when POI is prolonged it can significantly impact patient outcomes including delayed oral feeding, slowed wound healing, increased risk of infection, and increased hospital resource utilization. Consequently, it is estimated that the high prevalence and impact of POI costs the United States $1 Billion annually. Monitoring POI is, however, imprecise. The current standard of care is to perform unreliable, periodic physical examinations to assess abdominal girth, bowel sounds and movements, stool output, and flatus. To help medical professionals better monitor POI, we introduce the novel AbStats acoustic monitoring system. With AbStats, patients recovering from POI will be monitored continuously and accurately for gut motility rather than periodically. Researchers hypothesize that AbStats has the capacity to detect earlier motility; allowing patients with POI to be fed earlier and discharged sooner than might otherwise occur without AbStats.

Methods Used: Patients were recruited at the West Los Angeles VA Hospital based on specific inclusion criteria for POI. Patients were divided into three AbStats groups; healthy subjects (HS), post-surgery no nutrition (PSNN), and post-surgery returning to nutrition (PSRN). Data from the device was then extrapolated and compared to identify differences in motility.

Summary of Results: The HS group had motility event rates/sec between 0.150-0.208 (mean = 0.1917), PSNN between 0.008–0.022 (mean =0.014), and PSRN between 0.045–0.062 (mean=0.0544).

Conclusions: AbStats is able to reliably show distinct patterns of motility among HS, PSNN, and PSRN patients groups. Additionally, AbStats is able to show when a post-operative patient is returning to a motility pattern suitable for feeding.

ANTIBODY-MEDIATED REJECTION: AN IMPORTANT AND UNDERDIAGNOSED CAUSE OF LIVER GRAFT DYSFUNCTION

Bhattacharyya S1, Swanson E2, Naini B1, Wozniak L1, 1David Geffen School of Medicine, Los Angeles, CA; 2David Geffen School of Medicine, Los Angeles, CA and 1David Geffen School of Medicine, Los Angeles, CA.

Purpose of Study: Antibody-mediated rejection (AMR) is uncommon following liver transplantation (LTx). As such diagnostic criteria and optimal treatment remain poorly defined, and most reports have applied the same criteria used in renal and cardiac transplantation: a) clinical signs of graft dysfunction; b) histopathology indicative of acute injury; c) complement deposition (C4d staining); d) presence of HLA donor-specific antibodies (DSA). The aim of this study was to describe the clinical characteristics and outcomes of three pediatric LTx recipients diagnosed with AMR.

Methods Used: A retrospective review identified three pediatric LTx recipients diagnosed with AMR at UCLA from September 2012 to May 2013. For each patient, liver biochemical markers, immunogenetic tests, and immunosuppression protocols were longitudinally assessed.

Summary of Results: All three patients presented with clinical signs of allograft dysfunction, indicated by peak ALT levels of 454–699 U/L, and peak GGT levels of 67–234 U/L. Two patients were initially diagnosed with acute cellular rejection refractory to steroid therapy. Additional testing of all three patients showed positive HLA Class II DSA with values ranging from 1372-1191 MFI. Two patients were treated with IVIG and rituximab, and the other with IVIG alone. All three exhibited resolution of allograft dysfunction 1 to 4 weeks after receiving treatment for AMR and continue to have normal allograft function at most recent follow-up.

Conclusions: Historically AMR has been considered rare after LTx. There are now increasing numbers of case reports, including ours, supporting its existence. Clinicians need to be aware of AMR as it may be an underdiagnosed cause of LTx allograft dysfunction.

OUTCOMES AND COMPILICATIONS OF CAPSULE ENDOSCOPY IN A COMMUNITY GASTROENTEROLOGY PRACTICE

Smith JD1, Gonzales CM2, 1Weber State University, Ogden, UT and 2McKay Dee Hospital, Ogden, UT.

Purpose of Study: Capsule endoscopy (CE) is used to diagnose small bowel pathology and has favorable diagnostic yield when compared to other available technologies. Primary indications for CE include obscure gastrointestinal bleeding in adults, suspected Crohn's disease, and small bowel tumors. While CE has been successful in this regard, there are relatively few studies that evaluate outcomes specific to a small community private practice environment.

Methods Used: Between 2007 and 2012, 265 patients underwent CE testing in a community GI clinic. A retrospective chart review of these patients was conducted. Electronic and paper medical records were analyzed for demographic information, CE indications, pertinent findings and interventions. Sub-group analysis was performed.

Summary of Results: CE was performed for evaluation of iron deficiency anemia in 65.7% of patients, occult GI bleeding (39.3%), rectal bleeding (31.7%), abdominal pain (20.7%) and diarrhea (18.1%). Overall diagnostic yield was 82.3%. The most common findings were gastritis (34%), artery venous malformations (AVMs) (19.9%), small bowel ulcers or erosions (9.9%) and miscellaneous (18.5%). 17.7% of studies were normal. Relevant pathological findings were identified in patients with iron deficiency anemia (72.9%), occult GI bleeding (76.9%), rectal bleeding (76.2%) and abdominal pain (80%). Complications due to capsule retention occurred in 3 patients (1.1%) all of whom had Crohn's disease with small bowel strictures, ulcers or erosions. The capsule passed spontaneously in 2 patients by 3 weeks. The capsule was retained for 3 months in the other patient with known Crohn's and was removed by surgery. Capsule transit to the colon was delayed in 18 patients (6.8%) affecting completeness of the study. NSAID discontinuation was recommended in 21.5% of patients. Additional diagnostic studies were recommended in 23% of patients. Iron replacement therapy in 12.3% of patients.

Conclusions: Wireless CE in community GI practice is a useful study in evaluation of small bowel pathology with high diagnostic yield. CE is safe with very few complications. Capsule retention was infrequent occurring in only 1% of patients. Abnormally slow capsule transit occurred in 5% of studies and impacted completeness of the study.
ANCILLARY DIAGNOSTIC TESTS TO DISTINGUISH THESE TWO LESIONS.

SUMMARY OF RESULTS: The analysis showed the genes MAPK1, CASP2, and CASP14 to be upregulated in the KA area vs. SCC area (fold change >1) while BAG1 and MMP14 were downregulated (fold change <1). This is consistent with the previous microarray data, and the functions of these genes are also consistent with the idea that KA is a neoplasm that regresses.

CONCLUSIONS: The differential gene expression in the histologically different KA and SCC areas of the scalp lesion further validates the results of previous expression microarray studies and supports the idea that KA and SCC are distinct entities. The differing molecular profiles may suggest targets for developing ancillary diagnostic tests to distinguish these two lesions.

GALACTOSE DETERMINES ADENO-ASSOCIATED VIRUS SEROTYPE 9'S CONE PHOTORECEPTOR TROPISM

Marshall T,1,2, Turunen H,2, Plovie E2, Chang R2, Carvalho L2, Xiao R2, Vandenbergh LH1, 1University of Washington School of Medicine, Seattle, WA and 2Harvard Medical School; Scheper's Eye Research Institute, Boston, MA.

PURPOSE OF STUDY: Therapeutic gene delivery to the retina with adeno-associated viral vectors (AAV) has been found safe and efficacious in early proof-of-concept clinical trials. Vectors in these studies targeted the retinal pigment epithelium, however, many forms of inherited blindness are due to gene defects in photoreceptor cells. AAV serotype 9 targets cone photoreceptors (PR) in non-human primate retinas with a greater efficiency than other serotypes. Furthermore, AAV9 is known to bind galactose moieties on both N-linked and O-linked extracellular glycan chains. The goal of this study is to identify if AAV9 targets cone PR through interaction with galactose moieties on the cell surface.

METHODS USED: The ability of AAV9 to bind galactose was analyzed both in vitro and in vivo using two methodologies: 1) the enzymatic digestion of extracellular glycan via neuraminidase (NA), to expose galactose, and 2) galactosidase to remove galactose; 2) a genetic mutant of AAV9, AAV9W503R, which has a single capsid mutation rendering it incapable of binding galactose. Binding assays were performed in vitro on 661 W cells, a mouse cone PR cell line and AAV binding was measured using qPCR. Sub-retinal injections of AAV for in vivo analysis was performed on 6-8 week old male C57BL/6 mice, harvested at 10 days post-injection, and analyzed via confocal microscopy for eGFP transgene expression.

SUMMARY OF RESULTS: AAV9 shows increased binding in vitro on 661 W cells when treated with NA to expose galactose residues, while AAV9W503R shows no greater binding affinity on NA treated cells. Initial in vivo data suggests that AAV9 better transduces in the mouse retina when NA treated. AAV9W503R shows efficient retinal transduction in vivo.

CONCLUSIONS: AAV9 targets retinal cone PR in vitro by binding extracellular galactose residues. Sub-retinal injections in mice demonstrated stark differences between in vivo and in vitro results and highlighted the potential of the mutant AAV9W503R as a novel vector for retinal gene therapy.

EXPANDING THE CLINICAL PHENOTYPE OF HDAC8 MUTATIONS

Atwal PS, L Hudgins, Stanford, Sunnyvale, CA.

CASE REPORT: The phenotype of HDAC8 mutations was initially described in 2012. The initial cohort of patients was described as having a craniofacial appearance similar to classical Cornelia de Lange Syndrome (CDLS) and severe developmental delay. We present a patient with an HDAC8 mutation who does not have a classical CDLS facies and only mild delays in development.

Our patient is now a 4 year old girl of Indian descent with mild growth restriction (height 3rd percentile), microcephaly (<-2 SD) of prenatal onset and mild developmental delay. Formal developmental assessment at 2-years-1-month showed a 50% delay in multiple domains including communication, gross motor and visual motor skills (DQ 46). At her present age of 4 years, she is walking, strings 2-3 word sentences together, has over 100 words and is able to follow commands. Pertinent features on physical exam included micro-brachycephaly, asymmetric facies, synophrys (also present in mother), a broad nasal root with a full tip, delayed tooth eruption, bilateral fifth finger brachy-dactyly, and hirsutism.

To ascertain the causal molecular diagnosis, whole exome sequencing was performed clinically and demonstrated a de novo c.1006-2A>G mutation in the HDAC8 gene, on chromosome X. This mutation is predicted to abolish the canonical upstream (3') splice site prior to exon 9 of the HDAC8 gene, resulting in a nonsense gene product.

The findings in our patient suggest that the clinical heterogeneity is wider than initially observed as our patient lacks classic CDLS craniofacial features and has only mild delays in growth and development. Classic CDLS is characterized by growth failure of prenatal onset, hirsutism, upper limb reduction defects and distinctive facial features including synophrys, arched eyebrows, long eyelashes, small upturned nose, long smooth philtrum with thin vermilion border and cupid's bow and small widely spaced teeth. Our patient's facial appearance is unlike classic CDLS in that she does not have arched eyebrows, long eyelashes or a thin vermilion with cupid's bow. HDAC8 mutations have been observed in heterozygous females previously with skewing of X-inactivation.

In summary, HDAC8 mutations have a broader phenotype than originally observed ranging from mild to severe developmental delays, minor facial anomalies to classic CDLS, and mild postnatal growth restriction.

TRANSCRIPT CHARACTERIZATION OF THE HUMAN-SPECIFIC NEURAL GENE HYDIN2

Dougherty M1, Nuttle X2, Eichler E2,3, 1University of Washington School of Medicine, Seattle, WA and 2University of Washington School of Medicine, Seattle, WA; 3University of Washington School of Medicine, Seattle, WA.

PURPOSE OF STUDY: Several internal exons of the ciliary gene HYDIN2 duplicated exclusively in the human lineage approximately 3.1 million years ago, giving birth to the human-specific gene HYDIN2. This novel gene is hypothesized to have played an important role in human brain evolution because mutations disrupting its ancestor have been associated with hydrocephalus and autism, its expression is largely confined to the brain (unlike its ancestor) and duplications including it have been implicated in microcephaly and macrocephaly, respectively. Although there is clear evidence of transcription from this locus, its genic potential remains largely unexplored. In depth characterization of HYDIN2 transcripts is critical for delineating HYDIN2 coding sequence and informing future efforts to associate genetic variation at this locus with disease.

METHODS USED: cDNA was generated from fetal brain RNA. Rapid amplification of cDNA ends (RACE) was used to isolate 5' and 3' ends of HYDIN2 transcripts for capillary sequencing.

SUMMARY OF RESULTS: Three distinct 5' ends of HYDIN2 transcripts were identified. Interestingly, these ends map outside of the HYDIN segmental duplication, suggesting that HYDIN2 acquired a new promoter and novel 5' exons not included in its ancestor. Long-range PCR experiments confirmed the existence of HYDIN2 transcripts spanning the duplication boundary and revealed a wide diversity of HYDIN2 splice isoforms, in that she does not have arched eyebrows, long eyelashes or a thin vermilion with cupid's bow. HDAC8 mutations have been observed in heterozygous females previously with skewing of X-inactivation.

In summary, HDAC8 mutations have a broader phenotype than originally observed ranging from mild to severe developmental delays, minor facial anomalies to classic CDLS, and mild postnatal growth restriction.

EXPANDING THE CLINICAL PHENOTYPE OF HDAC8 MUTATIONS

217 EXPANDING THE CLINICAL PHENOTYPE OF HDAC8 MUTATIONS

Atwal PS, L Hudgins, Stanford, Sunnyvale, CA.

CASE REPORT: The phenotype of HDAC8 mutations was initially described in 2012. The initial cohort of patients was described as having a craniofacial appearance similar to classical Cornelia de Lange Syndrome (CDLS) and severe developmental delay. We present a patient with an HDAC8 mutation who does not have a classical CDLS facies and only mild delays in development.

Our patient is now a 4 year old girl of Indian descent with mild growth restriction (height 3rd percentile), microcephaly (<-2 SD) of prenatal onset and mild developmental delay. Formal developmental assessment at 2-years-1-month showed a 50% delay in multiple domains including communication, gross motor and visual motor skills (DQ 46). At her present age of 4 years, she is walking, strings 2-3 word sentences together, has over 100 words and is able to follow commands. Pertinent features on physical exam included micro-brachycephaly, asymmetric facies, synophrys (also present in mother), a broad nasal root with a full tip, delayed tooth eruption, bilateral fifth finger brachy-dactyly, and hirsutism.

To ascertain the causal molecular diagnosis, whole exome sequencing was performed clinically and demonstrated a de novo c.1006-2A>G mutation in the HDAC8 gene, on chromosome X. This mutation is predicted to abolish the canonical upstream (3') splice site prior to exon 9 of the HDAC8 gene, resulting in a nonsense gene product.

The findings in our patient suggest that the clinical heterogeneity is wider than initially observed as our patient lacks classic CDLS craniofacial features and has only mild delays in growth and development. Classic CDLS is characterized by growth failure of prenatal onset, hirsutism, upper limb reduction defects and distinctive facial features including synophrys, arched eyebrows, long eyelashes, small upturned nose, long smooth philtrum with thin vermilion border and cupid's bow and small widely spaced teeth. Our patient's facial appearance is unlike classic CDLS in that she does not have arched eyebrows, long eyelashes or a thin vermilion with cupid's bow. HDAC8 mutations have been observed in heterozygous females previously with skewing of X-inactivation.

In summary, HDAC8 mutations have a broader phenotype than originally observed ranging from mild to severe developmental delays, minor facial anomalies to classic CDLS, and mild postnatal growth restriction.

FUNCTIONAL EXONIC SPlicing ELEMENTS DETERMINED BY MASSIVELY MULTIPLEX GENOME ENGINEERING

Findlay GM1,2, Boyle E1, Shendure J2, 1University of Washington, Seattle, WA and 2University of Washington School of Medicine, Seattle, WA.

PURPOSE OF STUDY: The recent development of highly specific and programmable endonucleases has allowed researchers to edit genomes of mammalian cells
with increasing efficiency. To date, such techniques have widely been used to make single changes in cell culture or animal models, such as the generation of mutant alleles or selectable markers. The goal of the present study is to engineer and assay many uniquely edited cells within a single sample. We show the utility of this approach by targeting 6 base pairs (bp) within an exon of the BRCA1 gene, within which a point mutation is known to cause deleterious exon skipping. By substituting thousands of 6 bp random sequences at this location, we can determine how each one affects splicing in a multiplex fashion.

Methods Used: A plasmid library containing >90% of all possible 4,096 DNA hexamers substituted at positions +5 to +10 of BRCA1 exon 18 was constructed using a partially degenerate oligonucleotide. Multiplex targeted editing of the human genome was achieved via homologous donor repair by co-transfecting the library into 293T cells with S. pyogenes Cas9 and a guide RNA complementary to exon 18 of BRCA1. DNA and RNA were harvested 5 days post-transfection, and PCR and deep sequencing were performed to quantify genomic integration and transcript inclusion for each hexamer.

Summary of Results: Hexamer substitution occurred with ~3% efficiency in 5x10^6 cells. Over 7.5x10^6 sequencing reads of gDNA and cDNA were generated to quantify genomic integration and transcript inclusion for each guide RNA complementary to exon 18 of BRCA1. DNA and RNA were harvested 5 days post-transfection, and PCR and deep sequencing were performed to quantify genomic integration and transcript inclusion for each hexamer.

In PRDM9, there is significant diversity, and as we continue to better characterize this phenomenon we hope to demonstrate the mechanism by which certain alleles cause sterility in humans.

Conclusions: We have demonstrated the ability to generate thousands of distinct mutations at a single locus in cell culture and have correlated our data to known biological phenomena for validation. To our knowledge, this is the first demonstration of multiplex, targeted genome editing followed by high-throughput functional analysis.

221 ANALYZING THE CLINICAL INDICATIONS WHEN TESTING FOR LYNCH SYNDROME USING NEXT GENERATION SEQUENCING

Perez M, Gallagher C, Bennett R, Jarvik G. University of Washington, Seattle, WA.

Purpose of Study: Massive parallel sequencing (MPS) allows physicians to sequence multiple genes at once to look for pathogenic variants in a patient's genome. The Colosq panel consists of 13 genes associated with colorectal polyps and malignancy including Lynch Syndrome (LS), an inherited susceptibility to cancer of the digestive tract and endometrium. Current guidelines recommend using age, family history, and histologic tests to screen for LS before proceeding to genetic testing. The Amsterdam II Criteria and Bethesda Guidelines have been used to help identify people and families at risk of LS. This study analyzes the efficacy of established guidelines when determining who should receive genetic testing using Colosq.

Methods Used: A chart review was performed on patients (n=101) who had Colosq performed at the University of Washington. An abstraction form was used to collect personal information, family history, and lab results. Patients were excluded if they had Colosq performed but results were not available.

Summary of Results: A total of 30 patients for whom the Colosq test was performed had a variant returned. Of these, 9 variants were pathogenic, 5 likely pathogenic, and 16 were variants of unknown significance (VUS). Of the 39 patients that fit Bethesda Guidelines and/or Amsterdam II Criteria, 8 (20.5%) were found to have a pathogenic or likely pathogenic variant. Four of these 8 were in LS genes. For subjects that did not meet Amsterdam II or Bethesda criteria the rate of identification of pathogenic or likely pathogenic mutations was 6/62 (9.7%); 3 of the 6 were in LS genes. Of the 9 patients that showed loss of protein expression from a LS gene by histologic tests, 4 had a pathogenic or likely pathogenic variant.

Conclusions: The sensitivity of the Colosq panel depended on clinical indication. Although patients meeting Amsterdam II and Bethesda Guidelines had a higher positive test rate, these guidelines lacked the sensitivity to identify all patients with pathogenic or likely pathogenic variants in LS genes. The extended panel improved yield vs. LS genes alone. With 16 of the 30 returned variants being VUSs emphasizes the need for shared pathogenicity information and for patient follow up when additional information is obtained.

222 COMBINING HOMOZYGOSITY AND TARGETED OR EXOME SEQUENCING TO Diagnose Rare Genetic Disorders

Beck AE1,2, Issaill HM1,2, Delgado F1,2, Conta BH1, Glass IA1,2, Curry C1,4, Phokher C1,2, Tsuchida KD1, Seattle Children's Hospital, Seattle, WA; 1University of Washington, Seattle, WA; 2Genetic Medicine Central California, Fresno, CA and 4University of California San Francisco, San Francisco, CA.

Purpose of Study: Single nucleotide polymorphism (SNP) microarrays can identify multiple blocks of long contiguous stretches of homozygosity consistent with shared ancestry/consanguinity. In individuals with suspected autosomal recessive genetic conditions, however, these regions of homozygosity can contain a large number of genes. We report 5 families in which a diagnosis was made by using knowledge of genes contained within regions of homozygosity to direct either targeted or exome sequencing.

Methods Used: The homozygous regions identified on SNP arrays were analyzed for size, percent of total autosomal homozygosity, and the number of genes contained within these regions (all, OMIM, and “disease-causing” OMIM genes). If the homozygous regions were relatively small or had candidate genes located within those regions, then targeted Sanger sequencing was performed. If the regions were large and encompassed a large number of candidate genes, then exome sequencing was carried out instead.

Summary of Results: While SNP array analysis did not identify any clinically relevant deletions or duplications in affected individuals, it did reveal significant autosomal homozygosity across multiple chromosomes ranging from 3–23%. Consanguinity was denied in all cases; however, in all 5 cases both parents were from the same ethnic and/or regional background. Two families had 2 affected children, but 3 families had only one affected child. In all 5 of these cases, the molecular investigation led to the discovery of homozygous, deleterious mutations within a gene that explained the child's phenotype. The size of the
specific homozygous block containing the causative gene ranged from 1.4 to ~10Mb, therefore not all of the homozygous blocks containing the causative gene were above the standard 3-5Mb cut-off often used by clinical laboratories.

Conclusions: The discovery of homozygous regions on SNP arrays, expected or unexpected, can be a valuable clinical tool in determining the molecular cause of autosomal recessive genetic conditions when combined with subsequent targeted or exome sequencing.

Neonatology – General II
Concurrent Session

12:30 PM
Friday, January 24, 2014

223
A RANDOMIZED CLINICAL TRIAL OF THERAPEUTIC HYPOTHERMIA DURING TRANSPORT FOR HYPOXIC ISCHEMIC ENCEPHALOPATHY: DEVICE SERVO-REGULATED COOLING VERSUS STANDARD PRACTICE

Akula V1, Joe P4, Thusu K1, Kim S10, Shimotake T3, Butler S5, Honold J9, Kuzniwicz MW4, DeSandre G1, Davis AS1, Gould JB2, Randall K1, Wallenstein M1, Van Meurs KP1, Stanford University School of Medicine, Palo Alto, CA; 2Palo Alto, CA; 3UCSF Medical Center, San Francisco, CA; 4Children's Hospital and Research Center Oakland, Oakland, CA; 5Sutter Medical Center, Sacramento, CA; 6Kaiser Permanente, Oakland, CA; 7Children's Hospital Central California, Madera, CA; 8Santa Clara Valley Medical Center, San Jose, CA; 9Rady Children's Hospital, San Diego, CA and 10Loma Linda University Children's Hospital, Loma Linda, CA.

Purpose of Study: Therapeutic hypothermia initiated within 6 hours of birth has been shown to significantly improve survival and outcome in newborns with moderate to severe hypoxic ischemic encephalopathy (HIE). Effective cooling during transport is critical for outborn infants. Our purpose was to compare temperature profiles during transport between device servo-regulated cooling and standard practice.

Methods Used: In this randomized clinical trial at 9 cooling centers in California, newborns with gestational age ≥35 weeks who met institutional criteria for therapeutic hypothermia, and in whom the decision had been made to perform cooling in transport, were randomly assigned to receive cooling according to usual center practice (passive cooling ± ice/gel packs) or device servo-regulated cooling using the TecothermNeo (Inspiration Healthcare LTD, Leicester, UK). Rectal or esophageal temperatures were collected every 15 minutes from arrival of transport team at the birth hospital until admission to the cooling center. The primary outcome was the percentage time in the target temperature range (33–34°C).

Summary of Results: Between October 2012 and September 2013, 100 newborns were enrolled; 49 to standard care and 51 to device. Device regulated cooling resulted in a higher percentage of temperatures in target range compared to standard care (63% vs 34%, p<.0001). More infants achieved target temperature at 1 hour using the device compared to standard care (72% vs 18%, p<.0001).

Conclusions: Device servo-regulated cooling improves temperature management during neonatal transport for HIE.

224
DANCE (DARBE ADMINISTRATION IN NEWBORNS UNDERGOING COOLING FOR ENCEPHALOPATHY): SAFETY AND PHARMACOKINETIC TRIAL

Roberts JK1, Beachy J1, Yoder B1, Ward R1, Sherwin C1, Spigarelli M2, DiGeronimo R1, Ohls RK2, Walsh W1, Mayock D3, Jaul S4, Christensen R4, Basgall P4, University of Utah, Salt Lake City, UT; 5University of New Mexico, Albuquerque, NM; 6Vanderbilt University, Nashville, TN; 7Seattle Children's, Seattle, WA and 8McKay Dee Hospital, Ogden, UT.

Purpose of Study: Despite early intervention using hypothermia, outcomes of death or major disability still occur in nearly 50% of babies with hypoxic-ischemic encephalopathy (HIE). In neonatal animal models, erythropoietin (EPO) has been shown to provide neuroprotection, improving short and long-term neurologic outcome following HIE. Darbepoetin (darbe) has comparable biological activity to EPO but offers extended circulating half-life, requiring less frequent dosing. We hypothesize that darbe can be administered in a safe manner as an adjunctive therapy to cooling in newborn infants with moderate to severe HIE.

Methods Used: In this ongoing Phase I multicenter trial, 30 infants (n=10 in each arm) ≥36 weeks gestational age (GA) with HIE were randomized to receive darbe low dose (2 μg/kg IV), high dose (10 μg/kg IV), or placebo. First study drug dose was given within 12 hours of life and a 2nd dose 7 days later. Safety was examined by documenting adverse events (AE). To determine darbe PK in this population, serum samples were obtained for measurement of EPO concentrations (ELISA), and analyzed using PK modeling (Phoenix WinNonLin).

Summary of Results: 24 are enrolled up to date: 11 females/13 males with a mean birth weight of 3015 gr and median GA of 39 weeks. There was 1 death in a patient with multi-organ failure not attributable to the study. There were no other serious adverse events. Most common AE reported included hypertension, hypotension, altered renal and hepatic function, persistent pulmonary hypertension, and thrombocytopenia. These AE were attributable to HIE and hypothermia. A non-compartmental analysis was performed on the preliminary data. Parameters estimated for the 10 μg/kg group: Area Under the Curve (AUC) = 163.7 h*ng/mL, terminal half life (T1/2) = 53.4 h. Parameters estimated for the 2 μg/kg group: AUC = 27.2 h*ng/mL, T1/2 = 37.3 h.

Conclusions: Preliminary results show darbe PK parameters comparable to those previously published, indicating the desired plasma concentrations were reached. Importantly, darbe appears to be safe in critically ill newborns.

225
THE ROLE OF MATERNAL IMMUNE ACTIVATION IN EPILEPSY

Washington JA1, Pineda E2, Shim D3, Mazzarati A2, Sankar R2, UCLA, Los Angeles, CA and 1UCLA, Los Angeles, CA.

Purpose of Study: Recent studies show maternal viral infection resulting in maternal immune activation (MIA) is a significant risk factor in the development of autism in offspring. 30% of patients with autism develop epilepsy. It is not known whether MIA also leads to epilepsy. Although our lab has previously demonstrated that MIA facilitates epileptogenesis using the kindling model, limitations of this model include face and construct validity. In the present study we used a more relevant mouse model of temporal lobe epilepsy (TLE) induced by an intrahippocampal injection of kainic acid (KIA). We hypothesized that MIA will exacerbate the severity and frequency of seizure in mice subjected to KIA.

Methods Used: MIA was induced in C57BL/6 pregnant mice by the injection of polyinosinic-polycytidylic acid (PIC) during embryonic days 12 to 16. Control treatment consisted of the injection of normal saline. Postnatal day 40, the propensity of the offspring to epilepsy was examined using the IKA model of TLE. One month after, IKA mice were monitored for an additional month for the presence and frequency of spontaneous recurrent seizures. After the seizure monitoring, mouse brains were processed for hippocampal histological analysis using NeuN to measure the degree of neuronal degeneration and glial fibrillary acidic protein (GFAP) to measure the degree of astrocyte activation in CA1, CA3 and hilus of hippocampi.

Summary of Results: IKA alone (i.e in the absence of MIA) produced significant neuronal cell loss in CA1 (NeuN-positive cells 133±16.5 vs 186.5±9.6 in controls; p<0.01). Preexisting MIA significantly exacerbated kainic acid-induced neurodegeneration in CA1 (NeuN-positive cell count 94±38.7 vs kainic acid alone; p<0.05). Neither IKA alone nor the IKA+MIA led to significant cell loss in CA3 or hilus. There were no differences in frequency or severity of seizures amongst groups.

Conclusions: MIA selectively exacerbated IKA neuronal injury to CA1. Results have not shown a significant difference in seizure incidence or severity associated with maternal inflammation or IKA. We are currently performing GFAP staining. Future studies will include the addition of a MIA only group (i.e mothers injected with maternal inflammation or IKA). We are currently performing GFAP staining. Future studies will include the addition of a MIA only group (i.e mothers injected with maternal inflammation or IKA). We are currently performing GFAP staining. Future studies will include the addition of a MIA only group (i.e mothers injected with maternal inflammation or IKA). We are currently performing GFAP staining. Future studies will include the addition of a MIA only group (i.e mothers injected with maternal inflammation or IKA).

226
ERYTHROCYTE STIMULATING AGENT EFFECTS ON MAGNETIC RESONANCE SPECTROSCOPY IN CHILDREN BORN PREMATURELY

Van Meter J1, Ohls RK2, Phillips J1, Caprhan A1, Peceny S1, Cannon DC2, Lowe JP, Gasparovic C1, 1Mind Research Network, Albuquerque, NM and 2University of New Mexico Health Sciences Center, Albuquerque, NM.
Purpose of Study: In animal models, erythrocyte stimulating agents (ESAs) such as erythropoietin (Epo) and Darbepoetin (Darbe) are neuroprotective, showing evidence of oligodendrogenesis, decreased white matter injury, and decreased neuronal apoptosis. In several neonatal studies, Epo appeared to improve neurodevelopment in children formerly born prematurely. Limited information is available on potential neuroprotective effects of Darbe, which is a longer acting ESA than Epo, and the underlying mechanism of action of ESAs in preterm infants has not been clarified. MR spectroscopy provides an in vivo probe of important neurotransmitters and neurometabolites. We evaluated spectroscopy and cognitive outcomes in children born prematurely who had been randomized to receive Epo, Darbe or placebo during their initial hospitalization, compared to term born control children.

Methods Used: Children underwent developmental testing and magnetic resonance (MR) imaging between 3.5–4 years of age. Children previously born at term with uncomplicated hospital stays served as healthy controls. MR imaging included single voxel MR spectroscopy of the anterior cingulate and left frontal lobe white matter. Metabolites assessed include n-acetylaspartic acid, myoinositol, choline, creatine and glutamate/glutamine. Volumetric analysis was performed using the computer program FreeSurfer, allowing cortical segmentation to assist spectroscopy analysis.

Summary of Results: 48 children (21 male, 27 female) provided imaging and developmental datasets. We compared 3 groups: term healthy control children, untreated preterm children, and ESA treated preterm children. Trends toward normalization of n-acetylaspartic acid, creatine, myoinositol were noted in the anterior cingulate voxel. The frontal lobe white matter voxel demonstrated a trend toward normalization of myoinositol and glutamate/glutamine.

Conclusions: Several spectrophotometric trends were noted which, if confirmed in larger studies, may provide evidence for ESA effects on important neurometabolites. Further studies will help clarify the value of MR spectroscopy in assisting in the evaluation and treatment of children born prematurely who are treated with ESAs.

228
HISTONE MODIFICATIONS IN CORTICAL WHITE MATTER AT 3D OF VENTILATION DO NOT PERSIST IN FORMER PRETERM LAMBS
Hlavicka A, Rinehart K 2, Dong L 1, Wang Z 1, Dahl MJ 1, Null D 1, Yoder B 1, DiGeronimo R 3, Lane R 1, Albertine K 1, 4, University of Utah, Salt Lake City, UT and 2Lawrence University, Appleton, WI.

Purpose of Study: White matter injury in the cerebrum, partially characterized by loss of glia, frequently accompanies mechanical ventilation (MV) of preterm infants. A potential mechanism is epigenetic regulation of gene expression, which alters gene transcription through modifications of histone tags (acytela- tion and methylation of histone, such as H3). Our recent studies of preterm lambs show that MV for 3d leads to diffuse white matter injury that has hypacyetylated and hypomethylated histones relative to non-invasive high-frequency nasal ventilation (HFNV) for 3d. Whether the histone hypoacetylation and hypomethylation persist in white matter of former preterm lambs is not known. We hypothesized that histone modifications in white matter that occur at 3d of MV will persist later in life in former preterm lambs.

Methods Used: Preterm lambs (~128d gestation; term~150d), treated with antenatal steroids and postnatal surfactant and caffeine citrate, were managed by MV for 3d, weaned to non-invasive HFNV for 3d, and subsequently weaned from ventilation support. The former preterm lambs were recovered for up to 6 mo (n=4/group). Brain white matter in the temporal lobe was isolated and analyzed by immunoblot for acetylated histone tags. Weaning reference lambs were born at term and lived for 5 mo (matched for postnatal age after term gestation).

Summary of Results: Immunoblot relative protein abundance for the following histone modifications were the same between former preterm lambs and weaning reference lambs: histone 3 lysine 9 acetylated (H3K9ac), H3K18ac, H3K4me2, H3K9me3, H3K27me3, and H3K36me3.

Conclusions: Our results suggest that histone modifications that occur during 3d of MV are not persistently altered in the brain of former preterm lambs at 6 mo of age (~6 yr of human age). We speculate that the absence of persistence may reflect epigenetic adjustments (lability) after weaning from ventilation support. (HL110002, HL062875, LU-R1)

229
MECHANICAL VENTILATION INCREASES EXPRESSION OF INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN 5 IN RENAL CORTEX OF PRETERM LAMBS
Staub E, Dong L, Blair A, Dahl MJ, Albertine K. University of Utah, Salt Lake City, UT.

Purpose of Study: Preterm birth occurs at a time of ongoing nephrogenesis. Mechanical ventilation (MV) leads to shorter, more dilated glomerular capillary loops compared to gestational controls. Insulin-like growth factor binding protein 5 (IGF-BP5) has distinct spatio-temporal expression in developing glomerular mesangium and is a candidate protein for glomerular angiogenesis. We hypothesized that renal IGF-BP5 protein expression is altered by ventilation after preterm birth.

Methods Used: Preterm lambs were delivered at ~128d gestation (~28wk human gestation), intubated, given surfactant and caffeine citrate. They were managed by MV or high frequency nasal ventilation (HFNV) for 3d. Longterm weaned lambs were weaned from ventilation and lived for 3 or 6mo (~2 or ~6yr in humans). Age-matched lambs were references (n=4/group). Renal cortex was analyzed by immunoblot for IGF-BP5.

Summary of Results: IGF-BP5 protein abundance was significantly greater in the renal cortex of ventilated preterm lambs compared to fetal reference lambs, with MV significantly increased compared to HFNV lambs (Fig 1). IGF-BP5 protein remained higher in former preterm lambs at 3 and 6 mo postnatal age.

Conclusions: Our results indicate that IGF-BP5 protein expression is increased in the renal cortex of ventilated preterm lambs with the greatest increase in preterm lambs supported by MV. The increase persists for at least 3 mo after preterm birth. Upregulation of IGF-BP5 is associated with inhibited renal growth. Therefore, our findings provide new insight into the pathogenesis of renal development in ventilated preterm neonates. (HL110002, HL062875; Bangert Trust, Switzerland)
VENTILATION DECREASES CAPILLARY SURFACE DENSITY IN RENAL OUTER CORTEX OF PRETERM LAMBS


Purpose of Study: At the time of preterm birth, kidneys are developmentally immature and glomerular vasculization is ongoing. We hypothesized that ventilation after preterm birth reduces glomerular capillary formation. We compared surface density of glomerular capillaries (SVgc) in unventilated fetal and term lambs (for ontogeny), and 2 groups of preterm lambs: mechanical ventilation (MV) vs non-invasive high-frequency nasal ventilation (HFNV).

Methods Used: Reference lambs were delivered and killed at 128, 130, 133, 136 + 141d of gestation (term ~ 150d). Term lambs were either killed 1d after spontaneous delivery or lived for 3 or 10wk. Preterm lambs were delivered at 130d (~ 29wk human) gestation, intubated and given surfactant. Preterm lambs were ventilated by MV or HFNV for 3d. Kidney sections were immunostained with endothelial surface marker CD31. Stereological techniques were used to calculate SVgc.

Summary of Results: SVgc was constant from 128d of gestation to term. Within 3wk after birth at term, SVgc was significantly greater in the inner and the outer cortex. MV and HFNV preterm lambs had the same SVgc as in the inner cortex of 133d fetal reference lambs. In contrast, the outer cortex had significantly lower SVgc for the MV group compared to fetal reference lambs, but not for HFNV group. (Fig 1).

Conclusions: Our results show that MV after preterm birth is associated with lower SVgc in the outer, nephrogenic renal cortex compared to HFNV. As SVgc represents filtration surface area, our findings suggest that MV is associated with lower glomerular filtration capacity, which could lead to poor renal function later in life. (HL110002, HL062875, Bangerter-Trust, Switzerland).

PHENOTYPIC DIVERSITY IN PATIENTS DIAGNOSED WITH VACTERL ASSOCIATION

Husain M1, Wencel M2, Kimonis V2. UC Irvine, School of Medicine, Irvine, CA and 1UC Irvine, Irvine, CA.

Purpose of Study: The combination of vertebral, anal, cardiac, tracheoesophageal, renal and limb anomalies termed VACTERL association has been used as a clinical descriptor and a diagnosis of exclusion for a specific group of phenotypic manifestations observed to co-occur non-randomly and more frequently than expected by chance. Because VACTERL is clinically heterogeneous with an elusive etiology, we investigated the frequency and variety of these anomalies, other co-occurring manifestations and underlying causes of defects in embryogenesis or genetic mutations that elucidate VACTERL’s etiology.

Methods Used: Data from the UC Irvine Medical Center, Children’s Hospital of Orange County and Miller Children’s Hospital Long Beach was collected through an IRB-approved protocol. Medical records of patients with a final diagnosis of VACTERL were evaluated retrospectively.

Summary of Results: In 35 patients, the most common anomaly was vertebral - reported in 29 (82.9%) patients. 27 (77.1%) had cardiac, 25 (71.4%) tracheoesophageal, 22 (62.9%) renal, 20 (57.1%) anal and 19 (54.3%) had limb anomalies. 13 (37.1%) had 3 features, 12 (34.3%) had 4, 5 (14.3%) had 5, and 5 (14.3%) had 6 features of VACTERL. 14 (40.0%) also had urogenital anomalies. The most common vertebral anomalies were rib anomaly and scoliosis.

Rare 1q41 Duplication


Purpose of Study: Congenital diaphragmatic hernia (CDH) can be associated with other developmental abnormalities. With more children being followed after CDH repair, we are learning of new, very significant co-morbidities that can affect management.

Methods Used: We present an unusual clinical case of CDH and review morphogenesis, molecular genetic findings, and the potential importance of molecular diagnosis to complications.

Summary of Results: We present a term female infant born to a 38 year old mother. Her exam showed multiple dysmorphic features. Newborn abdominal ultrason showed Morgagni-type CDH containing a portion of the left hepatic lobe. Echocardiography revealed PFO and PDA. The baby underwent repair of diaphragmatic hernia and was found to have absent pericardium. Audiology revealed bilateral sensorineural hearing loss. Although these findings are not uncommon in CDH, there were several unusual findings.

The gallbladder was unexpectedly absent. Ophthalmologic exam revealed bilateral congenital lamellar cataracts. Cataract surgery was complicated by aphakic glaucoma, and the child underwent 21 ophthalmologic surgeries by 3 years of age. MRI brain showed no malformation.

Conclusions: CDH can be associated with pericardial defects, but the combination of CDH with an expanded set of anomalies (gallbladder agenesis and congenital cataracts) is unusual. Severe ophthalmologic complications occurred in this case, and array CGH showed a rare 2.55 Mb duplication at 1q41 region. Precise genes involved in this unique phenotype are unknown, but further studies could confirm whether the variant is useful for anticipating complications.
of anal it was imperforate anus, of cardiac if was VSD, of tracheo-esophageal it was TE fistula, of renal it was hydronephrosis/pelviectasis and of limb it was thumb anomalies. When VACTERL was suspected, 23 (65.7%) received genetic testing. Of those, 18 (78.3%) had chromosomal/karyotyping testing - all normal, 11 (47.8%) had microarray testing - 1 with an abnormal result and 5 (21.7%) had a chromosome DEB assay to rule out Fanconi's anemia - all normal.

**Conclusions:** VACTERL is more complicated than previously thought. Although we found no evidence of teratogenic exposure of the mother during pregnancy or other contributing factors, our findings of one microarray showing a 498kb interstitial deletion of chromosome 16p11.2 is promising and warrants further investigation because malformations associated with VACTERL are observed in up to 10% of 1st degree relatives of VACTERL patients. We hope that our findings enlarge upon the current understanding of VACTERL and guide research aimed at exploring its etiologies.

---

**235**

**RARE AND NOVEL FEATURES OF 49,XXXXY SYNDROME**

Wong L, Bird LM, Rady Children's Hospital of San Diego, University of California, San Diego, CA.

**Case Report:** 49,XXXXY is a rare sex chromosome aneuploidy with characteristic dysmorphisms, endocrine, neurologic, cardiac, and skeletal abnormalities. We present the first case of limbus vertebrae, posterior vertebral fusion defects, middle ear anomalies, and sensorineural hearing loss, none of which have been previously reported. This is the second report of hydrocephalus and syringomyelia in a patient but first of near holocord syrinx.

The patient is a 15-year-old boy with 49,XXXXY diagnosed at birth with characteristic facial features, radioulnar synostosis, clinodactyly, and shallow scrotum. He had a 3 week NICU stay for poor feeding and patent ductus arteriosus ligation. Left sensorineural hearing loss began at age 11 years with progression to bilateral hearing loss. A temporal bone CT showed small epitympanum and middle ear anomalies. MRI of the brain and spine showed an abnormality from the cervicomedullary junction to L2, thoracic and lumbar vertebrae, and posterior fusion defects of C1, C7, and T1. The patient underwent surgical decompression and post-operatively made a full recovery and is doing well.

Syringomyelia in 49,XXXXY may be subtle and overlooked so their incidence is likely under-recognized and under-reported. Limbus vertebrae form by intervertebral disc herniation through weak points between the ring apophysis and vertebral body. Posterior vertebral fusion defects occur in chondral and osseous abnormalities of the posterior neural arch. Both may be congenital or traumatic however the lack of trauma and multilevel involvement make a congenital process more likely. They may not be evident on radiographs, particularly posterior limbus vertebrae, which can cause spinal cord compression. A high index of suspicion for intracranial and spinal cord lesions should be maintained and sensitive imaging modalities such as CT and MRI considered when new neurologic symptoms arise in patients with 49,XXXXY.
aspects of patient’s hospital experiences and were given to all parents at discharge of their children. The grading was from Outstanding to Unsatisfactory levels. Patients were told that their response was voluntary and that there would be no identifiers and that this was only for quality improvement purposes. The time period of survey is from December 2012 to October 2013.

Summary of Results: Starting December 2012 thru March 2013, 66 parents participated in the survey. Out of 66 parents, 40 parents rated their experience as outstanding in all areas. 15 patients rated their experience as satisfactory to outstanding. 11 patients rated their experience in need of improvement or unsatisfactory in one or more areas. There were some areas identified to be unsatisfactory or needing improvement. The factors that were most consistent in getting a grade of unsatisfactory or in need of improvement were overall cheerfulness of hospital, staff’s response to concerns and complaints, attention paid to personal and special needs and pediatric staff’s efforts to include you in decisions about treatment.

Conclusions: Overall rating by patients of their experiences in critical areas of service at Children’s Hospital of Nevada was satisfactory to outstanding. Important areas were identified in need of improvement. Once more surveys are completed, plan for improvement in the areas identified will result in greater patient satisfaction at the Children’s Hospital of Nevada.

IMPACT OF DEFERRED CT IMAGING ON INTOXICATED PATIENTS PRESENTING WITH ALTERED MENTAL STATUS

Granata RT, Vilke GM. University of California, San Diego, La Jolla, CA.

Purpose of Study: Alcohol intoxication can confound the presentation of Traumatic Brain Injury (TBI), which can create the diagnostic dilemma of whether head computed tomography (CT) imaging should be done on intoxicated patient presenting with altered mental status. These cases traditionally have been taken in a case by case mode, with more conservative providers often ordering CT imaging on most drunk patients, while other providers will take a monitor and reassess approach confirming improving mental status over time with metabolism of alcohol. If a patient is allowed to metabolize but not neurologically “clear,” then the patient will then receive head CT imaging. This diagnostic presentation creates the need to balance optimal early detection of intracranial pathology with reasonable utilization of resources and the inability to scan every intoxicated patient presenting on a Friday night. The specific objective of this study is to assess whether there is a higher incidence of neurosurgical intervention in altered EtOH patients that receive delayed CT scans after being allowed to metabolize, as compared to altered EtOH patients receiving immediate head CT scans in the emergency department.

Methods Used: This is a structured retrospective chart review of all EtOH visits to a university ED between 2007 and 2012. Primary outcomes were whether patients received a head CT scan, any positive findings CT imaging, and whether patients required a neurosurgical intervention based on those CT findings, and were considered in each record. Patients were sorted into groups based on when the CT scan was ordered during the ED visit (within the first 60 minutes, or after 180 minutes) as well as the findings. Appropriate statistical analysis will be performed on these groups to determine the frequency of delayed findings that require operative management and if the incidence of neurosurgical intervention is significantly different between the two groups. Specifically, we will address the concern that delaying the CT scan has negative ramifications for the patient based on the aforementioned endpoint.

Summary of Results: Data are in review and will be available by the time of presentation.

Conclusions: Data are in review and will be available by the time of presentation.

PROMOTING SHARED DECISION-MAKING IN PATIENTS WITH MILD HEAD INJURY

Harris DM1,2, Kanzarla HK1, Hoffman JR1, 1David Geffen School of Medicine at UCLA, Los Angeles, CA;2UCLA, Los Angeles, CA. 3UCLA, Los Angeles, CA.

Purpose of Study: The purpose of this multi-year study is to a) develop a decision aid for patients with a GCS score of 15 following MHI, and b) evaluate the impact of the decision aid on imaging utilization and patient outcomes.

Methods Used: We will solicit input from create experts in EM and head injury to develop a decision aid that can inform appropriate patients about diagnostic and treatment options. We will then use qualitative methods to query both clinicians and patients, in order to improve the instrument, which will then be pilot tested in the UCLA ED. Ultimately, we will evaluate the tool’s performance in terms of patient knowledge and satisfaction, as well as its impact on imaging utilization rates and clinical outcomes.

ASSESSING CROSS-CULTURAL EQUIVALENCE OF A DECISION AID FOR SPANISH-SPEAKING MEN WITH PROSTATE CANCER: A SYSTEMATIC TRANSLATION PROCESS

Hubbard TR, Kaplan AL, Saeedco JD, Saigal, MPH, MD C. David Geffen School of Medicine, Los Angeles, CA.

Purpose of Study: In preference-sensitive conditions, such as prostate cancer, interactive decision aids have been shown to improve patient satisfaction and patient engagement. In order to effectively improve the process of shared decision-making in practice, decision aids need to be culturally and linguistically equivalent. Little is known regarding equivalence in decision aids for Spanish-speaking men with prostate cancer. Deliberate forward and back translation will ensure that the meaning and readability of the decision aid has not been affected.

Methods Used: To implement a prostate cancer decision aid in Spanish-speaking men from low socioeconomic status, we used a modified Brislin model to ensure cross-cultural equivalence. We employed the Comparability/Interpretablity Rating Scale between the original source and back translation to validate translation accuracy.

Summary of Results: While subtle linguistic discrepancies were identified, these were easily reconciled upon expert review. The Spanish-to-English translation interpretability score “Good to Excellent” confirming that the modified Brislin model was effective.

Conclusions: Using a modified Brislin approach, we successfully translated a prostate cancer decision aid into Spanish while maintaining linguistic equivalence. Pilot testing cross-cultural equivalence of the decision aid in this population of low socioeconomic status men with prostate cancer is needed to validate efficacy.

A COMPARISON OF VARIOUS CONTEMPORARY METHODS TO PREVENT A WET CAST

Nguyen S1,2, Medowell M2, Schlechter P1, 1College of Osteopathic Medicine of the Pacific, Pomona, CA and 2Western University of Health Sciences, Fullerton, CA.

Purpose of Study: To compare the various contemporary methods of preventing a wet cast in effectiveness, costs, and ease of use.

Methods Used: Using a synthetic a leg mode, a short leg cast was applied and six different methods were tested. Glad® Press and Seal, plastic bag with rubber band, plastic bag with duct tape, double plastic bag with duct tape, CVS® Reusable Cast Protector and Dry Corp® Dry Pro Cast Cover. Casts were submerged in water for two minutes and weighed. Each group had 10 individual trials. Effectiveness was measured by calculating amount of water absorption using cast weights before and after submersion. Comparison data, cost analysis and ease of application were evaluated.

Summary of Results: See table.

Conclusions: Our findings conclude that the six methods tested are effective in preventing the majority of water saturation. Although abstaining from contact with water is the most prudent approach, if a cast cover is to be used, we found that double plastic bags with duct tape or the CVS cast cover are the preferred contemporary methods to prevent a wet cast.
TYMPANIC TEMPERATURE AGREEMENT WITH VISCERAL TEMPERATURE BEFORE, DURING AND AFTER MAXIMAL BRUCE PROTOCOL TREADMILL EXERCISE

Raymond LW1,2, Willoughby JD3.1Univ of North Carolina at Chapel Hill, Charlotte, NC;2Carolinas HealthCare System, Charlotte, NC and 3Carolinas HealthCare System, Charlotte, NC.

Purpose of Study: Purpose of Study: Tympanic temperature (TT) has been widely studied and applied in pediatric practice but less is known of its use in exercising adults.

Methods Used: Methods Used: 38 healthy men and women (29 male, age 34 +/- 9SD, BMI 25.3 +/- 3.7) ingested disposable thermistors (CorTemp HT150002) which transmitted visceral temperature (VT) before, during and after maximal Bruce protocol treadmill exercise (BPTE). An infrared thermistor bolometer (Omron MC-505) was used to measure TT. Thermal discomfort was gauged by the Young Index (YI, 0-8, maximal heat discomfort = 8).

Summary of Results: BPTE duration was 13.9 +/- 3.1 minutes and YI was 6.2 +/- 1.0. TT rose by 1.6oF to 99.6oF and VT rose by 1.3oF to 100.1oF. Overall agreement between TT and VT was expressed by Bland plotting showed close agreement (VT - TT = 0.3 +/- 1.4oF) with only 1.3oF being one outlier. Pre-exercise TT was 0.8oF below VT, but exceeded VT by 1.3oF to 100.1oF. Pre-exercise TT was 0.8oF below VT, but exceeded VT by 1.3oF to 100.1oF.

Conclusions: Conclusions: TT is closely associated with VT in healthy adults before, during and after maximal Bruce protocol treadmill exercise. Anatomic differences in bodily heat transfer may account for TT changes that precede exercise-related changes in VT. A larger series of observations might further elucidate this latter thermal transient.
allows for relative proton stopping power (RSP) to determined directly. The purpose of this work was to create a digital head phantom that will allow the simulation of the Phase II pCT scanner.

Methods Used: A pediatric head phantom containing tissue equivalent material was scanned in a 64-detector-row CT scanner. Eight helical scans were performed with a 512x512 pixel matrix size and a display field of view of 9.6 cm, which corresponded to a pixel size of 0.1875mm x 0.1875mm and a slice thickness of 1.25 mm. The scans were combined into a single DICOM study using MATLAB. The images were analyzed in ImageJ using a series of thresholding macros to identify boundaries between tissues. These images were then overlapped in Microsoft Paint to reconstruct the original DICOM without noise.

Summary of Results: Appropriate thresholding of regions to differentiate tissue and knowledge of the anatomy of the skull base were instrumental in creating this phantom. Edge detection algorithms, thresholding, and hole- and gap-filling algorithms could be used to automate the process in the future. The phantom will now be used in simulating the performance of the Phase II pCT scanner.

Conclusions: A noise-less digital phantom was successfully created that will be useful in evaluating the expected performance of the Phase II pCT scanner at Loma Linda University.

FIGURE 1. Original CT image of the pediatric phantom and corresponding noise-less digital phantom slice.

246

DIAGNOSTIC IMAGING VIEWERS USED WHILE ON-CALL: A NATIONAL SURVEY OF CHIEF RESIDENTS AND PROGRAM DIRECTORS IN RADIOLOGY

Tesoriero JA1, Hasso A2. 1University of California, Irvine School of Medicine, Irvine, CA and 2University of California, Irvine Medical Center, Orange, CA.

Purpose of Study: To determine the prevalence of different diagnostic image viewing platforms used by radiologists while on-call. Also, to assess preferences and opinions amongst radiology program directors and chief residents with regards to the use of these image viewing platforms.

Methods Used: An online survey was sent electronically to radiology residency program directors and chief residents via the Association of Program Directors in Radiology and the American Alliance of Academic Chief Residents in Radiology, respectively.

Summary of Results: 42 radiology program directors and 25 chief residents completed the survey, yielding response rates of 24.9% and 8.5% respectively. From the survey results 10 different Picture Archiving Communications Systems (PACS) were identified; GE (25%), Philips (16%), and Agfa Impax (16%) were the most prevalent. Interestingly, only 5% of all respondents report using a secondary “Digital Imaging and Communications in Medicine” (DICOM) viewer different from PACS for on-call studies. Additionally, 41% of respondents report their institution’s PACS is not integrated into their Electronic Medical Records (EMR). In general, perceptions of PACS functionality were neutral to weakly positive. The majority of respondents strongly agreed that it is important to have a single integrated PACS for viewing on-call studies, and agreed that EMR should be integrated into PACS.

Conclusions: The vast majority of respondents (95%) use their institution’s PACS while on-call. The 5% that use a secondary DICOM viewer instead do so because of a lack of availability or access to their institution’s PACS for on-call studies. The results show there is still a wide variety of PACS platforms used by different institutions. However, GE, Philips, and Agfa Impax represent over 50% of all platforms used by survey respondents. Most radiologists surveyed have neutral to slightly positive perceptions about the functionality and ease of use of their PACS, however 10% of respondents believe their PACS is difficult to use and increases their radiologist report turnaround time. Furthermore, while radiologists agree that PACS should be integrated with EMR, only 53% of respondents report having this arrangement.
CHAPERONED FUNCTION OF HEAT SHOCK PROTEIN 72 IN GASTROENTEROLOGICAL CANCERS

Wang X1, Wang Q1, Lin H1, Xu B1, Fang J1, Zhang K1, Zhang J1, Yang Y2.

1Shaanxi University of Chinese Medicine, Xi’an, China; 2Emorpsia State University, Emporos, KS.

**Purpose of Study:** Heat shock protein 72 (HSP72) is highly expressed in cancer tissues. Recent studies indicate the possible roles of HSP72 in the development and progression of gastrointestinal carcinomas but detailed mechanisms are still ambiguous. The aim of the study is to investigate the chaperoned function of HSP72 in human gastrointestinal cancers.

**Methods Used:** The specimens were fixed in 10% buffered formalin and embedded in paraffin. Serial sections were cut and placed on poly-lysine coated glass slides. The immunofluorescence staining, confocal microscope analysis, immunoprecipitation, and western blot.

**Summary of Results:** Immunohistochemistry demonstrated that HSP72 expression was mainly stained in cytoplasm of cancer cells. HSP72 expressed higher in low differentiation of gastrointestinal carcinomas than that in tissues adjacent to cancers (P < 0.05). HSP72 positive rates in lymph node metastasis and remote metastasis groups were 100%. There were significant differences of HSP72 expression between metastasis groups and non-metastasis groups (P < 0.05). Our research showed that there only appeared a Mr 42000 clear CD44v6 fragment band under precipitated with anti-HSP72 antibody, indicating that over-expressed HSP72 is likely to assist in stabilizing and associating with CD44v6 precursor fragment in colonic cancer cell cytoplasm, integrating and transporting its complex to cell membrane and releasing it to the serum, which indirectly prompts and protects CD44v6 function. Further research demonstrated that HSP72 could co-localize and form a complex with HBx in cytoplasm of liver cancer cells.

**Conclusions:** HSP72 expression were significantly associated with the presence of tumor infiltration, lymph node and remote metastasis. The association of HSP72 and CD44v6 probably has some relationship with infiltration, metastasis and poor prognosis of human colonic cancers.

**Acknowledgments:** The Project of Shaanxi Provincial Education Department (No. 2007J233, 2010JK484), the Key Project of Ministry of Education of China (No.205002), and the National Natural Science Foundation of China (No.81172135/H1611, 81310108008).

---

EXPERIMENTAL STUDY ON EFFECT OF YI AIKANG CAPSULE IN THE TREATMENT OF FRIEND MURINE LEUKEMIA VIRUS IN MICE

Wei Z1, Xu L2, Xue Z1, Zhang J1, 1Wuyang University of Chinese Medicine, Nanjing. China; 2The First Affiliated Hospital of Henan University of Traditional Chinese Medicine, Zhengzhou, China and 3Henan Academy of Traditional Chinese Medicine, Zhengzhou, China.

**Purpose of Study:** Yi Aikang capsule is a kind of widely used in Chinese medicine treatment for AIDS/HIV in China. Through the establishment of immunodeficiency animal model in BALB/c mice caused by Friend murine leukemia virus (FLV), to study the Yi Aikang capsule in improving immune function on spleen index, thymus index and T cell subset.

**Methods Used:** FLV strain passaged two times, were randomly divided into FLV model group, ATZ control group, Tangcao tablets control group, Yi Aikang capsule large dose group, middle dose group, Yi Aikang capsule low dose group. Model group irrigated with saline, ATZ group according to 200mg/kg, i.g. continuous 21d. Then determine the spleen and thymus index. We take the eyeball blood with EDTA anticoagulant about 1h after the last administration. Flow cytometry was used to detect T cell subsets, including CD4+T lymphocytes, CD8+T lymphocytes, and CD4/CD8 ratio.

**Summary of Results:** Compared with the model group, Yi Aikang capsule had better inhibitory effects on it, but the effect is slightly inferior to the ATZ group. Yaikang group and Tangcao tablets group can also increase the weight of thymus, no difference between the two groups. Compared with model control group, Yi Aikang capsule has elevated the role of CD4+T cells (P < 0.05), each group had no difference between Yi Aikang increased CD4 +T lymphocyte function and Tangcao tablets group (P > 0.05).

**Conclusions:** Yi Aikang capsule can inhibit FLV induced immunodeficient mice and decreased splenomegaly, spleen index, protects the spleen, Yi Aikang capsule can increase FLV induced immunodeficient mice thymus weight and thymus index. Yi Aikang capsule can increase FLV immunodeficiency mouse CD4+T and CD4/CD8 ratio, enhanced FLV immunity in mice.
Conclusions: The CHL could enhance the MRT (0-∞), reduce the clearance and increase the system exposure of DAS. Furthermore, the cumulation of DAS in lung also increased, which illustrated CHL could enhance DAS targeted in lung.

EXPERIMENTAL STUDY ON CHEMOTHERAPY MULTIDRUG RESISTANCE MECHANISM OF OSTEOSARCOMA BY PROTEOMICS METHODS IN VITRO
Zhang L1, Li L1, Zhou Y2. 1Jilin province people's hospital, Changchun, China and 2Third Military Medical University, Chongqing, China.

Purpose of Study: In the past 10 years, many scholars tried to reveal the nature of MDR and its mechanism. However, drug resistance of tumor cells is still a major obstacle affecting its efficacy.

Methods Used: Specimens were obtained from 30 cases of patients with osteosarcoma of Jilin Provincial People's Hospital, including 19 males and 11 females and mean age was 18.5 years old. Chemotherapy drugs including cisplatin, doxorubicin, paclitaxel, bleomycin, vincristine and methotrexate were provided by Jilin Provincial People's Hospital. (1) Find resistant and sensitive osteosarcoma tissue samples. (2) Observing differentially expressed proteins in resistant and sensitive osteosarcoma tissue samples. The sequences of differentially expressed proteins were obtained to be identified comparing with protein databases by means of the analysis of mass spectrometry technology. (3) Confirm in vitro with different proteins in drug-sensitive differential expression in osteosarcoma tissue samples by experiments. Two three-representative-tissues on cisplatin-resistant and sensitive osteosarcoma were selected to test which is the differentially expressed one among 5 proteins by Western Blot technique in vitro.

Summary of Results: (1) The ratio of moderate and moderately above sensitivity of cisplatin and doxorubicin group was higher than that of other groups with statistically difference. (2)Five protein molecules were obtained. They were respectively: ENO1 (enolase 1), HMGBl(high mobility group box 1), GAPDH (glyceraldehyde-3-phosphate dehydrogenase), ALDOA (aldolase A, fructose-bisphosphate), PGK1(phosphoglycerate kinase 1). (3) Significant difference was found in ALDOA and PGK1 kinases expression of the two groups.

Conclusions: (1) Osteosarcoma has different sensitivity to various chemotherapy drugs. Cisplatin is an appropriate drug to find out differences in the protein research. (2)The exact results of two-dimensional electrophoresis and mass spectrometry analysis showed that there are differentially expressed proteins in tissues of cisplatin-resistant and sensitive osteosarcoma. (3)Expression of ALDOA and PGK1 were different in cisplatin treat human osteosarcoma with statistical significance. The two proteins may be the right marker in cisplatin chems in treating osteosarcoma.

Tools for Developing Intensity Modulated Proton Therapy
Choe M1, Selchau A1, Gonzales D2, Giacometti V3, Schulte R1. 1Loma Linda University, Loma Linda, CA; 2Southern Adventist University, Chattanooga, TN and 3University of Wallongong, New South Wales, NSW, Australia.

Purpose of Study: Purpose: Intensity-modulated proton therapy (IMPT) is an evolving, but far from fully-developed radiation technique for highly conformal dose delivery to tumors that are situated in close proximity to sensitive and critical organs at risk (OARs). IMPT requires that multiple proton Bragg peaks are directed at a target from many directions. The purpose of this work was to develop tools that will be used to solve the IMPRT dosage problem for a large number of beams.

Methods Used: Methods used: A pediatric head phantom was used to create partial scans of the head with a 64 detector-row CT scanner. The slices were stitched together to create a single CT DICOM study, which was segmented into different anatomical regions. Using Imaged and Microsoft Paint, the regions in each slice were defined, and a grayscale-value according to tissue type was assigned. Finally, by employing the E-anatomy application (www.imaios.com), a pituitary tumor, the chiasm, brainstem, optic nerves and hypothalamus were created in the digital phantom.

Summary of Results: Summary of Results: The digital phantom was successfully constructed. Each voxel was given one of 7 unique material compositions, which allows simulation of proton pencil beam delivery. We created a realistic pituitary tumor surrounded by OARs (Fig. 1). With these tools, we can now perform Monte Carlo simulation studies of proton pencil beams directed at a grid of beam aiming points within the target and apply novel mathematical algorithms to solve the IMPRT problem in determining the dosage to be delivered by the beams.

Conclusions: Conclusion: In this research, we created tools that will enable simulation and testing of novel methods for delivering IMPRT at Loma Linda University.
indicators and have well-established treatment guidelines. There is a general perception that primary LMS of bone has a poorer prognosis compared to these with little evidence supporting this belief. Further evidence regarding differences in outcome would be of benefit in understanding the disease and counseling patients with regards to prognosis.

Methods Used: A retrospective review of patients over the age of 18 treated for a primary sarcoma of bone at Seattle Cancer Care Alliance and University of Washington Medical Centers between 2001 and 2012 was conducted. For inclusion, all patients had localized disease at diagnosis, treatment with chemotherapy and surgery, and biopsy proven diagnosis of primary LMS of bone or other bone sarcoma treated with chemotherapy. Those with metastases at presentation, non-primary LMS of bone, and treatment not involving both chemotherapy and surgery were excluded. Disease specific outcomes, overall survival, and local recurrence were estimated and compared.

Summary of Results: A total of 36 patients met inclusion criteria. Patients with LMS of bone (n=6) had a median recent follow-up of 14 months. At this time, all LMS patients were alive and 50% were disease-free. The 3 patients with disease had both local and systemic recurrence. Patients with other primary bone sarcomas (n=30) had a recent median follow-up of 31 months, with 70% being free of disease. Following treatment 9 (30%) had systemic recurrences, 6 of which also had local recurrence. Two had died of disease. One patient's disease resolved with continued therapy. At most recent follow-up, 22 (73%) patients with non-LMS bone sarcoma were alive without disease.

Conclusions: A greater percentage of patients with primary LMS of bone had tumor recurrences in a shorter time period, suggesting a poorer prognosis. This evidence supports early diagnosis and aggressive treatment of these rare bone sarcomas.

254

THE VALUE OF PATHOLOGY REVIEW IN ADVANCED COMMON CANCERS

Oh D1, Goulart B2,3,1, Martino I2,3,1. 1University of Washington School of Medicine, Seattle, WA; 2Seattle Cancer Care Alliance, Seattle, WA and 3Fred Hutchinson Cancer Research Center, Seattle, WA.

Purpose of Study: Review of pathology (ROP) is a standard practice in many academic medical centers, and consists of a formal review of tumor biopsies and pathology reports that originate from outside institutions. The value of ROP in early stage cancers is to avoid unnecessary surgery in about 3% of cases in which a discordance in histologic diagnosis prompts changes in treatment. However, no studies have evaluated the clinical and economic value of ROP in advanced cancers, a sizable population in oncology centers. This is important because forgoing ROP may improve the efficiency of care while reducing healthcare costs. Thus, we sought to estimate the clinical value and medical costs of ROP for prevalent stage IV cancers at a large academic oncology practice.

Methods Used: This retrospective study included 263 patients with stage IV cancer (77 colorectal, 135 lung, 51 prostate) seen at the Seattle Cancer Care Alliance (SCCA) between July 2010 and December 2012, whose medical charts contained outside pathology reports and a ROP. We compared the outside diagnostic pathology to the ROP to determine the prevalence of major discordances (MD), which would have treatment implications, and minor discordances (mMD), which would not alter treatment. We then determined the Medicare reimbursement fee for ROP to estimate the cost to payers and the aggregate savings from forgoing this procedure.

Summary of Results: 2 out of 263 cases had MDs (0.8%, 95% confidence interval [CI] 0.00% to 2.7%), while 38 cases had mMDs (14.4%, 95% CI 10.4% to 19.3%). The two MDs were from fine-needle aspirates or cytology specimens of lung cancer. We estimated the savings from forgoing ROP as $5,260 in the 263 patients on this study and $838,280 in annual national costs for patients with advanced common cancers referred to teaching hospitals.

Conclusions: mMDs infrequently occurred in common advanced cancers, suggesting that the value of this had little in the patient group, which might not justify its costs. Future studies employing larger sample sizes should explore the value of ROP for lung cancer fine-needle aspirates and/or cytology specimens.

255

GENERALIZED PSORIASIS GREATLY IMPROVED WITH ONLY TWO EXPOSURES TO EXCIMER UVB LASER THERAPY: A CASE REPORT


Case Report: Background: Psoriasis affects up to 3% of the U.S. population and has been documented to cause severe, negative physical and psychosocial impact on patients, which is most severe in those with generalized psoriasis. While a variety of treatments for moderate-to-severe generalized psoriasis exist, they involve systemic medications such as biologics, methotrexate and cyclosporine that have the potential for serious side effects. One established way to treat generalized psoriasis without potential serious internal side effects is UVB phototherapy. However, traditional UVB phototherapy typically requires three exposures per week for two to three months to attain great improvement.

Case: The author describes a case in which a generalized psoriasis patient experienced 79% improvement in his Psoriasis Area Severity Index (PASI) score following only two treatments with 308-nm excimer UVB laser using a new and innovative way of determining the optimal dose of light called “the Psoriasis Plaque-Based Sub-Blistering” method. Biopsies taken before and after treatment revealed a dramatic decrease in T cells as well as cells producing TNF-alpha and IL-2, which are cytokines that mediate psoriasis. Conclusion: This is the first ever case of successfully treated generalized psoriasis with only two exposures to phototherapy instead of the usual 30 to 40 treatments using traditional UVB phototherapy. If repeatable, this method can make generalized psoriasis treatable conveniently without the risk of internal side effects of systemic agents.
In summary, there is still much to learn about multicentric reticulohistiocytosis and the effective treatment of this condition. We present this case to highlight the success of a TNF inhibitor in combination with methotrexate, Plisulone, and Plaquenil. Our patient responded dramatically to etanercept. Analysis of our case combined with those previously reported in literature indicates that a TNF inhibitor might be a great therapeutic option for patients with this disease.

Case Report:

A 78-year-old with remissive CLL developed diffuse erythematous papules and macules four days after being admitted to our institution for acute pancreatitis. The lesions were nontender and nonpruritic and appeared as blanching erythematous macules and papules (Fig 1) four days after being admitted to our institution. The lesions were negative for Pan-HPV and HSV-1, and focal viral cytopathic changes and multinucleated giant cells consistent with HSV-2. He was started on intravenous acyclovir and the lesions gradually improved.

Disseminated HSV infection is exceedingly rare, but can be fatal in immunocompromised patients even with prompt antiviral therapy. The vast majority of generalized HSV infections reflect reactivation of endogenous latent infection in patients with hematologic malignancies, congenital immunodeficiencies, and in organ and bone marrow recipients. Our patient had a history of CLL, placing him at risk for generalized HSV.

This case demonstrates the importance of a clinician’s awareness of the possibility of generalized HSV infection in patients who are immunocompromised. Prompt accurate diagnosis is crucial in order to avoid mortality outcomes for this aggressive disease.

FIG. 1. Diffuse, blanching erythematous macules and papules with central violaceous coloring.
treatment, we discharged the patient with oral steroids and acyclovir for 7 more days (total of 10 days). A follow up phone call 3 months after discharge demonstrated complete resolution of the disease with no sequelae.

**FIGURE 1.**

---

260

**THE PREVALENCE OF AVIAN INFLUENZA VIRUS IN RAINFOREST BIRDS FROM SOUTHERN CAMEROON**

Hamamoto JT, Njabo KY, Smith TB, David Geffen School of Medicine at UCLA, Los Angeles, CA; Charles R. Drew University of Medicine and Science, Los Angeles, CA and UCLA, Los Angeles, CA.

**Purpose of Study:** The avian influenza virus is an enveloped RNA virus that is highly unpredictable and capable of immense antigenic variability due to the high error rate of the RNA-dependent RNA polymerase enzyme. Therefore, it is important to constantly survey and monitor the spillover and transmission of influenza between humans, domesticated animals, and wild birds. Wild birds serve as the natural reservoir for influenza type A, giving it the potential to cause severe global pandemics. Our objective was to assess the prevalence of influenza type A and B in the Ebo region of Southern Cameroon in wild bird species.

**Methods Used:** Wild birds species were captured using mist nets. Cloacal swab samples were collected and processed at the Centre Pasteur in Yaoundé, Cameroon. To detect the virus real time reverse transcription-polymerase chain reaction was used targeting the matrix gene.

**Summary of Results:** A total of 62 wild birds were sampled but only 10 samples were analyzed due to a shortage of the reverse transcriptase enzyme. All 10 cloacal samples analyzed were negative for the matrix gene, indicating the absence of the influenza type A genome. Analysis for influenza type B was only performed if a positive result for influenza type A was found. Plans are underway to process the remaining samples.

**Conclusions:** Due to the small sample size of this project, no conclusions can be made regarding the prevalence of influenza in the region. However, our project illustrates the difficulties that researchers face when conducting research in developing countries. Continuous sampling and analysis, and improved research capacity will be necessary to monitor the spillover dynamics in Central Africa.

---

261

**ENVIRONMENTAL DETERMINANTS OF BURULI ULCER**

Kaganjo P, Ellis O, UCLA DGSOM, Los Angeles, CA; UCLA, LOS ANGELES, CA and UCLA, LOS ANGELES, CA.

**Purpose of Study:** To determine the environmental vectors of Mycobacterium ulcerans.

**Methods Used:** Environmental samples were collected from several areas within along the Nyong River, close to the villages where BU cases have been documented. Environmental and biological samples were taken along the Nyong river basin in Ndibi, Abong Mbong, Ayos, and common fishing areas in Akonolinga. The samples included samples taken from insects, fish, cow blood, cow dung, domestic dogs, frogs, porcupine, mud, turbid water, and algae. DNA extraction was performed along with RT-PCR using the insertion sequence IS2404, the genomic marker for BU.

**Summary of Results:** All of the samples were negative for M. ulcerans. 

**Conclusions:** It is possible that the samples did not harbor the M. ulcerans bacteria due to seasonal variance and fluctuation (wet versus dry). It can be recommended that continuous and repeat sampling should be done during the wet season to rule out seasonal variation as an inhibitory factor in the evaluation of environmental determinants of M. ulcerans.

---

262

**PREVENTING THE SPREAD OF CHLAMYDIA THROUGH ADOLESCENT EDUCATION IN BUTTE, MONTANA**

McQuinn D. University of Washington SOM, Seattle, WA.

**Purpose of Study:** Chlamydia rates are on the rise across the state of Montana, including Butte-Silver Bow County. According to the 2012 Montana STD End-of-Year Surveillance Report the highest rates of chlamydia infections are seen within the 20-24 year old age group. After talking with the staff at the Butte-Silver Bow Health Department, local physicians and patient encounters at the Community Health Center the great need for community education and awareness surrounding chlamydia prevention and treatment became apparent. The purpose of this project is to increase the awareness of the rising rates of chlamydia, educate the community through direct peer-to-peer discussion, inform the population about the disease, where to seek screening and treatment, and to distribute safe sex packets.

**Methods Used:** 300 safe sex packets and brochures were created and distributed, along with verbal education to numerous people amongst 15 different bars throughout the town of Butte. Studies have proved that face-to-face education and interactive awareness is the best approach. Packets including condoms, lubrication and information cards were distributed. Brochures containing, among other things, a list with directions to the clinics offering STD screening, were handed out as the issue of rising rate of chlamydia was verbally addressed.

**Summary of Results:** Although the results of this project have not been directly assessed, with the strong community input and support from the local Health Department useful supplies and educational materials were produced and distributed among a very responsive group of community members. The active participation and strong enthusiasm of the local bar owners to continue to distribute the packets and brochures was encouraging. The Butte Silver-Bow
Health Department plans to continue this method of education a few times throughout each year. **Conclusions:** Chlamydia is a serious disease with significant long-term health consequences if left untreated. As the disease is often asymptomatic, providing education and awareness to the "at risk" individuals of a community is vital in averting the rising rates of this disease.

263

**PROMOTING PERTUSSIS EDUCATION AND INCREASING VACCINATION RATES IN BUTTE, MONTANA**

Sherris MR. University of Washington, Seattle, WA.

**Purpose of Study:** The city of Butte, Montana has seen thirteen confirmed cases of whooping cough since the beginning of June. The Public Health Department is very concerned that school starting will prompt a more serious outbreak; in fact, the facility administers the DTaP and Tdap vaccines for free to minors and the uninsured. Research demonstrates that one of the primary obstacles for increasing vaccination rates is lack of education about the availability of affordable vaccines. Thus the purposes of this project were to promote awareness of pertussis in the community and to encourage increased vaccination.

**Methods Used:** Interviews were conducted with employees from the public health department to ascertain areas of need in the community. A literature review identified important components of vaccine education, particularly informing the public about free vaccines. A venue was chosen that would allow access to a wide range of community members: the weekly Butte Farmer's Market and the East-west Shrine Game Parade. Working in collaboration with the Health Department and the Community Health Center, an education event was coordinated in which Farmer's Market attendees were given information about pertussis and encouraged to vaccinate for free at the PHD. A poster with information was also displayed and a single page handout was distributed.

**Summary of Results:** Many of the event's 57 participants said that they didn't even know pertussis was present in the community and that they would get vaccinated. Interestingly, many people were already informed about the importance of vaccination, particularly parents of young babies. The number of participants and general effectiveness of the event were reported back to the Health Department, and the educational handout was adopted by the Community Health Center as a tool for patient education.

**Conclusions:** With the rise in pertussis rates in Butte, vaccine education and promotion is essential for curbing a larger outbreak. The community demonstrated interest in advocating for pertussis awareness. While Butte primary care physicians do promote pertussis vaccination, further education will be useful for the community. Broad-based educational opportunities like this one can advocate for increasing vaccine rates and encourage more appreciation for the dangers of a pertussis outbreak.

Family and Child

Concurrent Session

3:30 PM

Friday, January 24, 2014

264

**CAMPAIGN AGAINST TEXTING AND DRIVING**

Bains SS, Rhee P, Pandit V, Judkins D, Joseph B. University of Arizona College of Medicine, Tucson, AZ.

**Purpose of Study:** The primary aim was to identify the incidence of distracted driving (DD) among health care providers. Our secondary aim was to create awareness and prevention strategies against DD. We hypothesized that DD is prevalent among health care providers.

**Methods Used:** We performed a prospective interventional study of hospital staff. The trial involved three phases: Phase 1 was 1 week pre-intervention observation outside employee parking garage. Phase 2 was 1 week intervention phase carried out in hospital cafeteria, banners at garage exit, and survey questionnaire via email. Phase 3 was 1 week post-intervention observation. Observation was carried out at three time intervals: 6:30-8:30am, 4:40-5:30pm, and 6:30-7:30pm. We defined distracted driving as texting or talking on cell phones. Hospital employees were identified with: badges and scrubs, exit through employee exit, and parking pass on the car. Our primary outcome measure was incidence of distracted driving pre and post intervention. Univariate analysis was performed to compare incidence of distracted driving pre and post intervention.

**Summary of Results:** A total of 10,859 observations (Pre: 6,639, Post: 4,220) and 520 survey respondents were collected. The mean age of respondents was 44±27.5 years and 88% were female. 35.5% respondents admitted to texting while driving while 4.5% respondents were involved in an accident due to texting and driving. 77% respondents felt more informed after the survey and 91% respondents supported a state legislation against texting and driving. There was a significant reduction in distracted driving pre and post intervention in each of the time interval of observation. (Figure 1) On sub-analysis, there was a significant reduction in texting and texting while driving post intervention. (Figure 2).

**Conclusions:** DD is prevalent among healthcare professionals. We recorded greater than 50% reduction in the incidence of distracted driving during the post-intervention phase. Implementation of a national education campaign against distracted driving is warranted.

265

**HANDS-ONLY CPR AND AED OPERATION SEMINARS IN ANACONDA, MT**

Ulrich CL. University of Washington School of Medicine, Seattle, WA.

**Purpose of Study:** The purpose of this project was to increase hands-only Cardiopulmonary Resuscitation (CPR) and Automated External Defibrillator (AED) operation competency as well as build a foundation for future CPR/AED training initiatives in the school system. Anaconda is a former copper-smelting town that supported the copper mines of nearby Butte. The smelting plant closed in 1980, challenging the town to find an economic replacement. As this struggle has progressed, the average age of the town has increased. The leading cause of death in town is heart disease. Familiarity with hands-only CPR and AED operation has the potential to significantly increase out-of-hospital cardiac arrest survival rates, as well as survivor quality of life.

**Methods Used:** A hands-only CPR and AED operation seminar was created that included didactic instruction, a technique demonstration, and student practical application using training mannequins and AED trainers. The literature supports hands-only CPR and AED use as an intervention to increase out-of-hospital cardiac arrest survival rates as well as short blocks of instruction as a technique to increase bystander intervention rates and quality of CPR performed. Rotary, as the primary community partner, desires to continue this training initiative with the local high school. The literature supports this intervention as well, and Rotary was given online resources to provide this education to the students.

**Summary of Results:** Five seminar sessions were taught, and 29 members of the community ranging from a 911 dispatcher to teachers to retirees to courthouse personnel received the training. The participants in the training were very enthusiastic, and seemed to gain a great deal of confidence from the training. The overall feedback was very positive.

**Conclusions:** Hands-only CPR and AED training should be part of all high-school curricula. The project was a short-term success, but more importantly, it served to plant a seed for the local Rotary Club. They were receptive and supportive of learning hands-only CPR/AED operation so that they could successfully integrate what they learned into the schools. This project has the potential to be the starting point of a long-term partnership between the Rotary Club of Anaconda and Anaconda High School. If Rotary’s plans come to fruition, this will be the project’s greatest success.
WHO ARE THE PHYSICIANS SERVING SOUTH LOS ANGELES?
Blanding JD1, Dowling PT2, Moreno G2. 1David Geffen School of Medicine at UCLA, Los Angeles, CA and 2University of California Los Angeles, Los Angeles, CA.

Purpose of Study: To describe the distribution and demographics of physicians practicing in South Los Angeles, and to understand any aging trends of the workforce in this community.

Methods Used: Data was obtained from the Medical Board of California to identify the physician with a primary practice location in Service Provider Area (SPA). Physicians were cross-referenced with the American Board of Medical Specialties to determine board certification. Cross-tabulations and bar graphs were used to examine data trends.

Summary of Results: A total of 243 physicians with a primary practice location in South Los Angeles were identified. 32% were female, 18% were family medicine, 13% were internal medicine, 10% were medical subspecialties, and 59% were other specialties (including surgery). 25% of physicians in South Los Angeles were International Medical Graduates. 49% graduated > 30 years ago.

Conclusions: With aging physicians in South Los Angeles and the expected increase in insured patients due to the Affordable Care Act, there is a need to increase the physician workforce in this community to avoid exacerbating known access disparities. As physicians are more likely to practice in areas they self-identify with and/or have had exposure to, greater effort needs to be placed in recruitment of students and in the exposure of medical students to underserved areas.

DAY LABORER UTILIZATION OF HEALTH CARE SERVICES IN LOS ANGELES COUNTY
Nguyen C1, Lugo C2, Janio E2, Puvvula J3, Granados G3. 1David Geffen School of Medicine, Los Angeles, CA; 2UCLA, Los Angeles, CA and 3Harbor-UCLA, Harbor, CA.

Purpose of Study: Day laborers are individuals that seek temporary jobs on a day-to-day basis. Nationwide, there are an estimated 120,000 day laborers, most of who are immigrants and are uninsured. Factors such as immigration status, language barriers, and low wages greatly impact this population's use of health services. Those who are uninsured lack access to primary care providers and may potentially increase their use of various health care services, including the ER. This suggests a significant portion of the health care expenditure is due to the uninsured population. However, other studies have found that the day laborer population uses various health services at an overall diminished rate. Therefore, this study aims to determine the type and frequency of visits to health care services that are utilized by the day laborer population in LA County.

Methods Used: We conducted anonymous, in-person surveys at various day labor sites. After verbal consent, surveys were conducted in either English or Spanish, and queried the type of access and frequency of visits to health care services. Participants were compensated with $5. SPSS software was used for data analysis.

Summary of Results: Health insurance is a major indicator of access to health care services. Undocumented immigrants are more likely to lack health insurance (p<0.008). Those who are uninsured are significantly less likely to have a regular place for preventative (p<0.002) and sick care (p<0.012). County and community clinics were found to be the most utilized source for health services by the day laborer population.

Conclusions: Although being undocumented correlates with lack of routine preventative care, we found that insurance status plays a larger role in explaining reduced rates of health care utilization observed among the day laborer population. The Affordable Care Act (ACA) aims to increase health insurance coverage and puts a greater emphasis on preventative care to reduce health costs. However the ACA does not include undocumented immigrants, despite a majority of them reporting they would participate in such programs if eligible. By including immigrants in the ACA, we can increase access to health care services, improve rates of routine preventative care and decrease avoidable visits to the ER among this population.

END-OF-LIFE EDUCATION THROUGH COMMUNITY OUTREACH IN RED LODGE, MONTANA
Loomis JN. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: The 2012 California HealthCare Foundation Survey found that 82% of respondents said it is important to have end-of-life wishes in writing, but only 23% had done so. In addition, the survey found 80% of respondents expressed a desire to talk with their doctor about end-of-life care, but only 7% had. Feedback from the providers at the community clinic in Red Lodge, Montana revealed a similar demographic. This project was designed as an attempt to increase the number of community members with completed advanced directives.

Methods Used: A literature review confirmed that advanced directives increase many quality measures for both the patient and family during end-of-life care. Four documents were assembled in a handout packet, including two educational resources and two legal advanced directives. An information booth was set up where members of the community could come discuss end-of-life care and collect the packet of information. The event was supported by the Beartooth Billings Clinic, hosted at the Red Lodge Drug Store, and advertised in the Carbon County Newspaper and at the Red Lodge Senior Citizens Center. Additional flyers were posted around the community.

Summary of Results: Personal interactions with community members numbered over 50, and 38 packets of information were distributed. Many members of the community acknowledged that they needed to address their own end-of-life planning but admitted reluctance to filling out the paperwork. Most people that came to the event had misunderstandings about end-of-life planning, and nearly all of the 38 packets distributed also included clarifying conversations with the recipients. The Beartooth Billings Clinic is adopting the packet for use with patients considering end-of-life care.

Conclusions: Patient education about advanced directives is an important responsibility of any rural clinic. As clinic time is often focused on acute illness, community outreach is essential for proper education. For this project, the location of the event was able to capitalize on patients waiting for medication and provided a good environment for discussion. The packet was also well received as it provided the literature for review at the recipient's discretion. The positive response from the community members that came to the event was encouraging and indicates that further outreach would be well received.

EFFECTIVENESS OF THE STROKE HEROES ACT FAST CAMPAIGN IN A COMMUNITY HEALTH FAIR
Canales EM12, Puvvula J3, Granados G3. 1Charles Drew University of Medicine and Science, Los Angeles, CA; 2David Geffen School of Medicine, Los Angeles, CA and 3Harbor-UCLA Department of Family Medicine, Torrance, CA.

Purpose of Study: 795,000 people in the United States have a stroke every year and almost 130,000 die every year due to stroke. The inability of the public to recognize stroke warning signs and to quickly access emergency facilities is one of the barriers to acute stroke therapy and death prevention. The lack of stroke knowledge is greatly seen in minority communities. One way these communities obtain health education is at health fairs. At health fairs most stroke education is provided by handing out pamphlets accompanied by a short verbal explanation. This method can lead us to think that this is the best or only way to educate patients. However previous studies have shown that animated video can be a highly effective educational tool. Therefore, the aim of this study is to evaluate a quick and effective method to educate minority communities at health fairs about stroke.

Methods Used: Adult participants at a local health fair over the age of 18 were randomized to receive an educational pamphlet with verbal explanation or a brief 3-minute video regarding recognition of early stroke signs and appropriate response from The Stroke Heroes Act FAST Campaign.
Participants received a pre-test prior to the educational intervention early in the health fair and a post-test to evaluate retention of the information at the end of the health fair. The interventions were done in either English or Spanish based on participant preference.

Summary of Results: Nearly 3,000 participants attended the health fair of which 98 completed the educational intervention, pre and post-tests. A highly significant increase (p<.001) was observed in the participants ability to list at least 3 warning signs of stroke between pre-test and post-test. No significant difference was seen in the appropriate time to alert emergency services between pre-test and post-test. Video learning was associated with enthusiastic comments at the doctor's booth.

Conclusions: The Stroke Heroes Act FAST video or pamphlet can be useful for improving education regarding early warning signs of stroke via a brief intervention not only in time limited settings such as health fairs, but also at health clinics, hospitals and as public announcement messages to tackle this very important issue.

270 PERCEIVED OSTEOPOROSIS RISK AND GENDER

Vohra S1, Ochoa C2, Sathanthan A2.1Western University of Health Sciences College of Osteopathic Medicine, Pomona, CA and 2Western University of Health Sciences College of Osteopathic Medicine, Pomona, CA.

Purpose of Study: Osteoporotic fractures occur every 3 seconds worldwide resulting in approximately 8.9 million fractures annually. The World Health Organization Fracture Risk Assessment Tool, or FRAX, is a questionnaire based calculation tool used to estimate clinical osteoporosis risk. One advantage of the FRAX tool is it can be used with or without bone mineral density. In this study, we were looking at gender compared to self-estimation of fracture risk.

Methods Used: FRAX questionnaires were administered to patients and their family members at the Western University of Health Sciences Patient Care Center in Pomona, CA. Clinical osteoporosis risk factors were gathered and a 10-year risk of major osteoporotic and hip fracture probabilities were calculated using the FRAX assessment tool.

Summary of Results: A total of 76 men and women, over age 40, were recruited from the Western University of Health Sciences Patient Care Center. The average age was 53 years old (SD=8.8). Ethnic makeup was 59% Hispanic, 17% Caucasian, 14% African American, 8% Asian, and 1% other. The average 10-year major osteoporotic fracture risk and hip fracture risk were 4.38% (SD=3.96) and 0.59% (SD=1.12), respectively. The average self-estimated risks of major osteoporotic fracture and hip fracture were 33% (SD=30) and 26% (SD=28) respectively. Overestimations of osteoporotic and hip fracture risks occurred 71% and 70% of the time, respectively. Underestimations of major osteoporotic and hip fracture risk occurred 16% of the time. Interestingly, 33% of males underestimated their fracture risk, while only 8% of females underestimated their risk. Subjects were asked if osteoporosis was more common in men and of the 24 males in the study, 42% answered incorrectly.

Conclusions: This study investigated self-perceived osteoporotic fracture probability and gender. In this Pomona population most subjects overestimated their risk of fracture. Interestingly, male subjects showed an increased tendency to underestimate their osteoporosis risk compared to females. Providers should, during patient education, make an effort to educate patients about osteoporosis as well as the risk factors for the disease.

271 CARING FOR LESBIAN, GAY, BISEXUAL, AND TRANSGENDER PATIENTS: AN INTRODUCTION FOR CLINIC STAFF

Tran K. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: To educate clinic staff regarding care for LGBT people with three goals: 1) become familiar with LGBT terms and concepts, 2) learn about the health disparities LGBT people face, 3) describe ways to create a safe and accepting healthcare environment for LGBT patients. The lack of or barriers to safe and accepting clinics, where staff have had LGBT-sensitivity training, contributes to the many health disparities. This project works toward making an already culturally competent clinic, the International Community Health Services (ICHS) clinic in Seattle, WA, into an even more inclusive environment for all people in need.

Methods Used: Shadowing multiple healthcare providers demonstrated that most, if not all, clinic staff were unfamiliar with the term “LGBT” and had little to no experience providing care to LGBT patients. An hour-long presentation and Q&A session was given to medical clinic staff covering: 1) common terms used in the LGBT community and their level of appropriate- ness, 2) statistical data on LGBT-specific health disparities and relevant health screening recommendations, and 3) a checklist of tips for the clinic to be more inclusive and culturally competent. Printed materials provided: patient brochures explaining the importance of coming out to healthcare providers, copies of a list of local LGBT resource centers and their contact information, and rainbow stickers for ID badges.

Summary of Results: 21 staff members attended the workshop, which included physicians, psychologists, nurse practitioners, nurses, health educators, intake receptionists, medical assistants, and interpreters. Active engagement spurred new ideas for discussing LGBT health concerns with patients. All attendees placed rainbow stickers on their badges after the presentation. Printed materials were placed in the patient waiting room and in high traffic areas. Extra rainbow ID badge stickers were given to those who could not attend and saved for future staff.

Conclusions: LGBT health is complex, and relevant information is lacking in the curriculum for doctors, nurses, and medical assistants. Learning about the unique needs of the LGBT community and creating more safe and inclu- sive healthcare environments will work towards correcting the health disparities LGBT people face and provide the culturally competent care they greatly need.

272 ENCOURAGING BICYCLE USE FOR ACTIVE COMMUTING TO IMPROVE HEALTH OUTCOMES IN THE CITY OF CASPER, WYOMING

Sanderson M. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: While most of Casper is contained within a three mile radius, few citizens use bicycles for commuting. CVD, obesity, and diabetes are prevailing diseases within Casper's community. This project was meant to raise awareness of the health benefits of bicycle use for active commuting and to incentivize that use. It has been shown that physically inactive less active physicians discuss the importance of exercise with their patients more frequently than those who are active. Thus, physicians and other health professionals were included as a target audience along with community members.

Methods Used: A literature review was conducted to determine the best methods for reaching the community and to identify proven benefits of commuting with a bicycle. A “Bike to Work Day” was organized and advertised through flyers and word of mouth at the Wyoming Medical Center hospital, the event included a booth in a high traffic area at the hospital with educational material (digital presentation) about the health benefits of bicycling to work, healthy snacks, and coupons from a local bike shop for free bicycle tune-ups and discounted sale prices.

Summary of Results: The educational material at the booth was well received by members of the target audiences who stopped at the booth. Two-hundred people accepted the aforementioned coupons. Also, the project generated a discussion about obstacles that prevent hospital employees from bicycling to work, including scarce bicycle parking. This discussion alerted key hospital administrators to the problems, and remedies are already being discussed. One unexpected result was the positive peer pressuring that began once those that already bike to work were openly identified.

Conclusions: While education about the benefits of bicycling to work will continue to be important, many in the community expressed that they would already use their bicycles for transportation if the infrastructure was in place. Many felt unsafe biking because of the danger of cars in the developed city lack bicycle lanes. Community members must continue to raise awareness of this issue and stress the importance of improved bike lane
HELPING REDUCE TOBACCO EXPOSURE IN CHILDREN: USING SURVEYS TO PROVIDE SMOKING CESSATION IN A PEDIATRIC CLINICAL SETTING

Martin MR, Yang S, Tomajan D. UCSF Fresno Pediatric Residency, Fresno, CA.

Purpose of Study: Tobacco use and secondhand smoke exposure have well known adverse effects and long term health complications in children, such as asthma, recurrent infections, and decreased lung function. The purpose of this quality improvement study was to evaluate the effectiveness of implementing a smoking cessation survey as an instrument to help parents and caregivers stop smoking.

Methods Used: A standardize smoking exposure survey was employed in our resident community clinic as a means to discuss tobacco exposure among children, and to give families a way to stop smoking if they were ready. Each caregiver was provided with a standardized smoking cessation survey when they registered for all well child evaluations and clinic visits (excluding urgent care). Families were asked to complete the survey and give the survey to their respective providers. At the end of the visit the provider placed these forms in a bin labeled “fax” for those who requested help with quitting smoking or “no fax” for all other surveys. Completed forms indicating an interest in tobacco cessation, and were then faxed to California Smokers’ referral for smoking cessation.

Summary of Results: A total of 922 smoking exposure surveys were collected. From this total 51 care givers admitted to smoking in the past 7 days; 86 lived with someone who smoke; 32 had someone who smoked in their home, 12 had someone who smoked in their car. A total of 23 people stated they wanted help with quitting use of tobacco and all 23 forms were faxed to the California Smokers’ Cessation program. There were 70 incomplete surveys, and the remainder of the forms denied use tobacco or the form was left completely blank.

Conclusions: This quality improvement project demonstrated that providing families with a process to stop smoking, through the use of a survey could be an effective way to help reduce tobacco exposure in our pediatric population. Additionally, these forms also served as an education tool in discussing the affects of secondhand tobacco exposure in children.

THE CONTRIBUTION OF LABOR MANAGEMENT TO PREVENT THE FIRST CESAREAN SECTION, SINGLE CENTER STUDY

Oliva ME1, Walker S2, Benedetti T2. 1University of Washington School of Medicine, Seattle, WA and 2University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Cesarean section (CS) is an obstetric procedure that, due to a high variation in practice patterns, shows promise for improvement in health outcomes through standard interventions. Recent data has shown that as many as 40% of patients undergoing a CS delivery do not meet recommended criteria for a CS.

The goal of this retrospective study was to determine the extent to which labor management practices at the University of Washington Medical Center were consistent with the recommended guidelines. single center study

Methods Used: Four labor management bundle guidelines were developed as tools to evaluate labor practice: delay admission, latent phase, active phase, and second stage phase. The primary population of interest consisted of term singleton vertex primary CS deliveries in spontaneous labor at admission. A sample of 650 CS was selected over 2011-2013.

Summary of Results: Of the 650 CS deliveries, 204 were term singleton vertex primary CS. Of these, 100 were in labor and classified as in-study cases. 11% of the in-study cases had a CS before reaching the active phase of 6 cm cervical dilation, 48% during the active phase, and 41% during the second stage. Non-exclusive indications for CS were: failure to progress in either the latent or active phase (43%), fetal intolerance of labor (64%), and second stage arrest (39%).

In-study cases were eligible for 138 bundles: 16 delay admission, 21 latent phase, 60 active phase, and 41 second stage. Of these, 52 (38%) were ineligible for a pass-fail evaluation. In the delay admission bundle, the non-exclusive reasons for ineligibility were: inadequate pain control (93%), fetal heart rate tracing category II (57%), and maternal factors (36%). In the latent phase, active phase and second stage phase bundles, the reason for ineligibility was non-reassuring fetal heart rate (100%). Of the 86 bundles evaluated, 92% passed the bundle criteria, while 8% did not.

Conclusions: As opposed to nationally derived data, only 11% of the cases considered failed to reach 6 cm dilatation prior to the CS, and 92% percent of the bundles evaluated were consistent with the recommended guidelines. A large number of bundles (38%) was ineligible for further evaluation, mainly due to fetal intolerance of labor.

EXPERIENCE OF MOTHERS WHO EXCLUSIVELY BREASTFED UNTIL 6 MONTHS OF AGE IN THE CENTRAL VALLEY, CA

Patel K, Evans AE, Shilakhtsitsa K. UCSF Fresno, Fresno, CA.

Purpose of Study: Breastfeeding (BF) is the gold standard for infant nutrition and most medical organizations promote exclusive BF (EBF) to 6 months (m) of age. The US Government has published the Healthy People 2020 guidelines for BF which aims for 25.5% EBF through 6m. Our local initiation rate of 84.5% has exceeded the 81.9% target but our EBF rate drops to 47.1% before hospital discharge and is likely well below target at 6m. A statewide EBF rate to 6m is 21.7% with no local data available. Most of the current literature focuses on BF peripartum. While this is tantamount to initiation, there is a need for more of an emphasis on maintaining EBF with a paucity of research focusing on this. This study explored factors which helped mothers succeed in EBF in Fresno Co, which will help deliver targeted care to promote EBF to 6m.

Methods Used: We recruited mothers from various practice settings in the surrounding Fresno Co area and found 96 to be eligible. Criteria for inclusion was EBF their babies until 6m with no solids or liquids other than medications and/or vitamins. They participated in a detailed written survey exploring their experience and probing into issues such as motivation, source of information and support as well as difficulties encountered.

Summary of Results: Although many of these mothers were unaware of specific guidelines, they had planned to BF prior to delivery as the majority felt EBF was best and knew the health benefits. Many reported education through their doctors with additional from their peers. Mothers faced various challenges including learning to latch, juggling ADL’s, handling medical complications, social pressures to start solids, supply issues, pumping, and lifestyle changes- however they expressed empowerment through this experience. Despite all, they were able to attain their goals of EBF with the support of their family and friends. Maternal choice prior to delivery, social support and help from physicians seemed to be most significant factors that helped mothers overcome the obstacles and allowed them to succeed.

Conclusions: EBF to 6m does pose many challenges for the dyad and support is essential. As doctors we need to have the skills and resources to help mothers, babies and the families as they establish EBF. Physician education, family support and societal promotion are critical to help mothers achieve their BF goals.
Methods Used: An initial survey was conducted in the clinic to assess patients’ knowledge of urgent care services as an alternative to the emergency department. In response to the pre-intervention survey results, a poster about the clinic’s extended hours and a poster about common urgent care complaints that could be dealt with in the office were hung in every exam room as well as in the clinic waiting room. The clinic’s web presence was updated to reflect the new hours. A page was also added to the clinic webpage explaining the difference between emergency department care and urgent care. The effectiveness of this intervention was assessed using a post-intervention survey with questions related to the educational materials.

Summary of Results: The pre-intervention survey showed that a large percentage of patients from the practice use the emergency department (42% in the past year). Many patients (42%) were also unaware of the clinic’s capacity to accommodate same-day appointments for urgent concerns. Additionally, relatively few patients (31%) were aware of the clinic’s plan to extend hours despite a practice-wide mailing advertising the new hours. Post-intervention survey results revealed no statistically significant change in patient awareness after the intervention.

Conclusions: There was no statistically significant difference in patient responses before and after the intervention signaling that mailings, posters, and web updates are probably ineffective ways of communicating information to patients. On average, 39% of the clinic patient population used the emergency department in the past year, roughly double the national average of 20% (CDC, 2011). This is unlikely to be an issue of insurance, since almost all patients of this practice are insured. Having the physician educate the patient about these issues is most likely a more effective way of informing the patient. The next step in this project will be to encourage clinicians to remind all patients during the visit about the clinic’s new extended hours, urgent care capabilities, and the spectrum of what constitutes “urgent care.”

### Table 1. Factors Predicting Patient Satisfaction with Pain Management

<table>
<thead>
<tr>
<th>Very Strongly Correlated at P&lt;0.05</th>
<th>Strongly Correlated at P&lt;0.02</th>
<th>Correlated at P&lt;0.05</th>
<th>Not Significantly Correlated</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Lowest level of pain during the first 24 hours (R² = 0.34, p=0.0001)</td>
<td>% Allowed to participate in decision-making about pain treatment (R² = 0.16, p=0.013)</td>
<td>% How helpless the pain is making you feel (R² = 0.13, p=0.025)</td>
<td>% Pain interfering with falling asleep (R² = 0.54, p=0.016)</td>
</tr>
<tr>
<td>% Highest level of pain during the first 24 hours (R² = 0.16, p=0.013)</td>
<td>% How much pain interferes with staying asleep (R² = 0.13, p=0.026)</td>
<td>% How anxious, depressed, frightened the pain made you feel (R² = 0.043, p=0.022)</td>
<td>% Experience of side effects: nausea, dizziness, (R² = 0.0009, p=0.96)</td>
</tr>
<tr>
<td>% Percentage of first 24 hours spent in severe pain (R² = 0.15, p=0.018)</td>
<td>% Pain interfering with sitting up/turning/positioning in bed (R² = 0.016, p=0.043)</td>
<td>% Pain interfering with walking/sitting in a chair/standing at the sink (R² = 0.011, p=0.044)</td>
<td>% If you received pain treatment option information, how helpful was it? (R² = 0.10, p=0.17, df=18)</td>
</tr>
</tbody>
</table>

### 278 THE USE OF REMOTE ACCESS CLINICS TO TREAT AND INFORM MEN WITH SEXUAL DYSFUNCTION

Bayona E1, Keller T1, Clavijo R2, J Shelton1,2, Bergman J1,2, Bennett CJ1,2

David Geffen School of Medicine at UCLA, Los Angeles, CA and Greater Los Angeles VA Medical Center, Los Angeles, CA.

**Purpose of Study:** Telemedicine has been shown to effectively increase access to medical care in distant locations. The Greater Los Angeles (GLA) Veterans Affairs (VA) Healthcare System has implemented telemedicine to increase access to care throughout an expansive urban community. The GLA service area spans across five counties, serving approximately 1.4 million veterans. Although 10 community-based outpatient clinics exist within the GLA service area, veterans must often travel great distances for healthcare found exclusively at VA medical centers. This study examines patient satisfaction with monthly telehealth seminars for men diagnosed with sexual dysfunction.

**Methods Used:** 18 patients participated in this study from July to September, 2013. We administered two anonymous questionnaires following seminar attendance. To assess seminar satisfaction, participants completed a survey about their preference and overall experience. The preliminary data from this ongoing study indicate telehealth seminar participants were satisfied with their experience. The majority of telehealth participants “strongly agree” to choosing telehealth again in the future and recommending telehealth to others. The telehealth group had a mean satisfaction of 82%, demonstrating a high degree of satisfaction. The in-person group had a mean satisfaction of 77%, also indicating high satisfaction. At present, our study illustrates similar satisfaction scores between both groups. SHIM scores indicate that men attending the seminars present with a baseline sexual function of moderate to severe erectile dysfunction (Mean = 9.2).

**Conclusions:** The results of our study indicate similar satisfaction levels between telehealth and in-person seminar participants. As the study progresses, we expect to show that telehealth seminars provide equal or greater satisfaction than in-person seminars.
THE UTILIZATION OF CASELOAD REGISTRIES: PERCEPTIONS OF CARE COORDINATORS IN THE MENTAL HEALTH INTEGRATION PROGRAM

Eckstrom J, Williams D, Avery M, Unutzer J. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: With more Americans receiving mental health care from their primary care provider than from a specialist and few receiving adequate mental health care, the use of evidence-based integrated care models has recently expanded. The caseload registry, a web-based data management tool that helps guide and track patient care, is a critical component to success of these models and the improved management of mental health conditions in primary care. To date, there has been little research to assess the utilization of these registries. This study evaluates the utilization of the Mental Health Integrated Tracking System (MHITS), the caseload registry used by care coordinators (CCs) in the Mental Health Integration Program (MHIP) in Washington State. We assess CC impressions of working with MHITS and its effects on treating chronic mental health conditions.

Methods Used: We conducted a web-based survey of MHIP CCs in primary care clinics. Phone based follow-up semi-structured interviews were conducted with a subset of CCs. Survey responses and comments made by CCs during follow-up interviews were statistically and thematically analyzed.

Summary of Results: 64 (54%) of 118 eligible CCs completed the survey, and 27 follow-up interviews were conducted. On average, CCs agreed on 4 of 7 survey questions regarding specific benefits of MHITS. CCs agreed MHITS helps track patients and patient progress. On average, CCs only 4 of 7 survey questions of MHITS. CCs agreed with a subset of CCs. Survey responses and comments made by CCs during follow-up interviews; notably, all CCs greatly appreciated the patient populations and more education should be provided on the proper use of caseload registries.

Conclusions: CCs value MHITS; they find it helps provide more comprehensive care and tracks patient progress well. However, CCs also find that MHITS is time consuming and doesn't reflect how the patient is doing overall. To further improve patient outcomes and expand integrated care models, development of caseload registries should be focused on the needs of specific patient populations and more education should be provided on the proper use of caseload registries.

281 PHYSICIAN ASSESSMENT OF CMS ELIGIBILITY FOR HOSPICE (PACE-H)

Aminifard O, Buckholz G, Kazmi S, Achar S. UCSD School of Medicine, San Diego, CA; UCSD Health System, San Diego, CA; University of Michigan, Ann Arbor, MI and UCSD Health System, San Diego, CA.

Purpose of Study: Although Medicare funded hospice care is available to qualified patients in the last 6 months of life, the median time of hospice use is 17 days (MedPAC 2011). We hypothesized that under-utilization of hospice care in part be explained by physicians' inadequate knowledge of the criteria for hospice eligibility as established by Center for Medicare and Medicaid Services (CMS). A brief questionnaire was used to assess physicians' knowledge of such non-cancer diagnoses as dementia, heart, pulmonary and renal disease, and stroke, as these are the largest percentage of hospice admissions (NHPCO 2010).

Methods Used: Questionnaire responses were quantified by assigning a (+1) value to correct answers and unmarked incorrect answers, and (-1) for incorrect.

Summary of Results: On average, participants scored 53%; however, performance on some criteria was poor. For example, only 7% correctly identified one of the listed terminal lung disease criteria and 41% chose an incorrect response instead; only 11% recognized the correct Karnovsky Performance Score for hospice eligibility. In addition, over 67% chose an incorrect criterion for dementia, and 52% did not know the value of ejection fraction in significant congestive heart failure. Also, only 47% of doctors knew the glomerular filtration rate value necessary for hospice referral.

Conclusions: The findings of our study suggest a significant lack of knowledge of the CMS criteria for hospice referral and a need to either simplify the criteria or create a continued education program for physicians in order to help increase utilization of hospice and thus improve patient satisfaction and reduce medical care costs.
282

INCREASING ADVANCE DIRECTIVE COMPLETION AMONG END-OF-LIFE PATIENTS

Peseshki BB1, Kuo A2, Stevens C3, 1UCLA David Geffen School of Medicine, Los Angeles, CA; 2UCLA David Geffen School of Medicine, Los Angeles, CA and 3Harbor-UCLA Medical Center, Los Angeles, CA.

Purpose of Study: To examine how we could increase the prevalence of advance directives among the sickest patients in a practice.

Methods Used: We would identify 60 of the most ill patients of our practice, Santa Monica UCLA Internal Medicine-Pediatrics, then examine their medical records for an advance directive. We then contacted the primary care physicians of patients to understand what barriers the physicians were facing to attain an advance directive.

Summary of Results: It was concluded that 17% of patients did not have an advance directive. The four main barriers physicians faced were (1) time, (2) patient preparedness, (3) patient willingness, and (4) physician prioritization.

Conclusions: The best solutions for these barriers were determined to be: (1) create a new appointment type in the practice schedule—a 30 minute appointment at the end of the day, (2) prior to the appointment, distribute multilingual literature that is understandable to patients so that they could be prepared for discussion with their physician, and (3) to add advance directives to routine health maintenance check list in CareConnect.

ENVIRONMENTAL SCAN OF BEREAVALMENT SERVICES AT NORTH AMERICAN PEDIATRIC AND MATERNITY HOSPITALS: A QUALITY ASSURANCE STUDY

Ma V, Webber E, Crowell P. Children's and Women's Hospital of British Columbia, Vancouver, BC, Canada.

Purpose of Study: Bereavement is defined by BC Children's and Women's Hospital's Bereavement Committee as “the therapeutic process of dealing with loss of, or potential loss of, a life”. Bereavement services include those offered to patients and families leading up to the end of life, during and after the death of a patient or family member within the workplace. As such, bereavement is a valued component for patients’ families and vital in providing complete patient care according to the biopsychosocial model of health. While a unified set of protocols exists in the United Kingdom, the literature does not show whether the same consistency is in place in North America. Consequently, this environmental scan aims to identify whether formal procedures are in place for bereavement services.

Methods Used: Semi-structured phone interviews were conducted with bereavement representatives according to the Children’s Hospital Association Membership List. Interviews focused around five themes pertaining to patients and staff. These include whether a formal bereavement program was present and elements of the program, if they had a designated bereavement coordinator, guiding principles in providing patient care, support systems for staff and protocols, guidelines or standards for staff support following a patient’s death.

Summary of Results: Most hospitals were found to have a formal bereavement program in place for patients and a designated bereavement coordinator in charge of those services. Furthermore, all institutions followed some form of protocols, guidelines or standards, though they were often established in-house, and therefore not consistent throughout all institutions. Trends in terms of services included end of life memory making, bereavement resources, and a follow-up protocol following the death of a patient. Staff support was largely informal. Few hospitals followed a set of protocols for supporting staff after a patient’s death. Rather, informal ward debriefings or peer support from the manager or pastoral care were the main avenues of support.

Conclusions: Although there are no national guidelines for bereavement services for patients, certain themes persist enough throughout the majority of institutions to be considered as the minimum standard of care.

Infectious Diseases 1
Concurrent Session
3:30 PM
Friday, January 24, 2014

284

REDUCTION OF CLOSTRIDIUM DIFFICILE INFECTION USING ANTIMICROBIAL STEWARDSHIP IN A CHILDREN’S HOSPITAL WITHIN A HOSPITAL


Purpose of Study: To evaluate C. difficile infection (CDI) rates before and after implementation of antimicrobial stewardship.

Methods Used: To introduce the concept of stewardship, we instituted an antimicrobial stewardship pilot (ASP) project in the pediatric intensive care unit (PICU) and used the 27 months prior to stewardship as the non-intervention period of comparison (Period 1, P1). The initial stewardship program involved an infectious disease (ID) physician rounding with the PICU team from June 2010 to July 2011 (PICU stewardship, Period 2, P2). To increase the number of children evaluated, this model was transitioned to prospective audit with real time feedback from September 2011 to present (Prospective audit stewardship, Period 3, P3). Our team consists of a pediatric ID physician and clinical pharmacists with ID training. Three days a week, the pharmacist generates a list of all pediatric antimicrobial recipients and reviews selected patients with the ID physician. We compared days of antimicrobial therapy (DOT) per 1000 patient days and number of CDI cases per 10,000 patient days, estimated cost savings and evaluated negative outcomes (30-day readmission; all-cause mortality).

Summary of Results: Statistical analysis employed was Poisson regression. Adjusted rate ratios (RR) showed significant reduction in DOT for P1 vs P3 and P2 vs P3 (P<0.001) but not P1 vs P2 (P=0.76). RR for CDI showed significant reduction compared to the pre-intervention period. P1 vs P2 (68% reduction; P<0.001), P1 vs P3 (86% reduction; P<0.001), with a trend toward significance for P2 vs P3 (P=0.18). We performed statistical adjustment for seasonal effects and for the H1N1 outbreak using cosinor analysis. We demonstrated a $176,000 cost savings using prospective audit. There was no increase in 30-day readmission and no change in all-cause mortality attributable to stewardship.

Conclusions: Stewardship achieved a significant decrease in DOT with prospective audit appearing to be more robust than PICU ASP. However, both PICU ASP and prospective audit achieved a significant decrease in CDI compared to the pre-intervention period. There was a large cost savings attributed primarily to avoidance of CDI and no negative impact noted.

CHEST RADIOGRAPHIC PATTERNS IN PATIENTS HOSPITALIZED WITH RESPIRATORY SYNCTYIAL VIRUS (RSV) INFECTION

Hughes G1, Amini L1, Gasga A2, Reddy V1, Le D1, Le B1, Leung P1, H Wong 1, Garcia G1, B Afghani1,2. 1University of California, Irvine School of Medicine, Irvine, CA and 2CHOC Hospital, Orange, CA.

Purpose of Study: The objective of this study was to evaluate the association of the chest radiographic findings and disease severity of infants hospitalized with Respiratory Syncytial Virus (RSV) infection.

Methods Used: A retrospective cohort study was conducted at CHOC Hospital in Orange County, California. All infants less than one year of age hospitalized during the 2011-12 and 2012-13 with primary diagnosis RSV were identified. Chest radiograph results and the characteristics such as age, gender, underlying conditions, gestational age, treatments, length of hospitalization and oxygen requirement were recorded.

Summary of Results: A total of 592 infants less than one year of age were hospitalized during the 2011-12 and 2012-13 seasons. Those with consolidaed chest radiograph had longer LOS and oxygen requirement when compared to those with perihilar infiltrates or normal CXR. There were no significant differences in LOS for those who did not get an x-ray vs. those...
with normal x-rays or those with perihilar infiltrates (See Table). Of 337 patients who did not need oxygen, 18% did not get an x-ray, 23% had normal, 44% had perihilar infiltrates and 14% had consolidation on their chest radiograph. Of 255 patients who required oxygen, 9% did not get an x-ray, 16% had normal, 39% had perihilar infiltrates and, 36% had consolidation on their chest radiograph.

**Conclusions:** Infants hospitalized with RSV infection who had consolidation on their chest radiograph.

**Table 1. Chest Radiograph Patterns and Characteristics of Infants Hospitalized with RSV Infection**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No X-Ray</th>
<th>Normal X-Ray</th>
<th>Perihilar Infiltrate</th>
<th>Consolidation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females (N)</td>
<td>44 (32%)</td>
<td>50 (43%)</td>
<td>85 (43%)</td>
<td>53 (38%)</td>
</tr>
<tr>
<td>&lt; 2 months age (N)</td>
<td>53 (62%)</td>
<td>57 (48%)</td>
<td>85 (34%)</td>
<td>49 (35%)</td>
</tr>
<tr>
<td>Prematurity &lt; 33 weeks GA (N)</td>
<td>14 (16%)</td>
<td>15 (13%)</td>
<td>56 (14%)</td>
<td>30 (22%)</td>
</tr>
<tr>
<td>Underlying Condition (N)</td>
<td>3 (4%)</td>
<td>12 (10%)</td>
<td>34 (14%)</td>
<td>29 (21%)</td>
</tr>
<tr>
<td>Required Oxygen (N)</td>
<td>24 (28%)</td>
<td>41 (34%)</td>
<td>99 (40%)</td>
<td>9 (65%)</td>
</tr>
<tr>
<td>Mechanical Ventilation (N)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2 (1%)</td>
<td>9 (6%)</td>
</tr>
<tr>
<td>Length of Oxygen Requirement (Avg Days)</td>
<td>2.67</td>
<td>2.66</td>
<td>3.20</td>
<td>4.62</td>
</tr>
<tr>
<td>Length of Stay (Avg Days)</td>
<td>3.32</td>
<td>3.48</td>
<td>3.74</td>
<td>5.58</td>
</tr>
</tbody>
</table>

287

**WHOLE GENOME SEQUENCING OF 366 CLINICAL E. COLI ISOLATES COMPARES GENOTYPE WITH PHENOTYPE AND SHOWS THE MOLECULAR EPIDEMIOLOGY AMONG STRAINS**

Roach DJ, Salipante S, Shendure J, Kitzman J, Snyder M. University of Washington, Seattle, WA.

**Purpose of Study:** Escherichia coli is a bacterial species responsible for a range of clinical conditions and represents a significant burden of disease in the USA. Though the genome of E. coli is well characterized in many laboratory strains and outbreak isolates, there is a paucity of data on the genomic landscape of common pathogenic strains of the bacteria. The goal of this study is to utilize DNA sequencing to interrogate the interaction between virulence factors (VFVs) and clinical presentation, as well as to reconstruct the epidemiology of the strains present in the Seattle region.

**Methods Used:** We performed whole genome sequencing on 366 clinical isolates, 274 from patients with UTIs and 92 isolated from patients with bacteremia. Antibiotic resistance profiles and hemolysis states were ascertained by the UW Microbiology Lab for all strains. Additionally, complete medical records were obtained for all patients from whom the E. coli isolates were grown. Computational analyses were performed to interrogate epidemiology and to establish associations of bacterial genotype and phenotype, allowing for the identification of potentially novel VFVs and antibiotic resistance genes.

**Summary of Results:** This dataset enabled a large-scale analysis of the genetic diversity of pathogenic E. coli in the Seattle area, the elucidation of the pan-genome in the region, and a reconstruction of the molecular epidemiology among strains. Additionally, our computational analysis enabled the agnostic identification of known antibiotic resistance factors in resistant strains and several putative factors that are currently undergoing functional validation.

**Conclusions:** This study represents the largest whole-genome sequencing effort of a single bacterial species undertaken to date and provides a model for the integration of genomic science and clinical practice. We have shed light on the population structure of E. coli in the region and have detailed its pan-genome. Importantly, we developed a method for the large-scale identification of novel VFVs and antibiotic resistance genes and for improving our characterization of those already known. The pipeline utilized in this study is well-suited to other pathogenic bacterial species, and represents a potential breakthrough in using genomics to study infectious disease.

288

**THE PROTEOME OF PROPIONIBACTERIUM ACNES**

Yu Y1, Champer J1, Kim J2,3, UCLA, Los Angeles, CA and 2 Greater Los Angeles Healthcare System Veteran’s Affairs, Los Angeles, CA.

**Purpose of Study:** Propionibacterium acnes plays a major role in the development of acne vulgaris, a highly prevalent inflammatory skin disease. The need exists for novel approaches to develop treatments as the bacteria are becoming increasingly resistant to antibiotic therapy, and other treatment regimens have low efficacy or poor patient compliance. A full study of the P. acnes proteome will reveal protein drug targets or vaccine candidates and will allow us to gain insight into the bacteria’s mechanisms of pathogenesis.

**Methods Used:** To characterize the P. acnes proteome, we will first separate acne clinical isolate strain ATCC 6919 into different protein fractions, in including total cell extract, cell wall, cell membrane, cytolsic, and secreted proteins. These proteins will be subjected to mass spectrometry using an orbitrap for quantitative protein identification. In addition, we will compare the proteome of relatively benign type III P. acnes to that of type I bacteria, the most common in skin disease.

**Summary of Results:** Thus far, we have identified 205 proteins by mass spectrometry. Total cell extracts and cytoplasm fractions show commonly known proteins among the most abundant. Analysis of secreted fractions shows several potentially interesting highly expressed proteins of unknown function (Table 1). Additional work has revealed the proteome of relatively benign type III P. acnes to that of type I bacteria, the most common in skin disease.

**Conclusions:** Mass spectrometry has allowed for identification and quantification of a large number of proteins in our P. acnes fractions. Several uncharacterized proteins in the secreted fraction are potential virulence factors that could serve as targets for therapeutic intervention.
factors, and further analysis of other fractions will reveal additional proteins of interest that represent drug and vaccine targets.

### Table 1. The 10 Most Abundant Secreted Proteins of *P. acnes*

<table>
<thead>
<tr>
<th>Protein</th>
<th>Accession (gi)</th>
<th>MW (kDa)</th>
<th>fmoi/300ng Total Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>hypothetical protein PA1939</td>
<td>50840990</td>
<td>17</td>
<td>48.24</td>
</tr>
<tr>
<td>hypothetical protein PA1712</td>
<td>50840777</td>
<td>69</td>
<td>126.31</td>
</tr>
<tr>
<td>endoglycosidase</td>
<td>50839753</td>
<td>57</td>
<td>99.22</td>
</tr>
<tr>
<td>ral lipoprotein A, RlhA family</td>
<td>50841370</td>
<td>52</td>
<td>74.42</td>
</tr>
<tr>
<td>CAMP factor</td>
<td>50839777</td>
<td>29</td>
<td>71.94</td>
</tr>
<tr>
<td>adhesin or 5-layer protein</td>
<td>50840936</td>
<td>32</td>
<td>69.46</td>
</tr>
<tr>
<td>endoglycosidase</td>
<td>50841166</td>
<td>54</td>
<td>54.57</td>
</tr>
<tr>
<td>conserved protein</td>
<td>50841276</td>
<td>41</td>
<td>49.61</td>
</tr>
<tr>
<td>cell wall-associated hydrolase</td>
<td>50841012</td>
<td>43</td>
<td>37.21</td>
</tr>
<tr>
<td>NPF/PSO family secreted protein</td>
<td>50839811</td>
<td>41</td>
<td>32.25</td>
</tr>
</tbody>
</table>

### Role of a LysM Domain-Containing Streptococcus Pneumoniae Protein in the Activation of Dendritic and Natural Killer Cells and Pathogenicity

Toutouâlote J.1,2, Schmidt R.1,2, Eshkeman E.1,2, White J.1,2, Lenz L.1,2. University of Colorado, Denver, CO and 3National Jewish Health, Denver, CO.

**Purpose of Study:** Streptococcus pneumoniae (Sp) is a bacterium that can cause sepsis, meningitis, and pneumonia. It is responsible for a significant percentage of pediatric deaths, in spite of effective vaccines and antibiotics. The burden of this microbe necessitates ongoing investigation into its mechanisms of pathogenicity in order to identify novel vaccine and antibiotic targets. Recently, a Sp LysM domain-containing protein, Spr1875, was demonstrated to act as a virulence factor in mice. This LysM domain is similar in sequence to a region of the Listeria monocytogenes p60 protein that has been shown to stimulate activation of the dendritic cells (DC) and natural killer (NK) cells. We hypothesize the Spr1875 protein may illicit similar responses during Sp infection, which may serve a pathogenic role.

**Methods Used:** The ability of the Spr1875 LysM to activate the inflammasome will be assessed using established assays. Purified full-length, LysM only, and LysM deleted versions of recombinant Spr1875 will be used for induction of IL-1β and IL-18 secretion by DCs. NK cell activation will also be assayed in co-cultures with the treated DCs. The effects of Spr1875 on pathogenicity and host immune responses will also be studied in mice infected with WT, spr1875null or spr1875-LysM deleted pneumococcal strains.

**Summary of Results:** Treatment of DCs with full-length Spr1875 elicits significant IL-1β production and when naïve NK cells are added to the cultures they are stimulated by Spr1875 to produce IFNγ. Purification and testing of mutant Spr1875 and generation of mutant Sp strains is in progress.

**Conclusions:** The ability of purified full-length Spr1875 to activate the inflammasome and IFNγ production in culture suggests that this protein stimulates DC and NK cells as predicted. If we find this activity maps to the LysM domain it would suggest that Spr1875 and p60 proteins act via similar mechanisms. We are also working to determine if Spr1875 stimulates immune response during in vivo infection and host this affects pathogenicity.

### Inhibition of Polyamine Transport as a Target for Treatment of Toxoplasma Gondii Infection

Whitman JD.1,2, Chang S.2, Hawell L.2, Byus CV.2, Wilson EH.2. David Geffen School of Medicine at UCLA, Riverside, CA and 2University of California, Riverside, Riverside, CA.

**Purpose of Study:** Toxoplasma gondii is an intracellular parasite responsible for toxoplasmosis, a neglected infectious disease worldwide. Though the disease is largely asymptomatic, congenital transfusion can occur during acute infection leading to fetal death, hydrocephalus, and chorioretinitis. At the moment, the current approved drugs for toxoplasmosis include sulfadiazine and pyrimethamine, even though they are contraindicated for use in utero and in infants due to the possibility of teratogenicity and leukopenia. Our research seeks to explore polyamine uptake inhibitors (PATi), ANT-4, ANT-44, and 44-ANT-44, as a novel mechanism for treatment of toxoplasmosis, with a focus on congenital cases. Our hypothesis is that blocking polyamine uptake (necessary molecules for DNA synthesis) in *T. gondii* will lead to decreased parasite proliferation, while leaving cultured human cells unaffected due to de novo polyamine biosynthesis.

**Methods Used:** The effects of PATi on *T. gondii* infection of human fibroblasts were measured using chamber slide cultures. In addition to controls, PATi was added to parasite-infected cultures both concurrent with infection and after three-hours of infection. This allowed the effect of PATi inhibition on *T. gondii* cell invasion and parasite replication to be quantified. After twenty-four hours, slides were stained with H&E and analyzed by light microscopy.

**Summary of Results:** Quantification demonstrated a 78.59% (P=0.0074) decrease in the ability of *T. gondii* to infect fibroblasts when PATi was added concurrent with infection. Parasite replication was similarly significantly inhibited: 59.34% (P=0.0128). When PATi was added three hours following infection a 35.13% (P=0.0125) decrease in average number of parasites per infected cell was observed.

**Conclusions:** Our proposed PATi showed a statistically significant reduction in parasite invasion of human fibroblasts when given concurrently with *CVB1* infection were reported, eight of whom had myocarditis due to very closely related strains of *CVB1*. This represents a major shift in the virulence of *CVB1*, which while intermittently detected in the United States, caused neither neonatal mortality nor clinical myocarditis. We sought to identify genetic changes associated with this enhanced virulence.

**Methods Used:** The newly isolated *CVB1-Chi07* virus exhibited markedly greater myocardial replication than the prototype strain, however, the changes in the IRES sequence alone did not seem to be responsible for this effect. Full genome sequencing and comparison to other recently circulating enteroviruses revealed areas of conservation and divergence that are intriguing for further study.
292
INCREASED PRO-INFLAMMATORY CYTOKINE EXPRESSION IN RESPONSE TO TLR3 AND TLR9 STIMULATION USING HSV1
Martins TB1, Woodbury KO2, Tardif KD1, Augustine NH2, La Pine TR2, Kumanovics A1,2, Hill HR1,2 1ABRI Institute, Salt Lake City, UT and 2University of Utah School of Medicine, Salt Lake City, UT.

Purpose of Study: Toll-Like Receptors (TLRs) play a critical role in innate immumity by recognizing highly conserved structural components of microbes. Patients with HSV1 encephalitis have been reported to have defects in TLR3 and TLR9. TLR3 recognizes double-stranded RNA (dsRNA) and is primarily involved in the innate defense against viral infection, while TLR9 recognizes dsDNA with CpG motifs. Poly(I:C), a synthetic analog of dsRNA, has been shown to be an effective stimulant of the TLR3 signaling pathway via production of pro-inflammatory cytokines in murine models, but is not as effective in stimulating human peripheral blood mononuclear cells (PBMC’s) in commonly used TLR functional assays. The purpose of this study was to find a more potent stimulator of the human endosomic TLR3 and TLR9 pathways in the study of patients with HSV1 encephalitis.

Methods Used: PBMC’s were isolated from whole blood and cultured 24 hours with either Poly(I:C) or HSV1 virus. Cytokine concentrations were measured in the PBMC supernatant using an in-house developed multiplexed immunoassay.

Summary of Results: Mean pro-inflammatory responses were dramatically increased in the HSV1 vs. Poly(I:C) stimulated cells (n=5) for TNF-α (961 vs. 58 pg/ml, p=0.03), IL-1β (1,213 vs. 17.8 pg/ml, p=0.0047) and IL-6 (13,442 vs. 462 pg/ml, p=0.007). All HSV1 stimulated cytokine responses were dose-dependent and exhibited much higher concentrations at 24 hour compared to 5 day incubation times.

Conclusions: The use of HSV1 as a TLR3 and TLR 9 stimulant showed a more consistent and increased response in pro-inflammatory cytokines compared to the commonly used Poly(I:C). The use of HSV1 as a TLR3 and TLR 9 stimulant followed by pro-inflammatory cytokine quantitation should be useful in the evaluation of patients who suffer HSV encephalitis in the investigation of TLR function and its role in the susceptibility in HSV infections.

FIGURE 1.

293
MOLECULAR DETECTION AND IDENTIFICATION OF STAPHYLOCOCCUS AUREUS IN AIRWAY SAMPLES FROM CHILDREN WITH CYSTIC FIBROSIS
Johnson E, Wagner BD, Accurso FJ, Harris JK. University of Colorado School of Medicine, Denver, CO.

Purpose of Study: Staphylococcus aureus (Sau) is a common and significant pathogen in cystic fibrosis (CF). Quantitative PCR (qPCR) may provide a rapid, culture-independent approach to diagnosis of Sau airway infections, but a previously evaluated 16S rRNA gene (16S) qPCR assay demonstrated poor sensitivity with respect to Sau compared to other airway pathogens. We sought to determine the sensitivity of an alternative qPCR assay that targets amplification of the femA gene to identify Sau directly from airway samples in comparison with qPCR detection by 16S qPCR.

Methods Used: DNA extraction was performed with and without enzymatic digestion. Results of the qPCR assay were compared to culture to determine the sensitivity. We examined 87 samples (42 oropharyngeal [OP], 45 expectorated sputum [ES]), 59 of which were culture positive for Sau.

Summary of Results: qPCR detection of Sau was greater in ES (82.1% <70.3-94.0%>) than in OP (50.0% <34.9-65.1%>) with enzymatic digestion (p=0.02). Samples analyzed without enzymatic digestion had decreased sensitivity for OP but not for ES. Sensitivity in samples with greater than 10^4 CFU/mL was 100% but 0% for samples with less than 10^3 CFU/mL. Analysis by 16S qPCR had even lower sensitivity consistent with previous studies.

Conclusions: We conclude that the femA qPCR assay improves the detection of Sau in ES compared to the previously reported 16S qPCR assay. However, the sensitivity of the femA qPCR does not approach clinical utility. In addition, molecular identification of Sau in OP shows decreased sensitivity compared to sputum.

294
Juvenile Xanthogranuloma in Noonan Syndrome
Ali MM1, Gilliam AE2, Gilliam AC2, Rauen KA1. 1University of California San Francisco, San Francisco, CA and 2Sutter Health - Palo Alto Medical Foundation, Palo Alto, CA.

Case Report: Noonan syndrome (NS) is a RASopathy and is a common, autosomal dominant, multiple congenital anomaly syndrome. The mutations causing NS are all involved in the Ras/mitogen-activated protein kinase (Ras/MAPK) pathway. Juvenile xanthogranuloma (JXG) is a benign disease of early childhood, affecting the skin, mucous membranes, eyes, and viscera. JXG presents as yellowish-red nodules and usually arise during the first 6 months of life with predilection for the head and neck. JXG is rarely associated with systemic manifestations and represents a self-limited dermatologic disorder. A RASopathy that is known to be associated with JXG is Neurofibromatosis Type 1 (NF1). Juvenile myelomonocytic leukemia (JMML) is a myelodysplastic and myeloproliferative disorder that accounts for 1-2% of childhood leukemias in the US. A JMML-like picture with spontaneous regression in infants with NS has been previously reported, with an estimate of the incidence of 10% in patients with NS.

The association of JXG, JMML and NF1, has been described before, however, this is still controversial. Children with both NF1 and JXG have been estimated to have a 20-32 times higher risk of developing JMML than those with NF1 alone.

In this report we present a case demonstrating a possible association between JXG and NS, and a comprehensive literature review. To date, there have been no published cases of Sau patients reported with JXG. We describe a 10 month old female patient with the clinical and molecular diagnosis of NS, resulting from a heterozygous p.Y62D missense mutation in Shp2 (PTPN11 gene). She was being evaluated for multiple skin lesions that were found to be biopsy proven JXG. The course of the diagnostic work-up is discussed along with her family history, DNA analysis, current condition, and plan for follow up, followed by a literature review. To our knowledge, this case represent the first reported case describing a NS patient with JXG, highlighting the importance of carefully examining such patients for these skin lesions.
RESPIRATORY INVOLVEMENT IN COSTELLO SYNDROME: A REPORT OF TWO CASES AND REVIEW OF THE LITERATURE

Gomez-Ospina N, Myers A, Brennan M, Bernstein JA, Hudgins L. Stanford Hospital, Stanford, CA.

Case Report: Costello Syndrome (CS) is a multisystem disorder caused by a heterozygous germline mutation in the HRAS proto-oncogene. It is characterized by coarse facial features, intellectual disability, postnatal failure to thrive and increased incidence of malignant solid tumors. Integumentary, musculoskeletal and cardiac involvement is also prevalent. Respiratory difficulties have also been reported in CS, however, there has been limited description of their origins. Here we present the clinical course of two patients diagnosed with CS in the neonatal period who presented with respiratory failure soon after birth. Patient 1 presented with respiratory distress requiring temporary intubation. Laringoscopy identified laryngomalacia. The symptoms improved after excision of ariepiglottic folds, laryngoplasty and tracheal reconstruction but on follow up had persistent obstructive sleep apnea. Patient 2 presented with respiratory distress due to hyperventilation and presumptive pulmonary hypoplasia. At follow up the patient was still CPAP dependent.

Review of the literature revealed additional reports documenting respiratory symptoms in patients with CS including respiratory insufficiency, laryngo/tracheo/bronchomalacia, hydro/chylothorax, upper airway obstruction, obstructive sleep apnea and small lungs. Postmortem and histopathological studies have shown evidence of lymphangiectasia, atypical elastic fibers in brochi and alveoli, as well as alveolar and bronchopulmonary dysplasia. Review of the literature also revealed a correlation between the presence of severe respiratory phenotype and uncommon mutations in the HRAS gene.

Our cases and review of the literature suggest respiratory insufficiency is a source of significant morbidity for patients with CS in the neonatal period. Reported mechanisms to explain the upper and lower respiratory tract involvement include impaired elastogenesis, lymphangiectasia and pulmonary hypoplasia. The possibility of respiratory compromise in the neonatal period should prompt adequate counseling and plan for delivery in cases of prenatally diagnosed Costello syndrome.

DUPLICATION OF SERPINF1 ON 17p13.3 LEADS TO AN UNCLASSIFIED TYPE OF METAPHYSICAL DYSPLASIA

Graham JM2, Shih EM1, Pitukcheewanont P1, Vitazka P1. 1Children’s Hospital Los Angeles, Los Angeles, CA; 2GeneDx, Gaithersburg, MD.

Purpose of Study: Autosomal recessive loss-of-function mutations in SERPINF1 typically lead to a severe type of osteogenesis imperfecta (OF-Type VI).

Methods Used: We report a duplication of this gene that was detected on whole exome sequencing in a patient with an unclassified type of metaphysical dysplasia.

Summary of Results: This patient is a 12 year old Korean male with metaphysical dysplasia associated with genu valgum, coxa valga, and a 2 cm leg length discrepancy. Gene testing for known types of metaphysical dysplasia (RMPS and COL11A1) was normal. X-ray findings showed lytic and sclerotic distal femoral, proximal tibial and distal tibial metaphyses. To correct his bone abnormalities, he had bilateral distal femoral and proximal tibial metaphyseal dysplasia associated with genu valgum, coxa valga, and a 2 cm head circumference. At follow up the patient was still CPAP dependent.

Summary of Findings: This patient is a 12 year old Korean male with metaphysical dysplasia associated with genu valgum, coxa valga, and a 2 cm leg length discrepancy. Gene testing for known types of metaphysical dysplasia (RMPS and COL11A1) was normal. X-ray findings showed lytic and sclerotic distal femoral, proximal tibial and distal tibial metaphyses. To correct his bone abnormalities, he had bilateral distal femoral and proximal tibial metaphyseal dysplasia associated with genu valgum, coxa valga, and a 2 cm head circumference. At follow up the patient was still CPAP dependent.

Summary of Findings: This patient is a 12 year old Korean male with metaphysical dysplasia associated with genu valgum, coxa valga, and a 2 cm leg length discrepancy. Gene testing for known types of metaphysical dysplasia (RMPS and COL11A1) was normal. X-ray findings showed lytic and sclerotic distal femoral, proximal tibial and distal tibial metaphyses. To correct his bone abnormalities, he had bilateral distal femoral and proximal tibial metaphyseal dysplasia associated with genu valgum, coxa valga, and a 2 cm head circumference. At follow up the patient was still CPAP dependent.
Conclusions: We have identified and described a unique subcategory of vascular anomalies that have clinical features of high flow malformations but radiological features of low flow malformations. From a practical treatment standpoint, these lesions behave like low flow malformations and should be treated as such. We propose that complex vascular malformations should best be evaluated by both clinical as well as specialized radiological (MRI/MRA/angiography) means, radiologic diagnoses should usurp what is found clinically, and ultimate treatment is preferentially based on a radiological diagnosis.

299

MATURELY INHERITED INTERRISTIAL DELETION 11p15p15.4 IN A PATIENT WITH LONG QT SYNDROME AND BECKWITH-WIEDEMANN SYNDROME

Niaki M1, Wilnai Y1, Dunn K1, Perez M2, Miyake CY2, M Manning1.
1Stanford University, Stanford, CA and 2Baylor College of Medicine, Houston, TX.

Case Report: Long QT syndrome (LQTS) is associated with a high risk of life-threatening arrhythmias and sudden cardiac death. The most prevalent LQTS variant (LQT1) is caused by mutations in the KCNQ1 gene, with approximately half of the genotyped patients carrying KCNQ1 mutations. Although most cases of LQTS are attributed to mutations in KCNQ1, deletions or duplications are not typical (~3%). Beckwith-Wiedemann syndrome (BWS) is a clinically variable disorder caused by multiple molecular mechanisms including methylation abnormalities, mutations in CDKN1C, uniparental disomy, and cytogenetically detectable translocations, inversions, or duplications. Cytogenetic abnormalities involving chromosome 11p15.5 are detectable in 5-10% of patients with BWS. We report a case demonstrating the association of a rare maternally inherited deletion at 11p15.5 with LQTS and BWS.

A five-week-old male born prematurely was primarily diagnosed with omphalocele. Workup revealed a maternally inherited 915 KB interstitial deletion involving exons 2-16 of KCNQ1 and all of CDKN1C. DNA methylation analysis revealed a loss of methylation on the maternal chromosome for the BWS-IC2 critical region on chromosome 11p15.5. Methylation analysis of the BWS-IC1 critical region was consistent with normal bi-parental inheritance. Physical exam revealed the characteristic features of BWS with antenatal polydactyly of right foot. There was no reported family history of LQTS or BWS; however, the patient’s maternal aunt almost drowned during her thirties. Baby’s EKG revealed prolonged QTc of 556 ms. The patient’s mother was also found to have LQTS.

KCNQ1 mutations have been associated with LQTS. Recently, two reports described LQTS in individuals with small KCNQ1 deletions. To our knowledge this is the largest reported deletion of the KCNQ1 gene. BWS with congenital LQTS is extremely rare; however, it should be evaluated for systematically in patients with BWS and 11p15 deletions or rearrangements due to the risk of lethal complications.

300

ORAL-FACIAL-DIGITAL SYNDROME TYPE 1 IN A GIRL WITH VARIANT TURNER SYNDROME

Ramanathan S, Clark RD. Loma Linda Health, San Bernardino, CA.

Purpose of Study: We present a case of a female with variant Turner syndrome, with a karyotype of 46,X,idi(X)(p11.2) and clinical features of oral-facial-digital syndrome, type 1.

Methods Used: On physical exam, she had hypertelorism, midline notch of cleft lip with cleft palate and bifid upper midline frenulum. She had nevus flammeus on her nose, but no facial milia. She had hypoplasia of the fifth, six, and seven fingers and a single transverse palmar crease on left. She had a nasal encephalocoele, detected on maxillofacial CT-scan. An MRI of the brain showed bilateral occular globe colobomas, absence of the corpus callosum, pituitary ectopia and mild “molar tooth” malformation. An abdominal ultrasound was normal. She has global developmental delays at 11 months of age. The family history is non-contributory, except for advanced paternal age (40). Her clinical features are suggestive of oral-facial-digital syndrome type 1 (OFD1). OFD1, a ciliopathy, is characterized by malformations of the face, oral cavity and digits and is caused by mutations in the OFD1 gene.

Summary of Results: The disorder is inherited in an X-linked dominant manner and is presumed to be lethal in males and in hemizygous females with Turner syndrome, like our patient. There is wide variability of clinical findings in sporadic and familial cases among heterozygous females. OFD1 is located at Xp22.2 and is one of the 20% of X-chromosomal genes that escape X-inactivation. Some genes that escape inactivation still have variable levels of expression in some tissues. However patterns of X-inactivation studied in families with OFD1 show no consistent correlation between the degree of skewing and clinical severity. We believe that the gene is deleted on the abnormal X-chromosome in our patient and that there must be skewing X-inactivation, with the structurally abnormal X being inactive in the majority of cells. This alone would not be sufficient for her to have clinical features of OFD1. Studies are underway in order to determine whether a disease-causing mutation in her maternal copy of the OFD1 gene can be identified in her. We will also perform microarray analysis to determine the deleted interval on the idic(X).

Conclusions: To our knowledge, she is the first female with Turner syndrome to be reported with OFD1. As such, we cannot explain why the condition is not lethal in her.

301

ADDITIONAL EVIDENCE FOR CACNA1A MUTATION AS A CAUSE OF PAROXYSMAL TONIC UPWARD GAZE: REPORT OF A SECOND FAMILY

Macmurd CF, Myers A, Bernstein JA. Stanford University School of Medicine, Stanford, CA.

Case Report: Paroxysmal tonic upward gaze is a syndrome of abnormal ocular movements that was first described by Ouvrier and Billson in 1988. Clinical features include sustained conjugate upward deviation of the eyes with an onset before one year of age and normal horizontal gaze. The spectrum of paroxysmal tonic upward gaze can include ataxia, developmental disorders, unsteady gait, and epilepsy but is generally considered benign with resolution by five years of age in most patients. In 2008, Rouberte et al reported a family with paroxysmal tonic upward gaze, paroxysmal torticollis of infancy, and episodic ataxia in association with a CACNA1A mutation. We report a second similarly affected family with two brothers with paroxysmal tonic upward gaze and mother with symptoms of torticollis and migraines. All three family members have a CACNA1A mutation in exon 11 c.1369G>A, p.Ala454Thr. This family provides additional evidence for CACNA1A mutation as a cause of paroxysmal tonic upward gaze and related phenotypes. We will present the clinical findings in this family and review those previously reported for this emerging syndrome.

Neonatology - General III
Concurrent Session
3:30 PM Friday, January 24, 2014
using gas chromatography. mRNA levels of FADS1 (Δ5-desaturase), FADS2 (Δ6-desaturase), ELOVL2 (elongase 2) and ELOVL5 (elongase 5) were measured using real-time RT PCR.

**Summary of Results:** Results are IUGR as % sex-matched control ± SD, (p < 0.05). In male serum, IUGR decreases conversion of ALA to EPA (21±11%) and increases conversion of EPA to DHA (260±74%). In male lung, IUGR decreases conversion of LA to AA (76±15%). In female serum, IUGR increases in conversion of LA to AA (115±9%). In male liver, IUGR decreases mRNA levels of FADS1 (65±31%), ELOVL2 (73±55%), and ELOVL5 (65±10%). In male lung, IUGR increases mRNA levels of FADS2 (142±26%). IUGR did not affect mRNA levels of conversion enzymes in female lung.

**Conclusions:** IUGR alters serum and lung EFA as well as mRNA of EFA conversion enzymes in a sex-dependent manner. Changes in expression of EFA conversion enzymes in rat serum and lung may contribute to altered EFA levels. Given that EPA acts as ligands for several transcriptional regulators, we speculate that dysregulated EPA will alter gene expression profiles in the lung.

---

**303**

**UTERINE-SPECIFIC ANTI-INFLAMMATORY ACTIONS OF THE PROGESTERONE SIGNALING PATHWAY**

Encino JM1, Goddard LM2, Iruela-Arispe M2. 1David Geffen School of Medicine at UCLA, Los Angeles, CA and 2UCLA, Los Angeles, CA.

**Purpose of Study:** The progesterone receptor (PR) is a member of a large family of ligand-activated nuclear receptors that binds to DNA as a receptor for steroids, retinoids, thyroid hormones, and vitamin D. The anti-inflammatory effects of glucocorticoids are well known, however the anti-inflammatory role of the hormone progesterone and the receptor interactions through which progestational agents exert their anti-inflammatory effects is less understood. The goal of this study is to understand the cell-specific role of PR in inflammation and determine more precisely the receptor interactions through which progesterone exerts its anti-inflammatory effects in vivo.

**Methods Used:** Uterine inflammation was evaluated in vivo in control mice and in mice with either global deletion of PR or conditional deletion of endothelial PR. Uterine leukocytes were isolated and innate immune cells were identified by Gr1 and CD11b staining and quantified by flow cytometry. The anti-inflammatory effects of the progesterin medroxyprogesterone (MPA) were assessed by treating with MPA 2.5 mg SQ. Effects of GR inhibition were assessed after treatment with MPA 2.5 mg SQ + RU486 500 mcg SQ.

**Summary of Results:** Mice with global (PRKO) and endothelial PR deletion (PR ECKO) had increased uterine inflammation compared with control mice as evidenced by increased recruitment of Gr1+CD11b+ cells (PMNs). This finding was unique to the uterus and not observed in other organs (i.e. lung) which lack PR expression. Treatment of PRKO and PR ECKO mice with MPA exerted an anti-inflammatory effect in the uterus, thus demonstrating a PR-independent effect of MPA. GR inhibition with RU486 abrogated the anti-inflammatory effect of MPA in both PRKO and PR ECKO mice, thus providing in vivo evidence that MPA exerts anti-inflammatory effects through GR-mediated signaling.

**Conclusions:** Our data support a role for PR in suppressing the innate immune response and lends insight into the anti-inflammatory action of progestins in vivo. Further understanding of the precise receptor-mediated actions of progestins may lead to new therapeutic approaches for modulating uterine inflammation associated with pathological processes such as preterm labor, endometriosis, and implantation failure.

---

**304**

**INTRAVENTRIS LOW DOSE SOYBEAN OIL IN PRETERM INFANTS: LONG-TERM FOLLOW-UP ON GROWTH AND NEURODEVELOPMENT**

Ong ML1, Purdy F2, Molchan L2, Grogan T3, Elashoff D4, Calkins KL2. 1David Geffen School of Medicine, UCLA, Los Angeles, CA; 2David Geffen School of Medicine, UCLA, Los Angeles, CA and 3Statistics Core, UCLA, Los Angeles, CA.

**Purpose of Study:** Preterm infants are at risk for developing failure-to-thrive, neurodevelopmental impairment, and parenteral nutrition associated liver disease (PNALD). Improved growth is associated with improved neurodevelopment in this population. However, a reduced incidence of PNALD has been associated with a reduced dose of soybean-based intravenous fat emulsions (IFE). The long-term safety of low dose IFE remains unclear. The objective of the study was to determine the effect of IFE dose reduction on long-term growth and neurodevelopment in preterm infants.

**Methods Used:** This is a follow-up retrospective study to a multi-center randomized controlled trial. Neonates with a gestational age ≤ 29 weeks were prescribed either 1g/kg/d (LOW) or approximately 3g/kg/d (CONTROL) IFE within the first 48 hours of birth for the duration of their parental nutrient. Growth measurements, z-scores, and Bayley Scales of Infant Development III scores were collected for LOW and CONTROL at approximately 6 (FU1) and 12 months corrected gestational age (FU2).

**Summary of Results:** Preliminary results are available for 37 subjects from one site (LOW=18, CONTROL=19). There were no differences in baseline characteristics between the two groups. There were no significant differences at FU1 and FU2 between the two groups for weight, length, and head circumference for absolute values (p > 0.5 for all) and z-scores (p > 0.7 for all). Bayley scores were also comparable between LOW and CONTROL at FU1 and FU2 for receptive language, expressive language, fine motor, and gross motor subscales (p > 0.1 for all).

**Conclusions:** At this time, IFE dose reduction does not appear to affect long-term growth and neurodevelopment in this study. However, follow-up on this cohort continues and is needed.

---

**305**

**IMPLEMENTATION OF A STANDARDIZED INPATIENT TREATMENT GUIDELINE FOR NEONATAL ABSTINENCE SYNDROME DECREASES LENGTH OF STAY**

Lampland A1,2, Engel M2, Symalla B3, Poster A3. 1Children's Hospitals and Clinics of Minnesota - St. Paul, St. Paul, MN; 2University of Minnesota, Minneapolis, MN and 3Children's Hospitals and Clinics of Minnesota - St. Paul, St. Paul, MN.

**Purpose of Study:** To test if implementation of a multi-disciplinary standardized in-patient methadone treatment algorithm for in-utero opioid exposed infants with neonatal abstinence syndrome (NAS) would decrease length of stay in our Level II/III NICUs and not adversely effect re-hospitalization rates.

**Methods Used:** Retrospective chart review was performed from January 2012 - June 1, 2013. Inclusion criteria: 1) ≥35 weeks gestational age at birth, 2) diagnosed with NAS and required in-patient methadone therapy 3) cared for exclusively by neonatologists, and 4) out-patient care with pain/palliative care clinic. 20 infants in 2012 and 6 infants through June 1, 2013 met inclusion criteria. Infants born in 2012 were not on a standardized NAS treatment protocol (2012PRE). Infants born in 2013 were treated using a standardized NAS treatment protocol that was implemented by the neonatology division on January 1, 2013 (2013POST). Data were analyzed using 2-sample t-test and Fisher's exact test as appropriate. P-values <0.05 were significant.

**Summary of Results:** Initial methadone treatment dose was significantly higher in the 2012PRE group versus the 2013POST group (p-value 0.017). Average length of stay for 2012PRE was 13.5 days and 2013POST was 11.2 days (p-value 0.35). The lowest, highest and average Finnegan neonatal abstinence scores were similar in both groups in the two days prior to discharge. Total days of methadone treatment, length of outpatient methadone treatment, NAS-related re-hospitalization rates within 7 days of discharge, breast feedings rates at hospital discharge, and breast feedings rates at conclusion of methadone therapy were similar in both groups.

**Conclusions:** On preliminary analysis after 5 months of implementation, the standardized NAS treatment protocol appears successful in achieving lower initial methadone treatment doses, shorter times of hospitalization, and no increase in re-hospitalization rates. Analysis will be repeated upon completion of one full year of post-intervention treatment.

---

**306**

**EFFECT OF PRE-MEDICATION REGIMEN ON INFANT PAIN AND STRESS RESPONSE TO ENDOTRACHEAL INTUBATION**

Caldwell C, Watterberg K. University of New Mexico, Albuquerque, NM.

**Purpose of Study:** Endotracheal intubation is a frequent procedure in the newborn intensive care unit (NICU). Although it is likely to be painful and stressful, many infants undergo this procedure without paraldehyde or sedation, and those that are medicated receive variable medication regimens.

**Methods Used:** For non-emergent endotracheal intubations, (1) medications were recorded; (2) the DAN pain score was recorded during the laryngoscopy...
null glucose was obtained on scavenged blood from the post-in- 
tubation blood gas, and the change from the most recent pre-procedure
glucose documented. Infant responses were compared by MANOVA.

Summary of Results: From 1-2012 to 6-2013, complete data were obtained on 
166 infants. Medications included: (1) none, 44 (27%); (2) fentanyl, 23 (14%); (3) 
fentanyl + midazolam (F+M), 32 (19%); (4) morphine, 31 (19%); (5) morphine + 
midazolam, 19 (11%); and (6) midazolam 17 (10%). No infant received muscle 
relaxant. Only F+M was associated with lower pain/stress measures vs. ‘no’ 
or other medications (DAN score, p<0.005; glucose, p<0.005) and with fewer 
pre-defined complications (p<0.004). There was no difference in laryngoscope 
dwell time (p = 0.55) or in the total number of attempts (p = 0.145) between 
medications. Infants <29 weeks showed pain/stress responses similar to more ma-
ture infants, but were less likely to receive medication (p = 0.023).

Conclusions: Of the medication regimens used for non-emergent endotra-
chlear intubation in our NICU, only F+M showed significant benefit. Al-
though preterm infants showed both clinical and biochemical evidence of 
pain/stress, they were less likely to receive medication.

307
NEONATAL ORGAN DONATION FOLLOWING 
CIRCULATORY DEATH: WHAT IS THE POTENTIAL?
Stiers J1, Aguayo C2, Siatta A2, DiGeronimo R1. 1University of Utah, SLC, UT and 
2Intermountain Healthcare, SLC, UT.

Purpose of Study: The demand for transplantable organs continues to in crease. 
Historically, newborns have not been eligible for solid organ donation given the 
technical difficulties of transplanting such small organs. However, recent im-
proved organ preservation and surgical techniques have led to a renewed interest 
on newborns as potential candidates for organ donation after circulatory determi-
nation of death (DCDD). We aimed to determine the percentage of neonatal 
deaths from a single, level-IV regional NICU that would meet current criteria 
for DCDD, as well as the primary reasons why infants were excluded.

Methods Used: This is a retrospective study of all newborns admitted into Pri-
mary Children’s Hospital (PCH) NICU between Jan 1, 2010 and May 7, 2013 
who died prior to discharge. De-identified data was collected prospectively on 
all admissions as part of the Children’s Hospital Neonatal Database (CHND). 
Primary outcome was theoretical eligibility for organ donation as determined by 
Intermountain Donor Services criteria (weight, ventilation status, and warm ischemic 
time). Secondary outcomes included: Primary diagnosis, cause of death, liver func-
tion, renal function and whether organs and/or tissues were donated.

Summary of Results: Of the 136 neonatal deaths at PCH during the study period, 
74 (54.4%) met weight criteria for organ donation. 13 of these deaths 
occurred without withdrawal of life sustaining interventions (LSI) and 72 did 
not require mechanical ventilation. 46 newborns (33.8%) met weight and 
ventilation criteria and died within 90 minutes. The most common diagnosis 
of eligible patients was multiple congenital anomalies/syndrome (n=20), 
followed by profound CNS injury (n=17). Median warm ischemic time 
was 51 minutes. No brain deaths occurred. Of the 46 eligible newborns, only 
4 (2.9%) underwent organ/tissue procurement for donation.

Conclusions: In our study population, a significant percentage of newborns 
appeared to be candidates for DCDD. However, the majority of those eligible 
for DCDD did not end up as donors. We speculate many patients were pre-
sumed ineligible based on historical standards and therefore not offered or-
gan donation as a component of end-of-life care. Further assessment of 
provider knowledge may provide opportunities to narrow the current gap be-
 tween potential and actual organ donation.

308
RELATIVE ADRENAL INSUFFICIENCY (RAI): UNRECOGNIZED 
IN BABIES WITH CONGENITAL HEART DISEASE (CHD)
Sondhi M, Tran J, Melwak M, Purdy I, Devaskar U. UCLA, Los Angeles, CA.

Purpose of Study: Intact Hypothalamus-Pituitary-Adrenal axis, involving 
complex interactions including metabolism & energy, is essential during 
stressful/diseased states. Cortisol is critical to the maintenance of normal ho-
moeostasis. Its deficiency can lead to hypoglycemia, hypotension, shock & 
death. RAI, the inability of a patient to mount an appropriate elevation in the 
capacity to respond to stressful stimuli, is essential during 
complex interactions including metabolism & energy, is essential during 
stressful/diseased states. Cortisol is critical to the maintenance of normal ho-
moeostasis. Its deficiency can lead to hypoglycemia, hypotension, shock & 
death. RAI, the inability of a patient to mount an appropriate elevation in the 
capacity to respond to stressful stimuli, is essential during

hypothalamic-pituitary-adrenal function, including metabolic & energy, is 
esential during stressful/diseased states. Cortisol is critical to the maintenance of 
normal homeostasis. Its deficiency can lead to hypoglycemia, hypotension, shock & death. RAI, the inability of a patient to mount an appropriate elevation in the capacity to respond to stressful stimuli, is essential during

309
FOCUSED PROTEOMIC PROFILING FOR RAPID DETECTION 
OF LATE-ONSET NEONATAL SEPSIS IN PRETERM INFANTS
Cannon DC1, Ohls RK2, Hartenberger C3, Peceny H4, Ballard K5, Mani S5, 1University of New Mexico Health Sciences Center, Albuquerque, NM; 4Myriad RBM, Austin, TX and 5UNM, Albuquerque, NM.

Purpose of Study: Present methods for diagnosing sepsis in preterm infants are 
less than ideal. Waiting for definitive blood culture results, which require 24 to 72 
hours to process and lack sensitivity, can lead to life-threatening delays in treat-
mant. Other diagnostic criteria using physiological parameters and clinical scores 
lack specificity and encourage over-treatment with antimicrobial agents, which 
can further the development of resistant organisms. Using recent advances in ma-
chine learning and proteomic assay technology, we sought to derive an algorithm 
for rapidly and reliably detecting sepsis in very low birth weight (VLBW) infants.

Methods Used: We enrolled 139 eligible VLBW infants (gestational age ≤ 32 
weeks, birth-weight ≤ 1500 grams, postnatal age ≥ 120 hours) over a five year 
period from 2007 to 2012. Using a procedure based upon the current best practice at 
MCJCH, we assigned gold-standard diagnostic labels to the infants; we categorized 
46 as cases (culture positive sepsis) and the remaining 93 as controls (sepsis negative). 
We used serum samples collected from each infant over a 21-day period to perform a 
focused proteomic assay of 90 potential biomarkers suspected to play a role in infec-
tion and inflammation. Using stratified 10-fold cross-validation, we evaluated a vari-
ety of machine learning methodologies including Random Forests (RF), C4.5, 
ADT, logistic regression, and Na"ive Bayes. To enhance the sensitivity of our 
model, we combined RF with SMOTE, a technique for constructing classifiers 
from imbalanced datasets, and MetaCost, a cost-sensitive meta-classifier.

Summary of Results: Unenhanced, RF significantly outperformed other ma-
chine learning algorithms with an AUC of 0.86, sensitivity of 56%, and spec-
ificity of 95%. Using SMOTE, we increased sensitivity to 65% while slightly 
decreasing specificity to 89%. With the additional use of MetaCost, we in-
creased sensitivity to 90% while specificity decreased to 51%.

Conclusions: While additional validation is necessary before contemplating 
clinical use, our results suggest the potential utility of a proteomics-based di-
agnostic tool for the detection of sepsis in preterm infants.

Nephrology and Hypertension
Concurrent Session
3:30 PM
Friday, January 24, 2014
310
ANTIBODY-DEPENDENT NK CELL ACTIVATION: AN 
IMPORTANT MEDIATOR OF ANTIBODY MEDIATED 
ALLOGRAFT REJECTION

235

© 2013 The American Federation for Medical Research
Conclusions: complement-independent ABMR.

Purpose of Study: Complement activation by donor-specific anti-HLA antibodies (DSA) is important for mediation of antibody-mediated rejection (ABMR). This is commonly detected by C4d deposition in biopsies or C1q activation in DSA testing. However, antibody-dependent cellular cytotoxicity (ADCC) mediated by (NK) cell involvement may play an important role in ABMR.

Methods Used: Here, we investigated the role of NK cell-mediated ADCC in ABMR utilizing an in vitro ADCC model that identified genes associated with ADCC using microarray analysis and subsequently evaluated the ADCC-activated gene expression in human kidney biopsies.

Summary of Results: We identified 13 ADCC-activated genes. Six genes (CCL3, CCL4, CD160, IFNG, NR4A3 and XCL2) were subsequently analyzed in 127 kidney biopsies obtained from HLA-sensitized (HS), non-HS patients and controls. Most ADCC-activated genes showed significantly higher expression in the transplant samples compared to the controls (p<0.0005). The gene expression levels in HS patients were high and not different between those with and without ABMR for most ADCC-activated genes, while only those with ABMR in non-HS patients showed ADCC-associated gene expression (p=0.002-0.001). Samples with high panel reactive HLA antibodies (>80%) or positive DSA showed higher gene expression compared to low PRA (<80%) and negative DSA (p=0.04-0.001).

Conclusions: In conclusion, ADCC pathways are active in HS patients and likely mediate allograft injury, providing a potential mechanism for complement-independent ABMR.

311

THE EFFECT OF CD4 T CELL KNOCKOUT ON CISPLATIN-INDUCED AKI AND LUNG CANCER IN MICE


Purpose of Study: Nephrotoxicity is cisplatin’s major dose-limiting side effect as a chemotherapeutic agent. Most previous in vivo studies of cisplatin-induced AKI (AKI) have been in models of acute (3 days), high dose (25mg/kg) cisplatin administration that leads to mortality in non-tumor bearing mice. We have previously described that inhibition of IL-33, CD4 T cells or CXCL1 is protective against AKI in a 3 day model. We have developed a model of 4 week, low dose cisplatin administration in mice with cancer, that closely resembles the cisplatin dosing regimen used in humans with non small cell lung cancer. In a 4 week model of AKI, the increase in IL-33, CD4 T cells and CXCL1 precedes the AKI and tubular injury suggesting that these proteins may play a causative role. The aim of the study was to determine the effect of CD4 T cell depletion on AKI and the growth of lung cancer.

Methods Used: Wild type (WT) C57BL/6 or CD4 T cell -/- mice were injected subcutaneously with murine lung cancer cells derived from C57BL/6 mice. Ten days later, cisplatin (10 mg/kg/week) was given for 4 weeks.

Summary of Results: See Table. The decrease in BUN and SCr in CD4 -/- mice vs. WT mice with AKI was not yet statistically significant. Tumor weight was double in CD4 -/- vs. WT mice. Cisplatin prevented the increase in tumor volume in WT mice but not in CD4 -/- mice. Tumors in CD4 -/- mice started enlarging at 1 week and were significantly larger at 3 and 4 weeks.

Conclusions: CD4 -/- mice with AKI have a lower BUN and SCr than WT mice with AKI. These results suggest autophagic flux protects from apoptosis during WR but does not prevent caspase-1 activation nor necrotic cell death. Autophagy inhibitors should be used with caution during donor kidney reperfusion.

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>CD4 -/-</th>
<th>CD4 -/-/CIS</th>
<th>CD4 -/-/CIS</th>
<th>CD4 -/-/Lung</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN mg/dl</td>
<td>21 20.7</td>
<td>128 23.5*</td>
<td>19 2.6</td>
<td>87 2.6*</td>
<td>87 2.6*</td>
</tr>
<tr>
<td>SCr mmol/l</td>
<td>0.7 0.03</td>
<td>0.7 0.02**</td>
<td>0.7 0.02</td>
<td>0.6 0.04**</td>
<td>0.6 0.04**</td>
</tr>
<tr>
<td>Tumor wt (g)</td>
<td>0.7 0.01</td>
<td>0.6 0.003</td>
<td>1.4 0.2</td>
<td>0.4 0.2</td>
<td>0.4 0.2</td>
</tr>
<tr>
<td>Tumor Volume Wk 1 (cubic mm)</td>
<td>68 12</td>
<td>62 17</td>
<td>102 24</td>
<td>89 16</td>
<td></td>
</tr>
<tr>
<td>Tumor Volume Wk 2</td>
<td>184 25</td>
<td>61 17*</td>
<td>507 93</td>
<td>94 2a 19**</td>
<td></td>
</tr>
<tr>
<td>Tumor Volume Wk 3</td>
<td>375 56</td>
<td>72 48*</td>
<td>714 11***</td>
<td>185 20**</td>
<td></td>
</tr>
<tr>
<td>Tumor Volume Wk 4</td>
<td>882 116</td>
<td>67 35*</td>
<td>152 16**</td>
<td>238 27**</td>
<td></td>
</tr>
</tbody>
</table>

Methods Used: cisplatin (10 mg/kg/week) was given for 4 weeks. To simulate rewarming, UW was replaced with DMEM containing bovine serum at 37°C for 24h. LLCPK cells incubated at 37°C served as controls. Immunoblot and densitometry were used to assess active caspase-3 and 1 and LC3-II, a marker of autophagic flux. Cells were incubated with Baflomycin, lysosomal inhibitor or wortmannin, a PI3 kinase inhibitor before CI.

Summary of Results: During CI, caspase-1 was not increased whereas apoptosis and active caspase 3 were significantly increased vs. controls (Table 1). Treatment with Baflomycin and wortmannin did not change LC-3 II protein expression during CI indicating that autophagic flux was not increased. In contrast, during WR, apoptosis and caspase-3 did not increase whereas caspase-1 and necrosis increased significantly. Treatment with Baflomycin during WR resulted in significantly more LC-3II expression (indicating increased autophagic flux) and apoptosis but had no effect on necrosis or caspase-1.

Conclusions: During CI, caspase-3 and apoptosis are increased but autophagic flux is not. In contrast, autophagic flux, caspase-1 and necrosis are increased during WR. Baflomycin and wortmannin increased caspase-3 and apoptosis during both CI and WR, but had no effect on caspase-1. These results suggest autophagic flux protects from apoptosis during WR but does not prevent caspase-1 activation nor necrotic cell death. Autophagy inhibitors should be used with caution during donor kidney reperfusion.

312

THE ROLE OF INCREASED AUTOPHAGIC FLUX IN RENAL TUBULAR EPITHELIAL CELLS UNDERGOING WARM REPERFUSION (WR) AFTER COLD ISCHEMIA (CI)

Jani A, Jain S, Nydam TL, Edelstein C. University of Colorado Denver, Aurora, CO.

Purpose of Study: Delayed graft function (DGF) is primarily caused by CI and WR. The mechanism by which CI and WR causes RTE cell death is not known. We hypothesized that increased autophagic flux and apoptosis occur during CI and WR of RTE cells.

Methods Used: RTECs (LLC-PK1) were subjected to CI in UW at 4°C for 24h. To simulate rewarming, UW was replaced with DMEM containing bovine serum at 37°C for 24h. LLCPK cells incubated at 37°C served as controls. Immunoblot and densitometry were used to assess active caspase-3 and 1 and LC3-II, a marker of autophagic flux. Cells were incubated with Baflomycin, lysosomal inhibitor or wortmannin, a PI3 kinase inhibitor before CI.

Summary of Results: During CI, caspase-1 was not increased whereas apoptosis and active caspase 3 were significantly increased vs. controls (Table 1). Treatment with Baflomycin and wortmannin did not change LC-3 II protein expression during CI indicating that autophagic flux was not increased. In contrast, during WR, apoptosis and caspase-3 did not increase whereas caspase-1 and necrosis increased significantly. Treatment with Baflomycin during WR resulted in significantly more LC-3II expression (indicating increased autophagic flux) and apoptosis but had no effect on necrosis or caspase-1.

Conclusions: During CI, caspase-3 and apoptosis are increased but autophagic flux is not. In contrast, autophagic flux, caspase-1 and necrosis are increased during WR. Baflomycin and wortmannin increased caspase-3 and apoptosis during both CI and WR, but had no effect on caspase-1. These results suggest autophagic flux protects from apoptosis during WR but does not prevent caspase-1 activation nor necrotic cell death. Autophagy inhibitors should be used with caution during donor kidney reperfusion.

313

IS THERE AN EFFECT OF ETHNICITY ON eGFR DETERMINATION AMONG NEW MEXICANS WITH PREDIABETES?

Camacho JE1, Wong C2, Burge M1. 1University of New Mexico, Albuquerque, NM and 2University of New Mexico, Albuquerque, NM.

Purpose of Study: Patients with prediabetes mellitus (PreDM) may exhibit microvascular complications of diabetes, such as retinal hyperfiltration and microalbuminuria, prior to the onset of overt type 2 diabetes (T2D). Because people of Hispanic ethnicity are disproportionately affected by T2D and diabetic kidney disease compared to Non-Hispanic Whites (NHW), we hypothesized that Hispanic PreDM patients would exhibit increased estimated glomerular filtration rate (eGFR) compared to NHW subjects at the time of PreDM diagnosis.

Methods Used: One hundred and ninety seven adults were screened to determine their glucose homeostasis status. Inclusion criteria were an age greater than 18 years plus at least one of the following risk factors: a family history of diabetes in a first degree relative, a history of gestational diabetes, Hispanic ethnicity, non-Caucasian race, or obesity. All subjects received a fasting 75 gram Oral Glucose Tolerance Test (OGTT) and A1c at screening. Serum
creatinine was determined enzymatically by a central laboratory. We utilized the MDRD equation to determine eGFR as our measure of kidney function.

**Summary of Results:** One hundred subjects had normal glucose tolerance (A1c < 5.7%). 90 subjects were determined to have PreDM (A1c = 5.7% - 6.4%) and 7 subjects were diagnosed with new T2D (A1c > 6.4%). Estimated GFR increased with worsening glycemic status (Spearman correlation coefficient = 0.16; p = 0.03). Although an effect of ethnicity on eGFR was initially apparent (see Table), this effect was no longer apparent after adjusting for age using ANCOVA (p = 0.22).

**Conclusions:** The apparent differences in eGFR between Hispanics and Non-Hispanic Whites with prediabetes in this study were attributable to age differences between the two groups. There is no independent effect of ethnicity on eGFR among New Mexicans with PreDM.

**Purpose of Study:** In order to standardize care of childhood nephrotic syndrome (NS) patients across the province of British Columbia (BC), the Nephrology division at BC Children's Hospital (BCH) developed an evidence-based clinical pathway (CPW). An important step of this CPW development was to determine the extent of practice variation locally and to determine how this has impacted patient outcomes at our center.

**Methods Used:** We performed a retrospective analysis of NS cases treated at BCH from 1990-2010. We excluded those with a secondary cause of NS, those <1 year of age at diagnosis and those with steroid resistance. We explored cumulative prednisone dose (mg/m²) and duration of induction treatment (days) as sources of practice variation. We defined “low” and “high” dose prednisone groups as those prescribed less than or greater than the mean cumulative dose, respectively. We defined “short” and “long” duration groups as those prescribed prednisone for less than or greater than the mean duration of treatment, respectively. The primary outcomes were the total number of relapses in 3 years and the time to first relapse after completion of induction treatment (days).

**Summary of Results:** Mean (SD) cumulative prednisone dosing at induction was 2688 mg/m² (915 mg/m²). Mean (SD) duration of prednisone treatment was 118 days (47 days). The number of relapses was significantly lower in the “low” vs “high” dose prednisone group (3.7 vs 2.5 relapses/patient) and in the “short” vs “long” prednisone group (3.9 vs 2.3 relapses/patient). Higher cumulative prednisone doses at induction and longer induction periods were also associated with better 3 year relapse-free survival.

**Conclusions:** Significant practice variation exists in the induction treatment of childhood NS within the province of BC. This has a direct impact on disease outcomes, including the number of future relapses and time to first relapse. The variation in practice and clinical outcomes supports the development and implementation of a CPW for the treatment of childhood NS. This will standardize and improve patient care across the province. These results will also serve as a historical control for future evaluation of the CPW.

**Diuretic Management of Patients with Stage 3 and 4 Chronic Kidney Disease**

Schulte SR, Darath KB, 1,2 University of Washington, School of Medicine, Spokane, WA and Washington State University, Spokane, WA.

**Purpose of Study:** Chronic kidney disease (CKD) is a highly prevalent disease with poor health outcomes that benefit from the use of evidence-based antihypertensive management. The small amount of evidence for the role of thiazides and loop diuretics in antihypertensive management of CKD is conflicting. The purpose of this study is to determine whether diuretic therapy in Eastern Washington corresponds with the KDOQI guidelines through the use of medication discharge summaries for individuals with Stage 3 and 4 CKD.

**Methods Used:** Patients hospitalized in Eastern Washington from April 2007 to September 2011 who survived to discharge (N=645) were classified as stage 3 and 4 CKD by application of the CKD-EPI equation to laboratory serum creatinine measures. Patients were further classified as having received or not receiving a diuretic by analysis of discharge records. Cox proportional hazard models controlling for age, sex, payer, comorbidity, previous hospitalization, primary diagnosis category, and length of stay were conducted for time to event analyses.

**Summary of Results:** Forty percent of patients did not receive diuretics. The diuretic cohort was more likely to have diabetes mellitus (p<0.05), CHF (p<0.01), obesity (p<0.01) and valvular disease (p<0.01). Both stages of CKD received diuretics at similar rates (p=0.27) but progression from stage 3 to stage 4 was associated with an increase in loop diuretic prescription (p<0.05). Diuretic prescription declined by year of study for patients with stage 3 CKD (p<0.01). The diuretic cohort was more likely to be hospitalized for congestive heart failure (p<0.05) but the two cohorts had similar risk for rehospitalization (p=0.40) and primary diagnoses for rehospitalization (p=0.07).

**Conclusions:** The trends observed in this study were not uniformly in accordance with the KDOQI diuretic guidelines. It was surprising to find that such a large portion of this population is not receiving diuretic medications, and that this prescription grew larger over the course of this study. Trends in diuretic management help to illuminate the care that patients are receiving and whether it is in accordance with the guidelines. Future studies should seek to further understand the care patients with CKD are receiving in order to improve the long-term outcome of these patients.

**Lupus Nephritis and Podocytopathy in an Adolescent Female: A Case for a Mutual Relationship**

Shirley B, Staples A. University of New Mexico, Albuquerque, NM.

**Case Report:** The International Society of Nephrology/Renal Pathology Society revised the lupus nephritis (LN) classification in 2003. This system grades severity of LN within the glomerulus and aids in management. Proteinuria, especially nephrotic range, is not unexpected in LN, however it generally coincides with disruption of the capillary wall by immune complexes (IC). Several reports of patients with lupus describe nephrotic range proteinuria in the absence of subendothelial or subepithelial immune complex deposition. Rather, effacement of the epithelial cell foot processes as seen in minimal change nephrotic syndrome (NS) appears to be the structural feature explaining such degree of proteinuria.

We report a case of a 15 yo Hispanic female who presented with acute onset of edema. Her initial urine protein to creatinine ratio was 4.1 and serum albumin 1.4 g/dL. A renal biopsy demonstrated normal glomeruli with open capillary loops by light microscopy, with no evidence of glomerular hypercellularity or necrosis. Immunofluorescence demonstrated mesangial staining for IgG, IgA, IgM, C3, C1q, lambda and kappa light chains. Electron microscopy revealed effacement of foot processes, with IC deposits localized to the mesangium and paramesangium. She had no systemic symptoms to suggest a diagnosis of systemic lupus erythematosus (SLE). Serologic evaluation exhibited qualifying criteria for SLE with positive ANA, dsDNA antibodies, antinuclear antibodies, IgG antibody and lymphopenia. The patient was started on a course of prednisone 60mg per day and mycophenolate 1000mg twice daily. The patient had a rapid response with resolution of her proteinuria such that weaning of the prednisone was possible. At 12 months from presentation she has quiescence of NS on mycophenolate alone.

Our patient is another example of NS related to loss of integrity in podocyte architecture in a patient with LN class I, consistent with a diagnosis of lupus podocytopathy. Furthermore, our patient had no diagnosis of SLE and thus the heralding manifestation was lupus podocytopathy. Perhaps this distinction may be considered in future revisions of the LN classification. Additionally, clinicians should be aware that while minimal change NS is common in pediatrics, maintaining suspicion of an underlying diagnosis of SLE is prudent.

**IN-CENTER PRACTICE VARIATION IN THE TREATMENT OF CHILDMOHLD Nephrotic Syndrome AFFECTS OUTCOMES**

Sibbey MA1,2, Sibley J,2 Kwock T2, Jobsis J,2 Alshami A, Matsell D,2 Mammen C,2 BC Children's Hospital, Vancouver, BC, Canada and University of British Columbia, Vancouver, BC, Canada.

**Purpose of Study:** In order to standardize care of childhood nephrotic syndrome (NS) patients across the province of British Columbia (BC), the Nephrology division at BC Children’s Hospital (BCH) developed an evidence-based clinical pathway (CPW). An important step of this CPW development was to determine the extent of practice variation locally and to determine how this has impacted patient outcomes at our center.

**Methods Used:** We performed a retrospective analysis of NS cases treated at BCH from 1990-2010. We excluded those with a secondary cause of NS, those <1 year of age at diagnosis and those with steroid resistance. We explored cumulative prednisone dose (mg/m²) and duration of induction treatment (days) as sources of practice variation. We defined “low” and “high” dose prednisone groups as those prescribed less than or greater than the mean cumulative dose, respectively. We defined “short” and “long” duration groups as those prescribed prednisone for less than or greater than the mean duration of treatment, respectively. The primary outcomes were the total number of relapses in 3 years and the time to first relapse after completion of induction treatment (days).

**Summary of Results:** Mean (SD) cumulative prednisone dosing at induction was 2688 mg/m² (915 mg/m²). Mean (SD) duration of prednisone treatment was 118 days (47 days). The number of relapses was significantly lower in the “low” vs “high” dose prednisone group (3.7 vs 2.5 relapses/patient) and in the “short” vs “long” prednisone group (3.9 vs 2.3 relapses/patient). Higher cumulative prednisone doses at induction and longer induction periods were also associated with better 3 year relapse-free survival.

**Conclusions:** Significant practice variation exists in the induction treatment of childhood NS within the province of BC. This has a direct impact on disease outcomes, including the number of future relapses and time to first relapse. The variation in practice and clinical outcomes supports the development and implementation of a CPW for the treatment of childhood NS. This will standardize and improve patient care across the province. These results will also serve as a historical control for future evaluation of the CPW.

**314**

**315 IN-CENTER PRACTICE VARIATION IN THE TREATMENT OF CHILDMOHLD Nephrotic Syndrome AFFECTS OUTCOMES**

Sibley MA1,2, Sibley JA2, Kwock T2, Jobsis J1,2, Alshami A1,2, Matsell D1,2, Mammen C1,2 BC Children's Hospital, Vancouver, BC, Canada and University of British Columbia, Vancouver, BC, Canada.

**Summary of Results:** One hundred subjects had normal glucose tolerance (A1c < 5.7%). 90 subjects were determined to have PreDM (A1c = 5.7% - 6.4%) and 7 subjects were diagnosed with new T2D (A1c > 6.4%). Estimated GFR increased with worsening glycemic status (Spearman correlation coefficient = 0.16; p = 0.03). Although an effect of ethnicity on eGFR was initially apparent (see Table), this effect was no longer apparent after adjusting for age using ANCOVA (p = 0.22).

**Conclusions:** The apparent differences in eGFR between Hispanics and Non-Hispanic Whites with prediabetes in this study were attributable to age differences between the two groups. There is no independent effect of ethnicity on eGFR among New Mexicans with PreDM.
Surgery B
Concurrent Session
3:30 PM
Friday, January 24, 2014
317
EVALUATION OF 3D PHOTOGRAPHIC IMAGING TO MEASURE DIFFERENTIAL VOLUMES IN RECONSTRUCTED BREAST TISSUE
Lewis P. Mattison G, Kim H, Gupta S. Loma Linda University, Loma Linda, CA.
Purpose of Study: Hemoglobin (Hb) measurements inform clinical transfusion decision-making. Multi-wavelength pulse CO-oximeters have been developed for mas- sectomy patients in the delayed breast reconstruction process. After mastectomy an inflatable tissue expander is placed in the subpectoral pocket and filled with saline; fixed volumes, determined qualitatively, are added over weeks until an adequate pocket is available to accommodate a permanent implant. This method relies on the physician’s subjective opinions of aesthetic targets and 2D measurements. 3D photo technology has the potential to quantitatively improve the process by measuring patients’ natural breast volume thereby setting a target for fill volumes during reconstruction.
Methods Used: Known tissue expander fill volumes were compared to mea- sured breast volumes using the 3dMD® imaging system in 17 breasts. Patients were imaged before and after saline expansion at clinic appoint- ments until permanent implant placement. A linear regression analysis was conducted of the measured to known volume, and known fill volumes were compared to the measured/filled ratio.
Summary of Results: 17 reconstructed breasts from 10 patients were ana- lyzed. The ratio of measured to known fill volume had a mean of 1.265 with a standard deviation of 1.429 and SEM of 0.215 (p=5.07E-14), 95% CI=0.843 - 1.688. The measured/fill ratio was closer to 1:1 at higher fill volumes; the volume correlating to 1 was 91.72cc. The difference between known and measured volumes had a mean of 38.336 with a standard deviation of 43.605 and SEM of 6.574 (p=0.012), 95% CI=25.451 - 51.220.
Conclusions: Imaging using 3D photographic imaging has a great deal of potential for use in reconstructive procedures. In this preliminary study, there appears to be a quanti- tative relationship between the volume added and achieved when measured with 3D imaging. Further data collection may elucidate a stronger relationship. Three dimensional imaging as a clin- ical tool has the potential to be a powerful adjunct in the astute clinician’s decision-making process for breast reconstruction.

318
TREND ACCURACY OF PULSE COOXIMETRY HEMOGLOBIN DURING SURGERY
Stoeck R, Hassanian M, Allard M, Applegate R. Loma Linda University School of Medicine, Loma Linda, CA.
Purpose of Study: Hemoglobin (Hb) measurements inform clinical transfu- sion decision-making. Multi-wavelength pulse CO-oximeters have been de- veloped which allow for continuous non-invasive hemoglobin monitoring (SpHb) along with pulse rate, SpO2, and perfusion index. Previous reports show SpHb agreement with Hb is not good enough to guide transfusion, par- ticularly in the “transfusion decision range” of 6 to 8 g/dL. If SpHb change accurately reflects Hb change, SpHb trend could indicate need for confirm- atory testing to guide transfusion decisions. This study evaluates absolute and trend accuracy of newer SpHb Rev K compared to ABG co-oximetry deter- mined Hb values.
Methods Used: IRB approved, convenience sampled prospective observa- tional study, requiring written informed consent. Included patients were scheduled for surgical procedures with expected blood loss ≥10-15% of the estimated blood volume. Patients had perioperative monitoring with ra- dial artery cannulation as standard in our practice. SpHb sensors placed on patients’ fingers were optically isolated from each other. Data were recorded continuously to a computer. When clinically indicated intraoperative ABG samples were obtained, with SpHb at the time of sampling. Results were evaluated for trend accuracy (sequential change in ABG Hb compared to se- quential change in SpHb) and absolute accuracy (SpHb obtained at the time of ABG sampling was compared to ABG Hb for linear correlation and Bland Altman analysis).
Summary of Results: Table. Both trend and absolute accuracy were better than previously published: trend R² 0.51; absolute R² 0.67 bias -0.47 and limits -2.4 to 1.4 g/dL. SpHb increased in only 2 of 20 samples in which the sequential decrease in Hb was larger than 1 g/dL.
Conclusions: This revision SpHb has better trend and absolute accuracy compared to previous. Absolute accuracy remains less than needed to guide clinical transfusion decisions. Further research may show SpHb useful as a trend monitor during surgery.

VITAMIN D DEFICIENCY AMELIORATES POST-ARTHROPLASTY S. AUREUS INFECTION IN AN IN VIVO MOUSE MODEL
Yung M1, Stavnakis A2, Loftin A2, Bernalth N2. 1David Geffen School of Medicine, UCLA, Los Angeles, CA and 2UCLA, Los Angeles, CA.
Purpose of Study: Infections are a serious complication of joint replacement surgeries. With the number of arthroplasty procedures still on the rise, the inci- dence of post-operative infections is projected to increase from 17,000 to 266,000 per year by 2030. The severity and rising prevalence of these in- fections necessitates more effective methods of prevention. Serum vitamin D levels, which modulate both innate and adaptive immunity, may influence the ability to combat infection. This study uses a mouse model to examine the impact of vitamin D deficiency on the extent and severity of post- arthroplasty infections.
Methods Used: Two groups of mice were fed ad libitum for four weeks with either a control diet or a diet deficient in vitamin D. Mice then underwent a simulated knee replacement surgery and received a 2 μl liquid preparation of bioluminescent S. aureus at the surgical site. Infections were monitored using in vivo bioluminescence imaging up to 14 days post-operation. The surgical implants and surrounding tissue were then cultured to quantify the extent of the infection.
Summary of Results: The total flux and maximum radiance of biolumines- cence signal was on average 35% and 36% lower for mice on the vitamin D deficient diet as compared to mice on the control diet. A 1:1 dilution culture of the prosthetic implants gave an average of 51.75 colony forming units (CFUs) for vitamin D deficient mice and 175.10 CFUs for the control group. Similar cultures of the surrounding tissue gave an average of 2381 CFUs for vitamin D deficient mice and 3492 CFUs for the control group.
Conclusions: Contrary to expectations, mice on a vitamin D deficient diet develop less severe post-arthroplasty infections than mice on a control diet. These results indicate that dietary modifications prior to elective arthroplasties can impact risk for post-surgical infections.

DA VINCI ROBOT TRAINING DILEMMA: EVALUATING THE RAVEN ROBOT AS A SOLUTION
Glassman D1, White L2, King H2, Lewis A2, Clark A2, Glassman TS, Lendway TS. 1University of Washington, Seattle, WA and 2University of Washington, Seattle, WA.
Purpose of Study: Robotic assisted surgery is being rapidly adopted as evidenced by a 25% growth rate in the number of robotic procedures performed in the last four years. This progression is challenging the ability of surgeons to receive adequate training on robotic systems to keep up with the demand. The limited availability of the da Vinci robot for training has in- creased the need for new training tools. The University of Washington devel- oped the Raven robot, a more compact system that is only 1/5th the cost of a da Vinci robot, that may provide a solution to the training demand. The pur- pose of this study was to determine whether training on the Raven robot...
would be non-inferior to training on the da Vinci robot for the Fundamentals of Laporoscopic Surgery (FLS) block transfer task.

Methods Used: A total of 30 medical students completed the protocol and were randomly assigned to Raven training (RT) or da Vinci training (DT). Both groups were allowed to practice to proficiency on their assigned robot for the FLS block transfer. Once proficient, both groups completed a criterion test on the da Vinci robot.

Summary of Results: Criterion task times between the RT and DT groups were significantly different (p = 0.004). However, path length and economy of motion (EOM) during criterion tasks were not statistically different. The RT group had an average path length of 355 ± 44 in and the DT group averaged 339 ± 49 in (p = 0.39, 95% CI -1.56 to 33.31). The average EOM for the RT and DT groups was 3.74 in² ± 0.99 and 4.43 in² ± 0.83, respectively (p = 0.06, 95% CI -1.04 to -0.33). Subjects in the RT group performed no errors while working on the da Vinci while the DT group had an error rate of 46% and 53% during their first and second training tasks, respectively.

Conclusions: This prospective randomized trial provided evidence that the Raven robot may be a valid surrogate training tool for inanimate tasks on the da Vinci robot system.

321

EXTRACELLULAR MATRIX REMODELING OF RABBIT VOCAL FOLDS AFTER WOUNDING

Gonzalez L1,2, Long J1, UCLA David Geffen School of Medicine, Los Angeles, CA and 2Charles Drew University of Medicine and Science, Los Angeles, CA.

Purpose of Study: There has been recent interest in developing a three-dimensional vocal fold replacement using tissue-engineering techniques for patients with severe vocal fold scarring from injury or radiation therapy. In order to be able to provide a benchmark for tissue-engineered constructs to meet or exceed, a “gold standard” of cover replacement is needed. The aim of this study is to develop such a gold standard for vivo replacement, using the ideal normal vocal fold layer in rabbits. The fundamental question that must be answered is whether the nature of the cover layer has healed without scarring that would otherwise impair its function. At this juncture of this study the aim in vivo replacement of the vocal fold cover layer is complete. This phase of the study will assess microstructural changes in the surgical and control vocal folds that have been previously harvested.

Methods Used: Fluorescent immunohistochemistry (IHC) staining of paraffin embedded vocal folds of 10 specimens from 5 rabbits was performed. IHC with antibody labeling was used to better characterize the deposition patterns of elastin and decorin. Fluorescent-tagged secondary antibodies were used to detect these primary antibodies. Methods were validated by including positive and negative control slides. Masson’s trichrome staining was used to detect areas of collagen deposition. H&E staining was performed to visualize nuclei, as well as other eosinophilic structures. Lastly, Verhoeff’s Elasticin stain was used to visualize elastin and collagen fibers.

Summary of Results: IHC staining technique is currently being refined. Masson’s staining did not reveal an increased deposition of collagen. H&E staining confirmed an intact and continuous epithelial layer in all surgical animals. Verhoeff’s Elasticin stain showed an overall partial preservation of elastin fibers.

Conclusions: The results support the premise that a vocal fold cover layer can attach and survive when applied to the underlying thyroarytenoid muscle. Additionally, our results showed healing of the surgical specimens without increased scarring that would otherwise impair its function. We conclude that this model of attaching a cover replacement at a sub-lamina propria plane is a good model for use in future tissue engineered vocal fold cover replacement procedures.

322

GAMMA KNIFE AS SALVAGE THERAPY FOR RECURRENT GINOBLASTOMA MULTIFORME

Larson EW, Peterson HE1,2, Lamoreaux WT2,3, MacKay AR1, Carlson JD1,2, Ling BC, Cooke BS1,2, Peresinetti B2, Lee CM1,2, 1University of Washington School of Medicine, Spokane, WA, 2 Gamma Knife of Spokane, Spokane, WA, 3 Mackay & Meyer MDs, Spokane, WA, 3 Inland Neurosurgery & Spine Associates, Spokane, WA and 4 DataWorks Northwest, Spokane, WA.

Purpose of Study: Glioblastoma multiforme (GBM) is the most malignant primary tumor of the brain. It has a dismal survival prognosis of 14-16 months following initial diagnosis. Despite aggressive upfront therapy, GBM tumors tend to recur in six months. Following this recurrence, some patients may benefit from Gamma Knife Radiosurgery (GKRS) treatment. This study analyzes survival outcomes in a case series compared to known prognostic indicators for GBM patients.

Methods Used: 63 patients with recurrent GBM were treated with GKRS as part of a multimodal treatment plan between 2002 and 2011. Overall survival from date of diagnosis, was compared to expected survival times as indicated by updated RTOG recursive partitioning analysis (RTOG-RPA) Classes. Survival post-GKRS salvage was also evaluated. Univariate and multivariate analyses were conducted to determine whether extent of resection, age, Karnofsky Performance Status (KPS), GKRS dose, or tumor volume were significant predictors of survival following GKRS salvage for recurrent GBM.

Summary of Results: Overall median survival from time of initial diagnosis was 20.2 ± 2.7 months for the entire group. 46 patients were in RTOG-RPA Class IV with a median overall survival of 20.2 ± 2.6 months. Median survival following GKRS salvage therapy was 9.9 ± 3.1 months for all patients. Multivariate analysis indicated that KPS was a significant predictor of survival. Patients with KPS of 100 experienced 17.9 ± 5.5 month post-GKRS survival.

Conclusions: GKRS may be a safe and effective salvage therapy for selected rGBM patients, providing prolonged survival and quality of life. Treatment options should be individually tailored to each patient’s unique situation.

323

EFFECT OF CRANIAL WINDOW DIAMETER ON POSTOPERATIVE PNEUMOCEPHALUS VOLUME

Sharim J, Pezeshkian P, DeSalles A, Pouratian N. David Geffen School of Medicine at UCLA, Los Angeles, CA.

Purpose of Study: Deep brain stimulation (DBS) is used routinely to treat the symptoms of movement disorders such as Parkinson’s disease and essential tremor. DBS and other stereotactic surgical procedures necessitate high accuracy in targeting specific intracranial nuclei. Brain shift upon dural opening, due to pneumocephalus, can decrease this accuracy significantly. It has been argued that a larger burr hole will increase pneumocephalus volume upon dural opening due to a greater degree of communication between the subdural space and extracranial air. The objective of this retrospective study is to determine if there is a statistically and clinically significant difference in post-operative pneumocephalus volume due to burr hole size.

Methods Used: DBS electrodes were surgically implanted through either large (14 mm) burr holes or small (4 mm) burr holes. Immediate post-operative computerized tomography (CT) scans of 165 electrode implantations in 85 patients between 2010 and 2013 were retrospectively analyzed. Pneumocephalus volume was determined using iPlanStereotaxy® and converted into a per-hemispheric volume so as to allow for comparison between bilateral surgeries and unilateral/staged surgeries.

Summary of Results: The average per-hemispheric pneumocephalus volume in patients with small 4 mm burr holes (n = 71 hemispheres) was 12.84 ± 9.79 cc (mean ± standard deviation) and in those with large 14 mm burr holes (n = 87) was 11.71 ± 7.47 cc. No statistically significant difference in pneumocephalus volume was found (p = 0.42). Similar results were found analyzing total pneumocephalus volume separately for patients with bilateral surgeries (p = 0.24) and unilateral/staged surgeries (p = 0.23).
Conclusions: Our data suggests that burr hole size does not affect pneumocephalus volume. These results suggest that increasing burr hole size to gain greater visual access to the cortical surface will not increase pneumocephalus, and thus subsequent brain shift. Burr hole size is not a modifiable factor in controlling pneumocephalus volume, and thus minimizing burr hole size cannot be used as a substitute for intraoperative physiological testing and image guidance.

OUTCOME FOLLOWING RENAL TRANSPLANTATION: THE IMPACT OF PARAOPERATIVE PARAMETERS
Carreras EM1,2, Campbell A1,2, Mammen C1,2, Matsell D1,2, 1B.C. Children’s Hospital, Vancouver, BC, Canada and 2University of British Columbia, Vancouver, BC, Canada.

Purpose of Study: Renal transplant remains the gold standard for management of ESRD irrespective of the patient’s age. Currently there are no accurate and reliable methods of acquiring a quantitatively based long-term prognosis for a renal transplant recipient immediately after surgery. At B.C. Children’s Hospital, we hypothesized that peri-operative factors would have the most significant impact on short- and long-term graft survival in this population of patients and undertook a retrospective study of all pediatric renal transplant patients in our province.

Methods Used: All patients who have undergone a primary renal transplant between the dates of January 1st, 1992 to May 31st, 2013 were included. A retrospective review of the subjects’ health records has been performed to look for data, including 55 perioperative variables, and the three following primary outcomes as a determinant of renal function: eGFR at time of discharge following transplantation, at 6 months postop, and at 12 months postop.

Summary of Results: This study includes 150 subjects. There were 85 males (57%) and 65 females (43%). Preliminary analysis shows a mean age of 58 years. The average clinical follow-up time was 21 months. Gender, instrumented index fusion, age, time between index fusion and ASD operation, and presence of a multi-level index fusion had no significant association with postoperative VAS score, postoperative ODI score, or need for additional surgery. Longer operative times were associated with greater VAS score at last follow-up (p=0.03). Longer hospital stays were associated with a decreased need for additional surgery (p=0.04). Higher preoperative VAS and ODI scores were associated with higher ODI scores at last follow-up (p=0.04 and p=0.005, respectively). Higher preoperative ODI scores were also significantly associated with higher ODI scores one month after surgery (p=0.04).

Conclusions: Potential risk factors for increased morbidity following surgery to treat ASD include longer operative time, shorter hospital stay, and higher preoperative VAS and ODI scores. Additional risk factor analyses regarding comorbidities, lifestyle, and radiological parameters remain to be studied.

IDENTIFYING RISK FACTORS IN PATIENTS UNDERGOING SURGERY FOR ADJACENT SEGMENT DISEASE
Hoffman H, Lu DC. David Geffen School of Medicine, Los Angeles, CA.

Purpose of Study: Adjacent segment disease (ASD) is characterized by symptomatic degenerative changes at a segment adjacent to a spinal fusion. Surgical treatment for ASD involves decompression of the adjacent segment or extending the index fusion. The postoperative course is variable, ranging from complete resolution of symptoms to significant morbidity and additional surgery. Risk factors affecting outcomes have not been described. We hypothesize that older age, female gender, use of instrumentation in the index fusion, shorter duration between index fusion and ASD operation, multi-level index fusion, longer operative time, longer hospital stay, higher preoperative Oswestry Disability Index (ODI), and higher preoperative Visual Analog Scale (VAS) pain score will be associated with poorer outcomes.

Methods Used: All patients who underwent surgery for lumbar or cervical ASD in the past 10 years by three surgeons at UCLA were identified. 85 patients completed ODI and VAS surveys regarding their preoperative and postoperative condition. Preoperative and perioperative data was collected from the electronic health record. Postoperative ODI and VAS scores as well as the need for additional surgery were used to measure outcomes.

Summary of Results: 47 females and 38 males were included and had a mean age of 58 years. The average clinical follow-up time was 21 months. Gender, instrumented index fusion, age, time between index fusion and ASD operation, and presence of a multi-level index fusion had no significant association with postoperative VAS score, postoperative ODI score, or need for additional surgery. Longer operative times were associated with greater VAS score at last follow-up (p=0.03). Longer hospital stays were associated with a decreased need for additional surgery (p=0.04). Higher preoperative VAS and ODI scores were associated with higher ODI scores at last follow-up (p=0.04 and p=0.005, respectively). Higher preoperative ODI scores were also significantly associated with higher ODI scores one month after surgery (p=0.04).

Conclusions: Potential risk factors for increased morbidity following surgery to treat ASD include longer operative time, shorter hospital stay, and higher preoperative VAS and ODI scores. Additional risk factor analyses regarding comorbidities, lifestyle, and radiological parameters remain to be studied.

EVALUATION OF SURGICAL OUTCOMES OF PEDIATRIC RENAL TRANSPLANTS
Jiwa K1, Afshar K2, Bedford F3, 1University of British Columbia, Vancouver, BC, Canada; 2BC Children’s Hospital, Vancouver, BC, Canada and 3BC Children’s Hospital, Vancouver, BC, Canada.

Purpose of Study: BC Children’s Hospital is the first and only Canadian pediatric hospital participating in the Pediatric National Surgical Quality Improvement Program (NSQIP-P) created by the American College of Surgeons. The NSQIP-P program provides risk-adjusted outcomes data that is used to enable targeted surgical quality improvement initiatives in participating hospitals. Solid organ transplants are currently excluded from the surgeries evaluated, thus limiting the applicability of results to all aspects of surgical care. Our aim was to evaluate surgical outcomes of renal transplants and compare these with results from other NSQIP-P risk-adjusted rates at our facility.

Methods Used: We performed a retrospective chart review of all renal transplants performed at BC Children’s Hospital between 2003-2013. At present, 47 charts from 2003-2008 have been reviewed with additional charts from 2009-present pending. Data collection was based on a modified NSQIP-P framework with an extended post-operative follow-up period of 1 year. Study outcomes were determined based on NSQIP-P variable definitions. Pre-operative data included patient demographics, etiology of renal failure, prior dialysis, co-morbid conditions, and medication use. Intra-operative data consisted of procedure duration, complications, vascular anastomotic time and type of donor graft. Post-operative data was collected over a 30-day follow-up as per the NSQIP-P model, consisting of respiratory, renal, cardiac, and CNS events. Other variables were included based upon previous studies done on outcomes for renal transplant patients. These consisted of ureteric and vascular complications, incidence of lymphocele, acute rejection, delayed graft function and need for dialysis, and were collected over a 1-year follow-up period.

Summary of Results: As data collection and analysis is ongoing, no preliminary findings can be made at this time. Our aim is to compare the 30-day outcomes from the renal transplant patients with the surgical patients captured in NSQIP-P.

Conclusions: Given that NSQIP-P currently excludes solid organ transplants from their surgical evaluation program, it is hoped that this study will prompt similar reviews in other centres.
Surgery II
Concurrent Session
3:30 PM
Friday, January 24, 2014
327
PREEMPTIVE ANALGESIA IN CHILDREN USING CAUDAL EPIDURAL ROPIVACAINE: A PROSPECTIVE, RANDOMIZED, DOUBLE-BLINDED, CONTROLLED STUDY
Romana R, Mulder S, Andrews G, Applegate R. Loma Linda University, Loma Linda, CA.
Purpose of Study: Administering analgesics before noxious stimuli onset such as surgery (preemptive analgesia) may reduce pain. Caudal epidural analgesia (caudal block) and local anesthesia infiltration are commonly used in children for surgeries below the diaphragm. This study was designed to compare pre-surgery caudal blocks, post-surgery caudal blocks and post-surgery local infiltration as means to decrease analgesic medication needed for postoperative pain in pediatric patients.
Methods Used: IRB-approved study registered in ClinicalTrials.gov. After written informed consent was obtained from responsible caregivers, patients ≤ 2 years of age scheduled for outpatient inguinal herniorrhapsy, orchiorraphy or orchietomy were enrolled. Patients > 25 kg or > ASA Class 3 were excluded. Patients were randomized to receive one of the following:
- Caudal Before (CB): 1 mL/kg (5.15 mL) 0.25% ropivacaine with 1,200,000 epinephrine caudally after induction of general anesthesia, prior to incision
- Caudal After (CA): 1 mL/kg (5.15 mL) 0.25% ropivacaine with 1,200,000 epinephrine caudally after surgery end, prior to emergence from anesthesia
- Local Infiltrate (LA): 1 mL/kg (5.15 mL) 0.25% ropivacaine infiltrated around surgery site after surgery end, prior to emergence from anesthesia

Blinded observers assessed postoperative pain (using the FLACC Scale) 0, 30, 60, 120, and 180 minutes after recovery room arrival. Parents recorded pain scores 2 and 4 hours after discharge and the morning after surgery. Dosage and frequency of pain medications needed were recorded. The primary outcome was intergroup difference in total analgesic use (mcg/kg morphine equivalents) post-surgery among the three study groups.

Summary of Results: Table.

Conclusions: CB and CA had lower average pain scores than LA despite similar amounts of opioid administration. Further enrollment is ongoing to elucidate impact on 24-hour analgesic requirements and pain scores.

| Age months mean, 95% CI | 16.4 ± 3.5 to 19.2 | 15.9 ± 1.2 to 18.7 | 15.5 ± 1.3 to 18.1 | < 0.05
| Weight kg mean, 95% CI | 13.9 ± 10.8 to 13.7 | 10.5 ± 9.3 to 11.7 | 10.5 ± 9.5 to 11.8 | < 0.05
| Intraoperative ME(mcg/kg median, 95% CI) | 118 ± 83 to 152 | 107 ± 85 to 129 | 133 ± 85 to 176 | 0.52
| PACU ME(mcg/kg median, 95% CI) | 1.5 ± 0.5 to 3.1 | 1.5 ± 0.5 to 3.1 | 2.5 ± 0.9 to 4.0 | 0.60
| PACU Average FLACC score median, 95% CI | 1.1 ± 0.4 to 1.8 | 1.4 ± 0.6 to 2.1 | 5.2 ± 2.5 to 3.9 | < 0.0001

*Pain score higher in LA than either CA or CB. CA and CB were not different.

328
EXTENDED ANTIBIOTIC PROPHYLAXIS IN UROLOGIC ONCOLOGY SURGERY: HOSPITAL-LEVEL VARIATION AND CLOSTRODIUM DIFFICILE
Calvert JK, Gore JL. University of Washington School of Medicine, Seattle, WA.
Purpose of Study: The use of perioperative antibiotic prophylaxis (ABP) for the prevention of postsurgical infections in urology has been well established. However, research indicates wide variation across hospitals when it comes to the selection of antibiotic class, dose and duration. The current study aims to elucidate patient and provider factors that determine extended ABP and ascertain the extent to which ABP predicts subsequent Clostridium difficile infection.
Methods Used: We conducted a review of all patient visits in the PREMIER database from 2007 through 2012. We identified patients who underwent prostatectomy, nephrectomy or cystectomy. The outcome of extended ABP was based on American Urologic Association (AUA) guidelines, with a cut-off of 24 hours post-surgery. Patients with switched antibiotic class within 48 hours post-surgery were removed from analysis. We flagged patients C. difficile diagnosis based on index visit and readmission. Hierarchical logistic regression models were constructed regressing extended ABP and C. difficile diagnosis against demographic, clinical, and hospital level variables, respectively.
Summary of Results: We identified 59184 patients who had a prostatectomy at 360 PREMIER facilities, 27921 patients who had a nephrectomy at 401 facilities, and 5425 cystectomy patients at 235 facilities. Cystectomy patients were significantly more likely to receive extended ABP (56.3%, compared to 17.7% for prostatectomy and 28.8% for nephrectomy, p < 0.001). Length of stay was also significantly associated with extended ABP (p < 0.001 for all cohorts). The highest quartile providers had the lowest rates of extended ABP (p < 0.001). 34.9% of the variability in ABP in the prostatectomy cohort can be explained by the hospital where procedure took place, compared with 23.4% in nephrectomy and 19.7% in cystectomy. Extended ABP was significantly predictive of C. difficile diagnosis for nephrectomy patients [OR 3.79 (2.46-5.84)] and cystectomy patients [1.64 (1.12-2.39)].
Conclusions: We demonstrated marked hospital-level variability in extended ABP following urologic surgery, and subsequent increased odds of constructing C. difficile. Efforts to systematize perioperative ABP and increase compliance with AUA guidelines will likely reduce the burden of C. difficile.

329
COINCIDENCE OF CARPAL AND CUBITAL TUNNEL SYNDROMES
Koh J, Kwan M, DeCesare G, Azari K, Benhaim P. David Geffen School of Medicine at UCLA, Los Angeles, CA.
Purpose of Study: To identify the incidence of coincident median and ulnar nerve compression.

To characterize patients with simultaneous carpal and cubital tunnel syndromes based on demographics, physical exam findings, and nerve conduction study findings.
Methods Used: Nerve compression releases from 1/1/2008 to 10/23/12 were retrospectively reviewed. Demographics, physical exam findings, and nerve conduction studies were recorded for each patient. A retrospective analysis was performed by chi squared contingency tests and a logistic multivariate regression analysis for continuous variables, comparing patients with a single nerve compression, and patients with multiple nerve involvement.
Summary of Results: A total of 392 patients underwent nerve decompression during this period. 244 patients (62.2%) underwent carpal tunnel release, 23 patients (5.9%) underwent cubital tunnel release, and 125 patients (31.9%) underwent both carpal and cubital tunnel releases. History of autoimmune disease proved to be strongly correlated with increased risk of simultaneous compressions (p = 0.002). Among physical exam findings, sensory loss in the ulnar and median nerve distributions were strongly correlated with diagnosis of coincident nerve compression in conjunction with other positive physical exam findings (Median - odds ratio: 0.06; 95% CI .003-1.17 || Ulnar - odds ratio: .17; 95% CI: .03-1.11).

Conclusions: To our knowledge, the relative incidence of multiple nerve compressions relative to single nerve compressions has not yet been reported. Among the demographic factors analyzed, a history of autoimmune disease was most strongly correlated with incidence of multiple nerve compression syndromes. Additionally, sensory loss in the ulnar and median nerve distributions was best correlated to diagnosis of multiple nerve compressions in the context of other physical findings. Previously reported sensitivities for nerve conduction studies at the carpal tunnel and at the cubital tunnel relative to physical exam-driven diagnosis were also confirmed.

330
REDUCED MORTALITY, SHORTER HOSPITAL LENGTH OF STAY, AND FEWER COMPlications: ACUTE CARE SURGEONS’ IMPACT ON PATIENTS WITH OPERATIVE CARDIAC INJURIES
Mempin RL, Plurad DS, Kim DY, Bricker SD. Harbor-UCLA Medical Center, Torrance, CA.
Conclusions: Patients with operative cardiac trauma experience fewer complications (0.000128-0.8, p = 0.039). Patients treated by ACS surgeons were also found to have shorter hospital (H-LOS) and ICU (ICU-LOS) lengths of stay, ventilator days (VENT-DAYS), and complications.

Summary of Results: During the study period, 424 patients presented with cardiac injuries following trauma. Of this population, 64 patients underwent surgery for cardiac repair, and comprised the study sample. The sample was then divided into cohorts based on the training of the primary surgeon (ACS vs. NON-ACS). Baseline demographics were not significantly different between the two groups. A significantly lower mortality rate was observed in patients treated by ACS surgeons (odds ratio = 0.0101, 95% CI = 0.000128-0.8, p = 0.039). Patients treated by ACS surgeons were also found to have a shorter H-LOS (β= -16.832, SE = 6.503, t = -2.588, p = 0.016) and fewer complications (β= -1.622, SE = 0.726, t = -2.232, p = 0.034).

Conclusions: Patients with operative cardiac trauma experience fewer complications, shorter hospital length of stay, and reduced mortality when treated by Acute Care Surgeons.

MINOR SURGERY PROCEDURES IN A PEDIATRIC POPULATION
Chan E1, Bucevcska M1, Verchere C2. 1University of British Columbia, Vancouver, BC, Canada and 2BC Children's Hospital, Vancouver, BC, Canada.

Purpose of Study: Minor surgery under local anesthesia is an appealing option for parents who want to minimize the risk of sedation in their children. Many surgeons hesitate to perform minor surgery in the unpredictable pediatric population. This study evaluates the success of minor surgery undertaken by a single plastic surgeon at BC Children's Hospital.

Methods Used: This study was designed as a combination of a 2-year retrospective chart review and a prospective patient survey. Eligible subjects for retrospective study were identified through the CERNER system for the period of May 1, 2011 to April 30, 2013. Parameters of interest included patient demographics, type of procedures, complications, and outcomes. Eligible subjects for the prospective survey included consecutive patients undergoing minor surgery procedures between June 12, 2013 and Dec 31, 2013. Parents of patients were also asked to participate. Questionnaires were emailed to each subject within 1-2 weeks of completing the minor procedure.

Summary of Results: 168 subjects (68 male, 100 female) undergoing a total of 219 procedures were included in the retrospective review. Ages ranged from 2 weeks to 18 years, with a mean of 13.1 years. The most common diagnosis and procedure performed was nevus (63%) and simple excision (75%) respectively. Median length of follow-up was 46 days and ranged between 4 and 606 days. A total of 45 complications were found in 36 patients. Complication rates were divided into crusting (4.6%), delayed wound healing (3.2%), hypoperfusion reaction (2.3%), scar hypertrophy (1.8%), infection (0.9%), and other (7.8%). Procedures were also categorized under one of four outcomes: patient and physician satisfied (93%), patient satisfied but physician unsatisfied (0.5%), patient unsatisfied and physician satisfied (2%), and both unsatisfied (4%). In the prospective study, 32 out of 36 eligible subjects consented to participate in the survey. Of those that consented, 10 children and 12 parents (69%) responded to the questionnaires. 83% of respondents indicated that their goals were accomplished by minor surgery. 82% of participants also indicated that they would be willing to undergo minor surgery again.

Conclusions: Minor surgery is possible and practical in pediatric plastic surgery clinics with few complications and high patient and surgeon satisfaction.

NASOEPHAL FLAP RECONSTRUCTION OF PEDIATRIC SELLAR DEFECTS
Shinn JR1, Purcell P2, Otto R3, Davis G1, Parikh S2. 1University of Washington, Seattle, WA; 2Seattle Children's Hospital, Seattle, WA and 3Seattle Children’s Hospital, Seattle, WA.

Purpose of Study: Endoscopic, endonasal approaches for resection of anterior skull base lesions spare the morbidity of an open craniofacial resection. Surgical challenges in pediatric patients include the need to manipulate instruments within a narrow workspace and concerns regarding the adequacy of tissue for reconstruction. In adult patients, a nasoseptal flap is often used to re-establish complete separation between the cranial and nasal cavities following endoscopic anterior skull base resection. There is question as to whether children have adequate facial structure to supply a nasoseptal flap large enough to cover a sellar defect. This study used computed tomography (CT) measurements to characterize the feasibility of performing nasoseptal flap reconstruction of sellar defects in children.

Methods Used: Seattle Children’s Hospital radiology records were queried for recent CT head, CT sinus, and CT maxillofacial studies. Anterior skull base or sinonasal anatomic abnormalities were excluded. Ten CT scans from subjects of each year of age from birth to age 18 were obtained, for a total of 180 subjects. OSIRIX radiology software was used to measure nasoseptal flap length and compare it with the length of anticipated sellar defect. Linear regression characterized the relationship between age, nasoseptal flap length, and sellar defect size.

Summary of Results: The ratio of nasoseptal flap length to sellar defect length was almost always greater than 1. In our cohort, only 5 patients, of varied ages, had nasoseptal length smaller than the sellar length. Our results found no association between age and the ratio of nasoseptal flap length to sellar defect size.

Conclusions: Almost all patients had a ratio of nasoseptal flap length to sellar defect length that was greater than 1 regardless of age. This is in contrast to prior studies that concluded nasoseptal flap reconstruction of endoscopic sellar defects may not be feasible in patients less than 6 years of age. Based on our measurements, nasoseptal flap length is not a limiting factor in reconstruction of pediatric sellar defects.

AN EXTENT OF RESECTION THRESHOLD FOR RECURRENT GliOBlastoma MULTIFORME
Pia J, Sarmiento JM, Mukherjee D, Ly D, Carico C, Nuño M, Patil CG, Cedars-Sinai Medical Center, Los Angeles, CA.

Purpose of Study: The prognostic value of extent of resection (EOR) for survival among patients with glioblastoma multiforme (GBM) is highly debated. To date, only one study has evaluated the prognostic significance of EOR at first recurrent surgery. This study is the first to use volumetric analysis to determine an EOR threshold that confers a survival benefit for GBM patients at their first recurrent surgery.

Methods Used: 113 adult recurrent GBM patients were retrospectively reviewed. Demographic, clinical, and outcome parameters including EOR at recurrent surgery based on volumetric analysis were obtained. Kaplan-Meier survival estimates and Cox proportional hazards models were used to evaluate the impact of EOR at recurrent surgery on overall survival (OS). We established a minimum EOR threshold value that predicted a significant survival benefit.

Summary of Results: Median age, KPS, EOR, and OS of all patients was 56 years, 80, 98.8%, and 21.4 months, respectively. An increment of 4.9 months survival was observed among patients with EOR levels above the 94% threshold (19.5 vs. 24.4 months, p = 0.04). In a multivariate analysis, we found EOR at recurrent surgery to be marginally significant in predicting OS (HR=0.98, p=0.10) after controlling for initial EOR (p=0.14), age (p=0.03), perioperative KPS (p=0.03), and radiation during initial surgery (p=0.01).

Conclusions: Our study established a survival benefit of 4.9 months among GBM patients who underwent recurrent surgery with an EOR of ≥ 94%.
Conclusions:

1. The current spiral fracture model in long bones includes sawing either a real or synthetic bone in a spiral pattern. A reproducible and inexpensive model for obtaining natural spiral fractures currently does not exist. This study explains how low energy spiral fractures can be obtained in sheep model.

Methods Used: Initially many different techniques were used in an attempt to produce spiral fractures, including torquing the femurs at a high rate with or without high axial compression, using multiple drill holes, and by opening a superficial spiral groove on the surface of the cortex. However, none of these methods produced acceptable results, as the fractures were inconsistent and therefore not reproducible.

Based on the knowledge acquired from these preliminary failure tests, we designed a method that allowed a reproducible, long, and isolated spiral fracture used in 25 sheep femurs. In our technique, we made a 1 cm long slit at a 40° angle with the longitudinal axis and cut through full cortical thickness using a rotary power tool (Dremel MultiPro 396 type 5, Mount Prospect, IL) with a #420 cut-off wheel (0.040” thickness). The ends of the femur were compressed with 500N. The specimen was then torqued at 0.1 deg/s until failure. The clockwise and counterclockwise rotations were applied in right and left femurs, respectively, yielding the same outward spiral fracture pattern in each femur.

Summary of Results: All 25 of the sheep femurs produced excellent spiral fractures that were nearly identical in pattern and length of fracture/femur diameter ratio. The average length of the fracture was 7.44 cm (6.00 cm-8.50 cm). The average diameter of the femurs was 2.24 cm (2.00 cm-2.55 cm). This gave us a fracture length that was on average 3.32 times longer than the diameter of the femur (3.00-3.78).

Conclusions: In this study we were able to develop a method for reproducible, non-communitive spiral fractures in inexpensive sheep femurs at safe and manageable torque levels.

SIMULATING SPIRAL FRACTURES IN LONG BONE: A SHEEP FEMUR MODEL

Burke C, Epperly S, Dajnowicz W, Inceoglu S, Basmajian H, Botimer G. Loma Linda University, Loma Linda, CA.

Purpose of Study: The current spiral fracture model in long bones includes sawing either a real or synthetic bone in a spiral pattern. A reproducible and inexpensive model for obtaining natural spiral fractures currently does not exist. This study explains how low energy spiral fractures can be obtained in sheep model.

Methods Used: Initially many different techniques were used in an attempt to produce spiral fractures, including torquing the femurs at a high rate with or without high axial compression, using multiple drill holes, and by opening a superficial spiral groove on the surface of the cortex. However, none of these methods produced acceptable results, as the fractures were inconsistent and therefore not reproducible.

Based on the knowledge acquired from these preliminary failure tests, we designed a method that allowed a reproducible, long, and isolated spiral fracture used in 25 sheep femurs. In our technique, we made a 1 cm long slit at a 40° angle with the longitudinal axis and cut through full cortical thickness using a rotary power tool (Dremel MultiPro 396 type 5, Mount Prospect, IL) with a #420 cut-off wheel (0.040” thickness). The ends of the femur were embedded in a metal alloy (Cerrobend, Chicago, IL), mounted to the universal biaxial materials testing machine (Electropuls E10000, Instron, Canton, MA), and compressed with 500 N. The specimen was then torqued at 0.1 deg/s until failure. The clockwise and counterclockwise rotations were applied in right and left femurs, respectively, yielding the same outward spiral fracture pattern in each femur.

Summary of Results: All 25 of the sheep femurs produced excellent spiral fractures that were nearly identical in pattern and length of fracture/femur diameter ratio. The average length of the fracture was 7.44 cm (6.00 cm-8.50 cm). The average diameter of the femurs was 2.24 cm (2.00 cm-2.55 cm). This gave us a fracture length that was on average 3.32 times longer than the diameter of the femur (3.00-3.78).

Conclusions: In this study we were able to develop a method for reproducible, non-communitive spiral fractures in inexpensive sheep femurs at safe and manageable torque levels.

TRENDS IN ULNAR COLLATERAL LIGAMENT RECONSTRUCTION AND ASSOCIATED ELBOW SURGERY

Rosenblum S1,2, Yeranosian M1, Terrell R1,2, McAllister D1,2, Petrigliano F1,2, 1UCLA, Los Angeles, CA and 2UCLA david geffen school of medicine, Los Angeles, CA.

Purpose of Study: The purpose of this study is to study novel surgical procedures in children with glaucoma whose original Ahmed aqueous shunt failed, and was replaced by a Baerveldt shunt in the same area of the eye. Ultimately, this may affect the surgical procedure used and give an alternative route of treating pediatric patients whose original shunt have failed.

Methods Used: The study methodology is a retrospective study of charts of pediatric patients with a diagnosis of glaucoma in at least one eye, and who had undergone an Ahmed shunt placement in the past. Descriptive statistics i.e. mean, median, standard deviation, and ranges are used and data was examined along a Kaplan-Meier curve. Intra-ocular pressures was analyzed to determine 1) how long the original Ahmed worked for and 2) if there was any regression in IOP after the placement of the Baerveldt.

Summary of Results: Because the patients had both Ahmed aqueous shunt procedure and Baerveldt procedure done in the same location of the same eye, results were analyzed to elucidate the effectiveness of the Baerveldt implantation in pediatric patients who had failed their original Ahmed shunt. To determine an alternative route of treatment to preserve the same area of the eye. There was a range of 1 mo-7 yrs after a Baerveldt implantation; the average IOP difference between the last visit and the implantation of the Baerveldt was an average of 15mmHg decrease for patients within the first year of the implantation and an average of 7.5mmHg decrease for patients whose last checkup was more than 2 years from the surgery. Despite this, patient's IOP and number of glaucoma medications were significantly lower (P<0.05*10-5, 1 test) after the Baerveldt transplant than it was after the first failed Ahmed transplant for a longer number of years after transplant.
Conclusions: Explantation of the Ahmed and implantation of a Baerveldt-350 may be a viable alternative in pediatric patient whose initial glaucoma treatment had failed. Further follow-up is indicated to track the course of patients in order to determine if these patients eventually had an increase in IOP.

337

IMPROVING TEEN ACCESS TO PLAN B: A PHARMACY OUTREACH MODEL IN AUBURN, WA

Mosheri S. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: The 2012 teen birth rate in Auburn, WA, was 19.7/1000; twice that of the greater King County area. Starting August 2013, Plan B One-Step will be available for purchase over-the-counter with no age restriction. In surveying local drugstores, a King County Public Health official encountered misinformation among pharmacists that could prevent some patients from receiving Plan B. The purpose of this project was to improve access to emergency contraceptives for teens by providing local pharmacists with a short presentation and educational materials on Plan B.

Methods Used: A literature review was conducted to identify barriers to obtaining Plan B and investigate the effects of policy changes on teen access. Studies supported pharmacist education to improve patient counseling and increase likelihood of emergency contraception dispensal. Auburn pharmacies were contacted to assess interest and knowledge about changes in emergency contraceptive legislation. An informational packet was assembled, and short presentation prepared; outlining local teen birth rates, Plan B legislation, pharmacodynamics, accessibility, payment options, and Medicaid coverage. Materials were included to help refer adolescents and low-income patients to obtain ongoing contraceptive support.

Summary of Results: 10 pharmacies in the city of Auburn received a presentation and informational packet about Plan B. The information was well-received, and pharmacist questions clarified. A relationship between Auburn pharmacies and the King County Public Health partner was established. This outreach program is expected to be replicated by South Seattle King County Public Health, and King County Public Health offices in Enumclaw, Federal Way, and Kent will utilize packet materials.

Conclusions: Increasing youth access to contraception is an important part of a multicomponent program to help reduce unintended pregnancy. In light of recent legislation, pharmacies have become a vitally important setting for patient education and access to Plan B. Specifically, small rural pharmacies that lack standing policy directives can benefit from outreach as a source of education and clarification. The pharmacists in Auburn, WA, are now armed with the resources to not only dispense Plan B properly, but also to help individual patients find ongoing family planning support.

338

HYPERSERONINOPHILIC SYNDROME PRESENTING WITH PERICARDIAL EFFUSION, TAMPONADE, AND MYOCARDITIS

Mehta A, Couch C, Lazerson J. UNSOM, Las Vegas, NV.

Case Report: Introduction: HES is a group of rare disorders defined by overproduction of eosinophils, with blood eosinophil counts >1,500/μL, resulting in infiltration and subsequent end organ damage. Clinical manifestations include dermatologic, pulmonary, and gastrointestinal. Life-threatening presentations include cardiac and neurologic manifestations. We report a pediatric case of idiopathic Hyperseroinophilic Syndrome (HES) presenting with cardiac, neurologic, pulmonary, and gastrointestinal manifestations.

Case Presentation: Patient is a 5-year-old female presenting with one week of vomiting, and diagnosis of presumptive urinary tract infection (abnormal urinalysis and prior history of grade 2 vesicoureteral reflux). Urine culture was negative. Serum laboratory analyses incidentally found an eosinophil count of 12,500/μL. She developed transient altered mental status and extensive workup ensued. Brain MRI showed trace ischemic changes, and hypercoagulability workup demonstrated decreased protein C levels and mutation of PAI gene (4G homozygous). Bone marrow was negative for malignancy. Pleural effusion was noted on imaging studies. She developed cardiac tamponade and echocardiogram showed large pericardial effusion. Pericardiocentesis was performed, and effusion composed of WBC 1,310/μL, with 80% eosinophils. She had impaired cardiac contractility with increased diastolic pressures, intracardiac thrombus, and BNP of 2,480 pg/mL. Abundant eosinophils, inflammatory changes, and early fibrosis were found on myocardial biopsy consistent with eosinophilic myocarditis. Enoxaparin was started for hypercoagulability, and enalapril for heart failure. She was given methylprednisolone and eosinophil counts decreased rapidly, undetectable on hospital discharge. She demonstrated marked clinical improvement, with no recurrence of pericardial effusion, and BNP trended down to 550 pg/mL.

Discussion: HES is a diagnosis of exclusion, considered when no underlying secondary cause is identified, eosinophil counts >1,500/μL, and resultant infiltration and end organ damage is observed. Patients presenting with markedly elevated eosinophils and cardiac manifestations require a complete evaluation for eosinophilic infiltration. Despite the lack of strong evidence, prompt treatment is required to prevent irreversible cardiac damage.

339

PREVENTING MYOPIA: THE ROLE OF BLURRED LENSES IN MODULATING AXIAL EYE LENGTH

Francis K, Neitz J, Neitz M. University of Washington, Seattle, WA.

Purpose of Study: Myopia, or nearsightedness, occurs when the eye has grown too long for its optics. This study sought to identify a means to prevent progression of myopia using lenses that blur the visual field periphery. Since distant objects are blurred in the myopic eye, it was hypothesized that blurring peripheral images could provide a signal to stop further eye growth and cause the choroid layer behind the retina to swell, pushing the retina forward. Two methods of inducing blur were compared; one was a standard diffuser and the other was a prototype lens designed to blur peripheral images but produce minimal degradation of central visual acuity.

Methods Used: A Zeiss IOL Master was used to monitor the axial length of the subjects’ (n=6) eyes and a Roland Consult - RETImap OCT instrument was used to image the retina and choroid layer. After a week of baseline measurements, subjects wore glasses with a untreated left eye (OS) lens and a Bangertler Occlusion Foil strip attached to the right eye (OD) lens. After four weeks, three subjects then switched to new prototype lenses on their left eyes. These lenses had a clear dot pattern printed on them with a small, unobstructed hole in the center.

Summary of Results: The axial length of OD of all six subjects decreased significantly (p<0.0001) after wearing the occlusion foils for four weeks. The difference in axial length of each eye (OD-OS) also decreased significantly, since each individual’s right eye was equal to or longer than their left eye (p=0.0025). The choroid significantly increased in thickness in the right eye (p<0.0001) and the difference between the choroid thickness between the left and right eyes (OS-OD) decreased significantly. When the OD glasses were removed and the OS eyes were treated, there was a corresponding significant decrease in the axial length of OS (p=0.0157) and increase in OD-OS value (p=0.003).

Conclusions: Blurring the periphery of the visual field significantly decreases the axial length of the eye and increases choroidal thickness. In myopia, the eye is too long, and images are focused in front of the retina. By increasing the thickness of the choroid layer, the retina is brought forward, improving optics in the eye. Lenses that produce blurred images in the periphery but have a clear center provide a potential means for preventing myopia progression.

340

ZINC HOMEOSTASIS IN MALAWIAN CHILDREN AT RISK FOR ZINC DEFICIENCY

Westcott C1, Ryan K2, May T3, Westcott J1, Miller L1, Manary M2, Young G3, Hambidge KM, Krebs N1, University of Colorado, Aurora, CO; 1Washington University in St. Louis, St. Louis, MO and 2Flinders University, Adelaide, SA, Australia.

Purpose of Study: Zinc (Zn) deficiency has been estimated to affect ~25% of the world’s population and can have detrimental effects on growth,
immune, and cognitive development. Children in Malawi are considered to be particularly susceptible to Zn deficiency due to high phytate, low animal source diet (Phytate/Zn > 20) and high prevalence of environmental enteropathy, an inflammatory condition proposed to impair absorption and/or increase losses of nutrients. Prior to undertaking an intervention designed to improve gut function, we studied zinc homeostasis in Malawian children.

**Methods Used:** This study measured Zn homeostasis in 19 apparently healthy rural Malawian children (mean age ± SD, 46 mo ± 6.4). Anthropometric measurements of participants were conducted by local nurses and included height, weight, and mid-upper arm circumference. Variables of Zn homeostasis were measured by administration of stable Zn isotopes or intravenously. Duplicate diets were collected to measure total dietary Zn (TDZ). Fractional absorption of Zn (FAZ) was measured by dual isotope ratios in urine. Total absorbed Zn (TAZ) = FAZ x TDZ. Endogenous Fecal Zinc (EFZ) was calculated by an isotope dilution method, using 2F (divided by F (u x d)) where F is total fecal zinc (mg); f is enrichment of IV Zn tracer in a pooled fecal sample, u is average IV tracer enrichment in urine during the collection period; and d is days.

**Summary of Results:** Participants were severely stunted (mean ± SD, HAZ=-3.27 ±0.77), and underweight (WAZ=-1.88 ±0.75). Results from the zinc stable isotope studies are presented in the Table.

**Conclusions:** Mean consumption of Zn was equal to the RDA. Mean FAZ was higher than expected, resulting in TAZ that exceeded estimated physiological requirement for this age (1.2 mg/d); and EFZ was not excessive relative to intake or absorbed Zn. These data do not support poor zinc status or perturbed zinc homeostasis.

### TABLE 1. Parameters of Zn Homeostasis

<table>
<thead>
<tr>
<th>TDZ (mg/d)</th>
<th>FAZ</th>
<th>TAZ (mg/d)</th>
<th>EFZ (mg/d)</th>
<th>EFZ/kg (mg/d/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.0 ±0.9</td>
<td>0.38±0.08</td>
<td>1.9±0.6</td>
<td>0.9±0.3</td>
<td>0.07±0.02</td>
</tr>
</tbody>
</table>

343

THE RELIABILITY OF CLINICAL TONSIL SIZE GRADING IN CHILDREN

Kumar DS1, Valenzuela D1, Kozak FK2, Ludemann JP2, Moxham P1,2, Lea J1,2, Chadha NK1,2. 1University of British Columbia, Vancouver, BC, Canada and 2British Columbia Children’s Hospital, Vancouver, BC, Canada.

**Purpose of Study:** Tonsillar enlargement is an underlying cause for several health problems in the pediatric population, most notably, Obstructive Sleep Apnea (OSA). Tonsil grading systems (scales) allow clinicians to record and communicate changes in tonsil size. However, the reliability of tonsil grading systems in a ‘real-life’ clinical setting has not been formally studied, and the significant variability associated with their use potentially makes tonsil grading difficult and unreliable. The objectives of this study were to compare the Brodsky, Friedman, and Modified 3-grade tonsil scales and to assess their inter-observer and intra-observer reliability/reproducibility in a clinical setting.

**Methods Used:** We aimed to recruit a minimum of 80 children between ages 3–18 with no major craniofacial abnormalities, who were attending the Pediatric Otolaryngology outpatient clinic at BC Children’s Hospital. For each child, 2 separate tonsil assessments (with at least a 5 minute interval in between) were conducted by 4 independent observers with different clinical backgrounds. These included: 2 staff Otolaryngologists, 1 Fellow/Resident, and 1 Medical Student. Each observer assessed and graded tonsil sizes using 3 different scales. Inter-observer and Intra-observer reliabilities were assessed by deriving the Intra-Class Correlation Coefficient (ICC) and Pearson Correlation Coefficient (PCC), respectively.

**Summary of Results:** Preliminary results (n=86) show mean Inter-observer ICCs to be highest for the Brodsky Grading Scale (0.748), followed by the Friedman Grading Scale (0.685), and Modified 3-Grade Scale (0.643). The mean Intra-observer PCCs for the Brodsky, Friedman, and Modified 3-grade scales were 0.966, 0.946, and 0.944, respectively.

**Conclusions:** The Brodsky grading scale exhibits a higher Inter-observer and Intra-observer reliability than the Friedman and Modified 3-Grade Scales. We hope that these findings will help reduce variability associated with assessing tonsil size and lead to improved clinical care for children.

342

SCREENING FOR DEPRESSION IN ADOLESCENTS IN A LOW-INCOME PEDIATRIC CLINIC IN FRESNO, CA: DOES THE PATIENT HEALTH QUESTIONNAIRE (PHQ-9) WORK?

Mayer MC, Tomajan D, Kammertan T, Kraus K, Yang S. UCSF Fresno, Fresno, CA.

**Purpose of Study:** Suicide is the third leading cause of death in youth ages 15-24 nationwide. Opportunities for depression screening in teens occur at annual physicals; however, children in California after age 9 who are insured with Medicaid are eligible for physicals only every 4 years. We implemented PHQ-9 depression screening at all types of adolescent visits (vaccine-only, urgent care, well-child checkups) at a medical home serving low-income children in downtown Fresno, CA. This quality improvement study investigates the feasibility of the PHQ-9 and provider performance in depression screening of adolescents in a pediatric community clinic.

**Methods Used:** For three months in 2013, 227 children ages 12-19 completed the PHQ-9. Pediatric providers evaluated patients for depression with a positive screen (score > 9/27). We reviewed medical records of all screened patients for their PHQ-9 scores; diagnoses of depression, suicidality, and other conditions; and the quality of providers’ care regarding their PHQ-9 use. Characteristics of depressed and non-depressed patients were analyzed using descriptive statistics, and mean PHQ scores were compared between groups using t-test.

**Summary of Results:** 8.4% of patients had diagnoses of depression. A chart review yielded 2 new diagnoses of depression from the PHQ-9, but there were 4 cases in which providers identified depression despite negative PHQ-9 screens. A significant difference in mean PHQ-9 scores exists between patients with and without depression (9.5 vs. 3.1 respectively, p<0.01). 39% of positive screens were not depression-related, but showed dysmenorrhea, ADHD, a past history of depression with no current depression, drug use, anger management, oppositional defiant disorder, behavior concerns, back pain, and insomnia. Half of positive screens went unaddressed.

**Conclusions:** In our clinic serving low-income children in Fresno, CA, the PHQ-9 identified youth with depression but also other conditions not depression-related. Further research is planned to validate the PHQ-9 in this setting. More education of providers is needed to reinforce depression screening at all adolescent encounters and that positive screens must be addressed with clear documentation in the medical record.

343

RAPID ASSESSMENT SURVEY OF A NEWLY ESTABLISHED NEWBORN CARE UNIT AT DHUALAGIRI ZONAL HOSPITAL, NEPAL

Levy D, Fasil B. University of Utah, Salt Lake City, UT.

**Purpose of Study:** Dhaulagiri Zonal Hospital (DZH) has recently been established in the hill region of Nepal to provide better care for the community. This includes a Special Care Newborn Unit (SCNU) that will focus on advanced care for newborns. This study was undertaken to conduct a facility assessment survey about the care capacity for newborns at the DZH; to describe the current care standards provided by hospital staff; and to identify areas of improvement in the future.

**Methods Used:** We conducted a site visit at the DZH in Baglung District during April and May 2013. Using a previously validated health facility (HF) assessment tool for Nepal, we evaluated the care capacity of DZH. We directly observed care delivery and qualitatively report on compliance with WHO newborn care standards. We conducted open-ended focus group surveys with key medical, administrative and governmental stakeholders to determine hospital strengths, weaknesses, and opportunities for improvement. Reporting of findings is descriptive.

**Summary of Results:** The HF assessment survey revealed 1) absence of essential equipment to provide basic newborn interventions (phototherapy, oxygen monitoring, bag and masks); 2) lack of key infrastructure elements such as reliable power and oxygen; 3) unfulfilled staff positions at the nursing, midwife and MD level.

© 2013 The American Federation for Medical Research
During direct observation of care delivery (12 deliveries, 155 in-patient encounters), the following issues were identified: Only 1/12 deliveries occurred with appropriate delivery room setup. Appropriate initial steps of newborn care occurred in 9/12 deliveries. Timely initiation of advanced resuscitation measures (bag mask ventilation) occurred in 0/3 cases for secondary apnea. 0/155 in-patients had vital signs recorded at least once daily. Hospital staff lacked a care plan for common neonatal conditions such as jaundice, respiratory distress, and also lacked knowledge and skills to identify and manage high-risk newborns. Focus group surveys showed hospital staff to be aware of skill deficiencies and the need for more training, especially with regards to WHO newborn care standards.

Conclusions: The DZH-SCNU staff will require significant investments in infrastructure and staff training to reach WHO newborn care standards.

Purpose of Study: The DZH-SCNU staff will require significant investments in infrastructure and staff training to reach WHO newborn care standards.

Methods Used: The DZH-SCNU staff will require significant investments in infrastructure and staff training to reach WHO newborn care standards.

Summary of Results: The DZH-SCNU staff will require significant investments in infrastructure and staff training to reach WHO newborn care standards.

Conclusions: The DZH-SCNU staff will require significant investments in infrastructure and staff training to reach WHO newborn care standards.

IMPROVING PARENTING OUTCOMES BY ESTABLISHING A POSTPARTUM HOME VISIT PROGRAM IN CHELAN, WASHINGTON

Hippe S. University of Washington School of Medicine, Spokane, WA. Purpose of Study: According to Center for Disease Control reports from 2003-2010, Chelan County has a teen birth rate 36% higher and infant mortality 8% higher than state averages. Residents of the county are also more likely to lack health insurance and to not have a regular doctor. There is need for sound parenting knowledge. In the past four years a postpartum home visit program (HVP) and lactation counselor position have been discontinued due to cuts in federal funding. Initiation of a volunteer-based HVP attempts to fill the void left in these programs’ absence by reaching out to families that could benefit from aforementioned services.

Methods Used: A volunteer training curriculum was arranged using material from the American Academy of Pediatrics and a HVP administered by Johns Hopkins University. Topics included infant care, breastfeeding, home safety, and postpartum depression.

Summary of Results: 15 people were interested in volunteering and 4 people received training. Qualitatively, community members were surprised Chelan County performs poorly in many health indicators. Volunteers were empowered by the training and excited to support mothers and newborns in the community. The two local clinics were receptive of the program.

Program logistics were laid out. There were encouraging signs it will be self-sustaining.

Conclusions: There is interest in Chelan to support families needing sound parenting knowledge. The HVP will be a convenient and effective way to reach out to these families. This study suggests volunteer-based programs may be a viable alternative when funding constraints limit federal- and state-supported programs. This project can be enhanced by gathering evidence to evaluate the impact it has on improving infant health and encouraging appropriate parenting behaviors.

YOUTH TRAUMA PREVENTION IN U.S. BORDER COMMUNITIES: INVESTIGATING THE ROLE OF CULTURAL PREFERENCE ON SELF-ESTEEM AND MOTIVATION FOR EMPLOYMENT AND EDUCATION

Garcia S1,2, Krotz S1, Chang D2, Coimbra R2. 1University of California, San Diego, La Jolla, CA; 2University of California, San Diego, San Diego, CA; and 3San Ysidro High School, San Diego, CA.

Purpose of Study: Motivation for education and work is associated with reduced risks of trauma among youth. Minority youth have increased high school drop-out rates creating a disproportionately large group with increased risk factors related to trauma. Therefore, we investigated factors that contribute to self-esteem and motivation for education and work.

Methods Used: Non-randomized intervention study in high school students of largely Mexican-descent in a U.S. border community. An 8-week intervention program to address barriers related to higher education and employment. Validated scales for self-esteem, motivation for school and employment were used.

Summary of Results: A total of 68 students were included, 27 of which were at-risk youth. There was a significant improvement in grades (3.14 vs. 3.43, p=0.005). No significant change was observed after the intervention in self-esteem, motivation for school or employment. However, there was a significant increase in preference for dominant culture (21.4 vs 23.1, p<0.001).

On multivariable regression, motivation for school was driven by self-esteem scores (+0.02, p=0.012), preference for dominant culture (+0.03, p=0.002), and being female (+0.26, p=0.006); preference for minority culture showed borderline negative association (-0.17, p=0.06). The only variable that had a significant positive association with motivation for employment was self-esteem (+0.03, p<0.001). In the self-esteem analysis, females had lower self-esteem than males (-3.1, p=0.051) and at-risk participants had lower self-esteem compared to all program participants (-3.6, p=0.08).

Conclusions: Improved self-esteem and dominant cultural preference positively correlate with improved grades and motivation for school and work. Future studies should focus on strengthening the link between youth’s ethnic minority culture and academic success.
EARLY CHILDHOOD CARIES PREVENTION IN HARDIN, MONTANA: PATIENT EDUCATION, “FIRST TOOTH, FIRST EXAM,” AND FLUORIDE VARNISH

Tam ML. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Early childhood caries (ECC)—tooth decay before the age of five—is the most common childhood chronic disease in Big Horn County, Montana. In 2000, treatment of ECC cost Medicaid $100 to $200 million. Left untreated, ECC can cause speech delays, malnutrition and impaired learning. Fluoride varnish combined with caregiver education can significantly reduce ECC prevalence. The purpose of this project was three-fold: unite healthcare providers around a shared message on oral healthcare, increase fluoride varnish treatments and educate caregivers on key oral care behaviors.

Methods Used: The target populations for this intervention were caregivers, children ages six months to two years and healthcare providers. Four interventions were carried out: fluoride treatments were incorporated into well-child visits at Hardin Clinic; educational materials on children’s oral care were developed and distributed at two health centers, Hardin Family Dental and Big Horn County Public Health Department; oral hygiene activities were conducted at a daycare and preschool reading time at the library; and a “First Tooth. First Exam.” program from Indian Health Services (IHS) was adapted for healthcare providers to prescribe dental visits for children.

Summary of Results: By collaborating with a variety of healthcare establishments this project connected leaders in each organization with a shared message on preventing ECC. This united front increased commitment from leaders in each organization. The prescription pads and brochures were adopted by both health centers in town, Hardin Family Dental and Big Horn County Public Health Department. Thirty-eight children attended the daycare activity, and 25 children and five parents attended the library activity. There were scheduling restraints that limited the number of parents who could attend, but the children present were very eager to participate.

Conclusions: The collaboration of healthcare providers in this project reinforced common messages on oral care behaviors, early dental visits and fluoride varnish. With the participation of many healthcare establishments, more caregivers and patients were exposed to the interventions. Through these efforts, more children may visit the dentist earlier in life and parents can work more closely with dentists to prevent ECC.

ENGAGING AND EDUCATING ADOLESCENT ATHLETES ON SUN PROTECTION IN BUTTE, MONTANA

Leyde S. University of Washington, Seattle, WA.

Purpose of Study: Rates of skin cancer are dramatically increasing despite the fact that skin cancer is largely preventable. The population of Butte, Montana is at high risk for developing skin cancer because of the high elevation (5,538 feet), 96.5% Caucasian population, and abundance of outdoor recreational activities. During informal interviews with community members, skin cancer was identified as a topic of interest and concern.

Methods Used: A literature review showed that counseling fair-skinned 10-24 year olds on avoiding UV radiation to prevent skin cancer is evidence-based. The literature also showed that using appearance-based messages (e.g., UV radiation causes skin cancer and worsens acne) for adolescents is effective in changing behavior. An hour-long talk was given to adolescent athletes attending the Lady Digger Hoop Camp at Montana Tech University. The camp leader (who operates several other sports camps in the area) was approached about revising camp policies to promote sun protection. In collaboration with the Butte Community Health Center, a booth was set up at the Butte Farmers’ Market to provide free sunscreen and answer questions about sun protection.

Summary of Results: 36 adolescent girls ages 9-16 were in attendance for the presentation. Although skeptical at first, the presentation was well-received and the campers engaged in a thoughtful discussion and Q&A session. Camp policies were revised to decrease sun exposure from 10am-2pm and encourage parents to pack sunscreen and sun-protective clothing. 53 community members stopped by the Butte Community Health Center booth at the Butte Farmers’ Market. Community members appreciated the free sunscreen and commented that the information presented at the booth was very useful to them.

Conclusion: Given the high elevation, predominantly fair-skinned population, and opportunities for outdoor recreation, adolescents in Butte, Montana are at high risk for developing skin cancer. Using an evidence-based approach to educate adolescent athletes about sun protection and skin cancer prevention should increase knowledge and promote sun-safe behaviors such as avoiding UV radiation and wearing sunscreen. Further studies are needed to show that increased education resulted in behavior change.

IMPROVING DENTAL HEALTH FOR LOW-INCOME CHILDREN IN CLALLAM COUNTY

Hallett B. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Washington State children are more than twice as likely as children nationally to have tooth decay. Moreover, Clallam County experiences higher than average decay and more untreated decay than the state average. Children from low-income families are at higher risk for oral disease and often have difficulty accessing dental care. In 2005, less than one third of toddlers enrolled in Medicaid visited a dentist.

The goal of the project was to improve dental health for low-income children in Clallam County through face-to-face oral health education for mothers during the prenatal and early parenthood time period, and increased pediatric dental referrals.

Methods Used: Community partners were identified through discussions with local medical professionals and public health officers. A literature review showed the need for timely oral health education, care referral and assessment, and behavioral interventions. Mothers were consented to learn about oral health during walk-in hours at First Step Family Support Center. Education targeted diet and oral hygiene. Summaries were included in a brochure, along with local dental referral information.

Summary of Results: There were ten participant families, and each family had an average of two children between one and five years of age. All families were covered by Medicaid. Prior to the education, none of the families were aware of the local dental resources accepting Medicaid coupons. Eight of ten families had a local primary pediatric provider for their children. All families expressed concern over dental health of at least one member in their family. All families expressed appreciation for the education and referral to local resources. First Step educators retained dental referral information to give to future families.

Conclusion: The project increased awareness of local dental resources serving children covered by Medicaid. However, challenges remain to improving oral health through diet, and improving access of non-pregnant mothers to dental care. Additionally, an increased ratio of dentists to Medicaid patients is needed, especially in rural areas where distance to care is a significant barrier. While primary care providers can administer some preventive oral health care, pediatric dental professionals are needed to address oral health problems that develop despite preventive efforts.

IDENTIFYING COMMUNITY PERCEIVED CAUSES OF CHILDHOOD OBESITY IN BOYLE HEIGHTS [CA] AND ANALYSIS OF ITS PEDIATRIC HEALTH PROFILE

Huynh PA1, Slussar W1, Whitley M2, Izadpanah N2, Solares J2, Mullennux N2, Lopez G1, Acala H1. 1David Geffen School of Medicine at UCLA, Los Angeles, CA;2AltaMed Health Services, Los Angeles, CA;3UCLA Fielding School of Public Health, Los Angeles, CA and 4UCLA Center for Health Policy Research, Los Angeles, CA.

Purpose of Study: Boyle Heights is an urban community in Los Angeles, CA whose residents endure problems such as chronic diseases and inadequate access to healthy foods. However, it is also an area with strong community...
cohesion. The aims of the study are to (1) understand community perceived causes of childhood obesity in Boyle Heights and (2) identify assets and strategies to prevent its prevalence in this community.

Methods Used: Surveys consisting of 10 questions pertaining to childhood obesity and community strengths were distributed to 49 community members. One focus group was conducted. Five independent readers reviewed data to determine recurring themes related to childhood obesity, identifying community strengths, weaknesses, opportunities, and threats (SWOT). The Boyle Heights Pediatric health profile was constructed using 2009 survey data from the California Health Interview Survey (CHIS) and CHIS Building Healthy Community (BHC) survey. The CHIS BHC oversample was generated in Boyle Heights where 333 adult interviews were conducted with 172 children and 64 teens.

Summary of Results: Respondents expressed several important perceptions regarding childhood obesity. Major themes included lack of knowledge, fast food, and sedentary lifestyles as contributors to obesity. Compared to all of California, LA County, and Service Planning Area (SPA) 4, Boyle Heights experienced poorer pediatric outcomes in a number of variables and better outcomes in others. There is strong perception of community unity and vested interest in building a healthier community. Themes of increasing education, building awareness, and promoting access to healthy foods were identified as ways to address obesity.

Conclusions: The Boyle Heights community attributed childhood obesity to many internal and external factors. Boyle Heights possesses key strengths and opportunities that can be used to create an environment in supporting healthy behaviors. Findings will assist in implementing strategies to leverage community strengths and reduce childhood obesity.
Methods Used: Adult male rats were randomized to four groups and fed for 15 weeks: intact rats on regular chow diet (RCD), intact rats on HFD (I+HFD), castrated rats on HFD (C+HFD), and castrated rats with T replacement on HFD (C+HFD+T). The HFD provided 71% energy whereas RCD provided 16% of energy from fat. Quantitative real time PCR was used to detect the mRNA changes of SCD-1, DGAT1, CPT-Ia, and ApoB. Western blotting validated the change in protein levels of ApoB100.

Summary of Results: T replacement attenuated hepatic steatosis in C+HFD rats. Compared to I+RCD, SCD-1 gene expression was suppressed in I+HFD, and was further suppressed in C+HFD, but not affected in C+HFD+T. No changes were detected in CPT-Ia and DGAT1. In comparison to that of I+RCD animals, ApoB gene expression was similarly suppressed in I+HFD and C+HFD. However, this difference was attenuated in C+HFD+T. Western blot confirmed suppression of ApoB100 protein levels in C+HFD, and reflected the restorative effect in C+HFD+T animals.

Conclusions: In castrated rats with insulin-independent NAFLD, low ApoB100 levels support defective triglyceride export from the liver.

Purpose of Study: There is a clear association between obesity and chronic, low-grade peripheral inflammation. We sought to determine the relative genetic and environmental contributions to obesity-associated peripheral inflammation through a cross-sectional twin study.

Methods Used: Same sex monozygotic (MZ) and dizygotic (DZ) twin pairs, aged 56-65 years were randomly selected from the University of Washington Twin Registry. Subjects with major medical conditions, disability, pregnancy, neuropathy or taking long-term pain medication were excluded. Anthropomorphic measures including body mass index (BMI) were collected along with blood for inflammatory markers including C-reactive protein (CRP) and interleukins 1a, 1b, and 6. Data were analyzed using overall statistical models in which all subjects were treated as unrelated individuals and then using within-pair models, which account for the similar genetics and environment of twins. Univariate and bivariate structural equation models were used to determine the relative genetic and environmental components. Directional analysis was performed to assess the relationship between BMI and CRP.

Summary of Results: There was a significant association between BMI and CRP in the overall model (P < 0.01) and in the within-pair models for MZ and DZ twins (P < 0.01 for both) suggesting little evidence of genetic or familial confounding. The magnitude of the association was similar in all models such that a 1-unit increase in BMI was associated with a 10.2% increase in CRP. There were no consistent associations between BMI and other inflammatory markers examined. In univariate analyses, BMI was strongly genetically determined (heritability=85%) as opposed to CRP (heritability=15%). Bivariate analyses showed no shared genetic component. In directional analysis, the effect of BMI on CRP was significant (P < 0.01) whereas the effect of CRP on BMI was not (P = 0.94).

Conclusions: Analyses of MZ and DZ twins in this study strongly suggest a causal association between BMI and CRP, which is independent of genetics. In addition, directional analysis indicates that elevated BMI is causal of elevated CRP.

Purpose of Study: Intrauterine growth restriction (IUGR) increases the development of adult onset obesity and associated metabolic disorders. Obesity and metabolic disorders stem from adipocyte dysfunction, including increased inflammation. Our group previously showed that, in male adolescent rat SAT, IUGR increases subcutaneous adipose tissue (SAT) expression of the inflammatory cytokine TNF-α, TNF-α signaling plays an important role in the activation of the unfolded protein response (UPR), a cell survival mechanism that mediates cellular dysfunction and apoptosis. UPR activation is accomplished by transcription factors ATF6, CHOP, and BIP as well as increased phosphorylated eIF2α protein. Whether IUGR activates the UPR in rat adipose tissue is unknown. We hypothesize that IUGR increases ATF6, CHOP, and BIP mRNA levels, as well as phosphorylated eIF2α protein, in male adolescent rat SAT.

Methods Used: IUGR was induced by bilateral uterine artery ligation in rat dams at E19 of gestation. Real-time PCR was used to measure mRNA levels of ATF6, CHOP, and BIP in IUGR and control d21 rat SAT. Western blotting was used to measure protein levels of phosphorylated and unphosphorylated eIF2α in the same groups.

Summary of Results: Results are IUGR as % of age and sex-matched control ± SEM. IUGR significantly increased mRNA levels of ATF6 (238 ± 25, p < 0.001), CHOP (214 ± 21, p < 0.001), and BIP (180 ± 18, p < 0.005) in male SAT. IUGR also significantly increased the ratio of phosphorylated to unphosphorylated eIF2α protein (589 ± 308, p < 0.05) in male SAT. No significant changes were found in female SAT.

Conclusions: We conclude that IUGR activates the UPR through increases in ATF6, CHOP, and BIP mRNA levels and increases in phosphorylated eIF2α protein in male adolescent rat SAT prior to the onset of obesity. We speculate that activation of the UPR increases adipocyte apoptosis and contributes to SAT dysfunction in male IUGR adolescent rats.
INTRAUTERINE GROWTH RESTRICTION ALTERS ESTRADIOL SIGNALING IN RAT ADIPOSE TISSUE IN A SEX DEPENDENT MANNER

Holliday D, Trevenzoli I, Zou C, Joss-Moore L. University of Utah, Salt Lake City, UT.

Purpose of Study: Intrauterine growth restriction (IUGR) increases the lifelong risk of visceral obesity and associated comorbidities, with males more severely affected. Our group previously showed that IUGR preferentially increases visceral adipose tissue deposition over subcutaneous adipose tissue (SAT) deposition in male rats, but not in female rats. Vat and SAT deposition and function is regulated by estrogen signaling, with suppressed estrogen signaling contributing to increased adipose deposition. Estrogen signaling is initiated by the binding of estrogen to estrogen receptors alpha (ERα) and beta (ERβ). Despite the role of estrogen and ER receptors in adipose deposition, the effects of IUGR on serum estrogen levels and ER expression in rat VAT and SAT are unknown. We hypothesize that IUGR will alter serum estrogen levels and ER protein abundance in rat SAT and VAT in a sex-dependent manner.

Methods Used: IUGR was induced by bilateral uterine artery ligation on gestational day 19 in Sprague Dawley rats. Offspring were killed at weaning (postnatal day 21) and serum, VAT and SAT collected. ELISA and western blotting were used to determine the serum estradiol (predominant estrogen) and ERα and ERβ protein abundance, respectively.

Summary of Results: Results are reported as IUGR as % of sex-matched control ± SD (*p < 0.05). In male rats, IUGR decreased serum estradiol levels (51 ± 24 %*) and increased ERα (149 ± 53 %*) and ERβ (397 ± 117 %%) protein abundance in SAT, with no effects in VAT. In female rats, IUGR did not alter serum estradiol levels, ERα or ERβ protein abundance in SAT or VAT.

Conclusions: In conclusion, IUGR decreased estradiol serum levels and increased ERα and ERβ protein abundance in SAT in male rats. We speculate that in male SAT, IUGR upregulates ERα and ERβ as a compensatory mechanism for decreased serum estradiol levels, suggesting overall normal estrogen signaling. However, in male VAT, lower estradiol levels in combination with no changes in ERs may result in an overall decrease of estrogen signaling, contributing to visceral obesity development.

IUGR COMBINED WITH A MATURENAL HIGH FAT DIET ADVERSELY PROGRAMS THE MicroRNA-96 - Insig2 - Srebp2 PATHWAY AND INCREASES HEPATIC CHOLESTEROL IN FEMALE, BUT NOT MALE RATS

Zinkhan E1, Yu B1, Yu X1, Schlegel A2, Joss-Moore L1. 1University of Utah, Salt Lake City, UT and 2University of Utah, Salt Lake City, UT.

Purpose of Study: Increased hepatic cholesterol increases morbidity and mortality. The risk of developing increased hepatic cholesterol is modulated by the in utero alteration of nutrient availability via intrauterine growth restriction (IUGR) or a maternal high fat diet (mHFD). IUGR and mHFD often occur together. However, little is known about how IUGR and mHFD combined program increased hepatic cholesterol. Hepatic cholesterol levels are regulated in part via the hepatic miR-96 - Insig2 - Srebp2 pathway. MicroRNA-96 decreases Insig2 mRNA. Insig2 forms part of a protein complex that senses hepatic cholesterol and prevents cleavage and activation of Srebp2 protein. Cleaved Srebp2 acts as a transcription factor for genes involved in cholesterol synthesis and uptake from the blood. We hypothesized that IUGR combined with a maternal HFD would adversely program the miR-96 - Insig2 - Srebp2 pathway and increase hepatic cholesterol in neonatal and juvenile rats.

Methods Used: Female rats were fed either a regular diet or a HFD prior to mating through gestation and weaning. IUGR was induced by uterine artery ligation at E19. Offspring were killed at birth or postnatal day 21. This produced four offspring groups per sex: control, IUGR, HFD, and IUGR-HFD. Hepatic miR-96, Insig2 and Srebp2 protein were quantified using real-time RTPCR and Western blot. Hepatic lipids were measured with a colorimetric kit.

Summary of Results: Compared to sex-matched control, IUGR, and HFD groups, both neonatal and juvenile female IUGR-HFD rats had increased miR-96*, decreased Insig2 protein*, increased cleaved Srebp2 protein*, and increased hepatic cholesterol*. In male rats, IUGR-HFD did not affect levels of miR-96, Insig2, or hepatic cholesterol in either neonatal or juvenile rats, but increased cleaved Srebp2 protein* in juvenile rats. *p < 0.05.

Conclusions: We conclude that IUGR combined with mHFD adversely programs the miR-96 - Insig2 - Srebp2 pathway and increases hepatic cholesterol in female, but not male, rats. We speculate that a sex-specific response to in utero nutrient stressors such as IUGR and mHFD may reflect a hepatic sex-specific microRNA stress response, and is an ongoing focus of our group.
and eye development. Our study was to determine if human milk is therapeutic for dry eye.

**Methods Used:** Benzalkonium chloride (BAK) at concentration of 0.2% was applied to the mouse ocular surface for 11 days. Dry eye was determined using thread tear volume and fluorescein tests on day 0, 1, 4, 7 and 11. Whole human milk, fat reduced human milk and Restasis (cyclosporine) were compared for therapeutic recovery of dry eye. The eyes were examined histologically at day 11 and corneal thickness measured.

**Summary of Results:** The mean corneal thickness at day 11 for saline control was 36.8μm, dry eye was 21.3μm, human milk was 33.2μm, fat reduced milk was 36.1μm, and Restasis 38.5μm. The punctate score as measured by fluorescein and thread tear volume tests were not reliable outcome measures in this model.

**Conclusions:** Treatment of dry eye with human milk and fat reduced milk for 7 days showed significant reduction of disease in comparison with standard of care, restasis.

### 362

**EFFECT OF MAGNETIC RESONANCE IMAGING RESULTS ON THE INTERPRETATION OF ELECTROMYOGRAMS IN PATIENTS WITH CERVICAL RADICULOPATHY**

Laney J1, Fish D2. 1UCLA DGSOM/CDU, Los Angeles, CA and 2UCLA, Los Angeles, CA.

**Purpose of Study:** Our study aims to expose the concordance of EMG in diagnosing cervical radiculopathy (CR); by evaluating EMG results with and without prior knowledge of MRI results.

**Methods Used:** This is a retrospective study in which a database of patients’ information (with CR) from 2011 to current who had both EMG and MRI from the UCLA Spine Center. Two groups of patients were analyzed by first procedure: EMG first and MRI first. A chi-squared analysis was done comparing the concordance between EMG and MRI for each of the groups.

**Summary of Results:** The results of this study indicate significant value of EMG for confirming CR. Of 131 total evaluated patients, 35 patients had EMG first, and 96 had MRI first. Results indicated that there was no interaction between the order of procedures and the agreement between them; there were 20 agreements amongst the EMG first group and 33 amongst the MRI first group (p=0.068). Agreement rates amongst the positive EMG tests (indicating CR) were 82% while negative EMG test agreement rates were 23.5%.

**Conclusions:** The results exhibit the diagnostic value of EMG studies in helping to determine presence of a CR. There does not appear to be a practitioner bias when the MRI results are available prior to the EMG. This study further supports the validity in ordering EMG even when an MRI is not available for determination of the presence of a CR.

![FIGURE 1. Chi-squared analysis shows no significant interaction between agreement rates and procedure order (p=0.068).](Image)

---

**A LUMP IN THE ELBOW—WHERE DID ALL THAT CALCIUM COME FROM?**

Dumas A, Parikh M, DeMartini J, Aronowitz P. UC Davis Medical Center, Sacramento, CA.

**Case Report:** A 62 year old man with a history of chronic kidney disease stage 5, diabetes mellitus, gout and hypertension, presented to the hospital after running out of solution for his chronic peritoneal dialysis. He had lost his insurance after an extended trip to his home country of Mexico, and thus was hospitalized for peritoneal dialysis. Initial labs were notable for hypercalcemia (12.0mg/dL) and hyperphosphatemia (7.4mg/dL). On review of systems he complained of mild right knee pain. Physical examination revealed firm, fixed, non-tender nodules on the right elbow and bilateral metacarpal joints with tenderness over the right olecranon bursa on flexion and extension. Additional labs were notable for normal parathyroid hormone and vitamin D levels as well as negative parathyroid hormone related peptide levels. Imaging of right knee showed vascular calcification, wrists and right elbow showed findings consistent with periarticular calcinosis as well as chronic olecranon bursitis with marked calcium deposition. On further investigation, the patient endorsed taking high dose calcium acetate presumably to prevent secondary hyperparathyroidism. While holding calcium acetate, his calcium levels normalized and his joint pain was stable. Tumoral calcinosis involves the deposition of calcium within periarticular soft tissue or larger joints forming lobular, radiodense masses. It is a rare, benign condition that is usually familial but in some instances can result from metabolic abnormalities including secondary hyperparathyroidism from chronic kidney disease or, as this patient demonstrated, high supplemental calcium intake.
363

COMPARING FRACTURE ABSOLUTE RISK ASSESSMENT TOOLS: AN OSTEOPOROSIS CLINICAL INFORMatics TOOL TO IMPROVE IDENTIFICATION AND CARE OF MALES AT HIGH RISK OF FIRST FRACTURE

Steenhoek CL1, LaFleur J1,2, Horne J1, Meier J1, Mambourg S1, Swislocki A1,3, Nebeker J2, Carmichael J1,2, Veterans Health Administration, Reno, NV; 2University of Utah, Salt Lake City, UT and 3University of California, Davis, CA.

Purpose of Study: Absolute risk assessment (ARA) is the preferred approach to guiding osteoporosis treatment decisions; however, male fracture absolute risk estimation is problematic due to poor discrimination of available tools. Although such tools are appealing for informatics-based population medication management, it is not known whether they are compatible with risk factor information derived from electronic health records (EHRs).

We compared two fracture ARA tools for such use: an adapted World Health Organization’s Fracture Risk Assessment Tool (FRAX) versus the Veterans Affairs (VA)-ARA.

Methods Used: In a case-control study of male veterans cared for in the VA’s Sierra Pacific network in 2002-2013, cases were those with a fracture during the study period. A control matched on age and encounter date was randomly selected for each case. We calculated absolute hip and any major fracture risks using VA-ARA and FRAX; calculations did not incorporate DEXA scans. We estimated the odds of fracture associated with a high-risk classification for each tool. Among cases, we compared the sensitivity of the two tools for correctly classifying patients as high risk.

Summary of Results: Among a total of 8,742 patients, the mean (SD) age was 67.0 (11.1). The VA-ARA correctly classified 40.1% of fracture patients as high risk (32.9% and 34.5% for the hip and any major fracture rules, respectively). The FRAX only classified 17.6% correctly (17.6% for hip and 0.2% for any major fracture). Patients classified as “high risk” using VA-ARA were 34% more likely to have a fracture (95% CI 23-47%, p < 0.0001) and patients classified as “high risk” using FRAX were only 16% more likely to have a fracture (95% CI 4-31%, p = 0.0081) compared to non-high-risk.

Conclusions: Results show that absolute fracture risk estimation with the VA-ARA is more predictive of a first fracture than FRAX when risk factors are collected passively as a routine part of healthcare operations. Decision support tools based on VA-ARA may improve early identification and care of males at risk for fracture.

364

MULTIPLE CHOICE AND IMAGE MAPPED ONLINE MODULES FOR TEACHING THORACIC RADIOLOGIC ANATOMY

Sue M1, Brown K2, Gu Z2, Krause S4, 1DGSOM at UCLA, Los Angeles, CA; 2DGSOM at UCLA, Los Angeles, CA; 3DGSOM at UCLA, Los Angeles, CA and 4DGSOM at UCLA, Los Angeles, CA.

Purpose of Study: This study aims to determine the efficacy of teaching thoracic radiologic anatomy using Perceptual and Adaptive Learning Modules (PALMs) in multiple-choice (MCQ) and image-mapped (IM) formats.

Methods Used: Repeated exposures to different images with the same underlying pattern increase the speed and accuracy of pattern recognition. Thoracic radiologic anatomy PALMs utilize this principle by presenting learners with a sequence of images, categorized by structure, and asking them to identify specified anatomic structures. PALMs adapt to a learner’s ability by sequencing the structures to be identified based on the learner’s previous accuracy and response time (RT) for each structure, and by removing learned structures as the module progresses. In MCQ PALMs, learners identify a structure from a list of 5 choices. IM PALMs ask the learner to click on the location of a given structure. After each trial, both formats provide feedback to the learner on accuracy and RT as well as the correct identity or location of the structure.

Both IM and MCQ PALMs were developed for PA and lateral chest X-rays and thoracic CT scans with and without contrast. We compared efficacy of the PALMs in enhancing performance of Year 2, 3 and 4 medical students based on pre- and post-tests. A Year 2 focus group was also used to compare the two formats and provide feedback about the PALMs.

Summary of Results: The use of either PALM format significantly and dramatically improved knowledge of thoracic anatomy with minimal time investment. Some modules showed significant differences in RTs and accuracies between MCQ and IM PALMs, but no systematic trends were observed. Knowledge transfer from the MCQ to the IM format showed a significant decrement. Students found both types of PALMs useful but preferred the IM to MCQ versions.

Conclusions: Both MCQ and IM PALMs are highly effective in teaching thoracic radiologic anatomy, with some differences between them. Because of the efficacy of PALMs, the introductory thoracic radiology lecture in the internal medicine clerkship at our medical school has been revised to allow greater focus on expanding student knowledge of image interpretation and thoracic pathology and physiology.

365

NOVEL MICROSPHERES FOR CONTROLLED RELEASE OF OLIGONUCLEOTIDES

Xie J1,2, Teng L1,2, Lu J1, Lee RJ1, 1Jilin University, Changchun, China and 2Jilin University, Changchun, China.

Purpose of Study: Antisense oligonucleotides (ASOs) can be designed to inhibit the expression of specific target genes as needed. However, due to their susceptibility to degradation by nucleases and high negative charge, ASOs have limited stability and capability to cross the cell membrane. Long-acting sustained-release microspheres are a novel drug delivery system that has advantages of sustained release, long duration, and thus reduced frequency of administration. In this study, novel microspheres for controlled release of oligonucleotides were prepared by a multiple emulsion-solvent evaporation method.

Methods Used: First, polyethylenimine (PEI, Mw=800) was added to an ASO aqueous solution. Then, 0.4mL of ASO/PEI were mixed with an organic phase with a homogenizer at 12000rpm for 3min. This water-in-oil (w/o) emulsion was then injected into 12mL of a 0.5% PVA aqueous solution and homogenized at 12000rpm for 1min. Then, microspheres were evaporated for 3.5h under stirring at 800 rpm.

Summary of Results: Changing the concentration of ASO/PEI impacted particle size, drug loading and release curves of microspheres. The microsphere particle size, an important parameter, was mainly determined by the size of the droplets formed during preparation. It was found that the greater the size of droplets, the greater the microsphere particle size, and the higher the drug loading.

Conclusions: In this experiment, we could increase the viscosity of the droplets by changing the ASO/PEI concentration. With an increase of ASO/PEI concentration, encapsulation efficiency of ASO was reduced from 54.07% to 46.32%, and the particle size of microspheres increased from 30.14 to 37.62μm.

Health Services A
Concurrent Session
8:00 AM
Saturday, January 25, 2014

366

OBESITY INTERVENTION: NUTRITION EDUCATION IN A RURAL IDAHO FOOD BANK

Grove L. University of Washington School of Medicine, Spokane, WA.

Purpose of Study: Weiser is a town of 5,537 people in Southwest Idaho, located approximately 70 miles northwest of Boise, ID. Weiser Memorial Hospital (WMH) serves a catch-area of approximately 10,000 people. Obesity is a known health issue in the United States and around the world that disproportionately affects low-income people in rural areas. Earlier this year, WMH completed a Community Health Needs Assessment identifying obesity as a top health concern specifically for this area.

Methods Used: Partnership with a local food bank and WMH led to the opportunity for presenting nutrition education at the regularly scheduled food...
distribution. A literature review of the most effective aspects of successful obesity interventions revealed that long-term programs emphasizing behavior change are most effective in achieving desired outcomes. Therefore, four separate materials were created for distribution that offered tips for implementing these strategies as well as nutrition information and healthy suggestions. These materials were distributed with a healthy snack and recipe cards at the food distribution, where meaningful conversations about nutrition were also had.

Summary of Results: More than half of the clients receiving food (75 of 130) stopped by the table to pick up materials, learn about better nutrition, and get a healthy snack. This was well-received by both the food bank coordinators and clients. This intervention opened the door for continued partnership between WMH (who sponsored the printing of materials) and the food bank by highlighting a potential niche that allows the food bank to offer more services and the hospital to reach out to a specific segment of the community. WMH later used these materials for community education at Weiser's annual National Oldtime Fiddlers Contest & Festival.

Conclusions: This brief intervention was part of a much bigger project of promoting health in Washington County. For the partnership and education established by this project was a step in the process of addressing the major health issue of obesity, reaching a relatively small number of people. However, its impact was large in illustrating the power of building partnerships and starting with small projects in order to make way for larger-scale interventions.

367
EVALUATING THE IMPACT OF HEALTH EDUCATION AT A FEDERALLY QUALIFIED HEALTH CENTER FOR PERSONS WITH DIABETES
Tukainen E1, Solares J3, Hochman M3, Steers N2, Mangione CM1,2.

Purpose of Study: To evaluate the effectiveness of a health education program implemented by AltaMed Health Services (a non-profit organization comprised of multiple FQHCs) in Los Angeles and Orange County. Our goal is to determine whether participation in a health education program leads to improvement in glycemic control, lipid profile, body mass index and blood pressure compared to patients receiving usual care but did not participate in the program.

Methods Used: We conducted an observational pre-post evaluation of patients with diabetes at AltaMed. We compared changes in HbA1C, BP, LDL-c levels, and BMI among those who attended the class compared to contemporaneous control group.

Summary of Results: We have analyzed data from 1355 patients with diabetes, of whom 368 patients received health education classes and 987 patients did not. Both intervention and control group were similar with approximately 56% female participants. Mean age for both groups was about 54 years and both groups were approximately 90% Hispanic. Unadjusted change in A1c from baseline to 6 months post for the intervention group was -1.4% (SD=0.1) and for the control group was -0.8% (SD=0.1). Both unadjusted and adjusted analyses of the change in BP, LDL-c, and BMI are currently underway.

Conclusions: Patients exposed to the health education program had significantly greater improvement of -0.6 (SD=0.1) in A1c. Improved glycemic control is associated with long-term reduction in microvascular complications.

368
PROMOTING THE ADOPTION OF APPROPRIATE INFANT AND YOUNG CHILD FEEDING PRACTICES IN RURAL VIETNAM THROUGH PEER-TO-PEER SUPPORT GROUPS
Rowan B. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Childhood malnutrition is a primary contributor to disease in La Hien, a rural commune in northern Vietnam. In 2012, 15% of children under 5 in the commune were underweight, despite national malnutrition control programs. Previous research suggests childhood malnutrition in the region is largely attributable to inappropriate infant and young child feeding (IYCF) practices. The goal of this project was to increase IYCF knowledge and promote the adoption of appropriate IYCF practices through the creation of village-level peer-to-peer support groups.

Methods Used: A 3-day training course in IYCF support group facilitation was developed using materials from various standard sources, focusing on communication skills and key IYCF recommendations. Vietnamese medical students participated in an initial training and helped to implement a cascade training for village health workers (VHWs) and partnered community members. Students then assisted the newly trained facilitators with their village’s first support group meeting.

Summary of Results: Four medical students completed the initial training and implemented the training of 3 VHWs and 3 community members. Each village hosted their first support group meeting with 7-9 participants. Facilitators led discussion, answered questions and distributed IYCF pamphlets, successfully integrating IYCF knowledge with their new facilitation skills. Participants agreed that the meetings were useful and at least two villages plan to continue meeting. Medical students and the local university have agreed to provide follow-up and support, and the commune health center hopes to potentially expand and integrate the project into its current nutrition program. The training materials have also been left with the university to guide future student-led projects.

Conclusions: Village-level peer-to-peer support groups can be an effective way of promoting IYCF discussion and increasing IYCF knowledge among caregivers. This project suggests that these support groups can be successfully implemented in rural areas through local, student-led trainings of VHWs and community members, especially if coupled with the continued support of a regional university. Future work will be necessary to determine if these meetings achieve the goal of increasing uptake of appropriate IYCF behaviors.

369
TOBACCO USE INITIATION PREVENTION IN BROWNING, MT
Welder ED. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Tobacco use is the number one cause of preventable death among American Indians, occurring at twice the mortality rate of other demographic groups in the US. Accordingly, 14.7% of American Indian students living within Montana reservations reported typically smoking 20 or more days per month, compared to 6.4% statewide. This project aims to reduce tobacco use by addressing the problem of tobacco use initiation among Browning youth.

Methods Used: This intervention specifically targeted the use of corporate tobacco, rather than ceremonial tobacco, because studies show that culturally sensitive tobacco use prevention is more effective than other interventions. Collaborative partners included both Tribal Health and local high school volunteers. Tribal Health helped to secure access to community events while high school volunteers, as young locals familiar to the community, made the booths more approachable for the youth. Youth were encouraged to pledge to be “corporate tobacco free” by tracing their hands and signing their names on poster boards while educators discussed the difference between corporate tobacco and ceremonial tobacco, as well as the dangers of tobacco use. Booths were set up at Blackfeet Youth Day and North American Indian Days, both...
ideal venues for interacting with Blackfeet youth in a receptive environment where healthy lifestyle choices were actively encouraged.

**Summary of Results:** Overall, 42 youth pledged not to use corporate tobacco and were briefly counseled on the dangers of tobacco use. Over 100 additional youth saw the posters on display. The booth was well received by the community as a whole because of its targeted message warning specifically against corporate tobacco use, as opposed to ceremonial tobacco use.

**Conclusions:** This project was effective because it was tailored to the target community and was presented in two ideal venues. Background research and collaborating with the right partners were critical in meeting these criteria. Tobacco use initiation among teenagers remains a major health concern for the Browning community. Fortunately, the community is receptive to culturally sensitive interventions that could reduce the rate of tobacco use initiation.

370  
**HEALTH EDUCATION AND HEALTH NEEDS ASSESSMENT THROUGH TARGETED HOMELESS OUTREACH IN MISSOULA, MT**

Moorhead MM, University of Washington, Seattle, WA.

**Purpose of Study:** The city of Missoula, MT is a temporary or permanent home to at least 1,064 homeless individuals yearly. Nationally, homelessness is an independent predictor of poor health outcomes. It is twice as likely that a homeless individual will report unmet medical care needs and twice as likely that they have had a hospital admission in the last year compared to their housed counterparts. The purpose of this project was to assess and address the unmet medical needs of Missoula's homeless population.

**Methods Used:** Three strategies were used to assess or address the unmet medical needs of Missoula's homeless population. Feedback from community leaders and a through literature review were instrumental in the development of this approach 1) A healthcare needs assessment survey was administered by Missoula's Homeless Outreach Team using convenience sampling of homeless individuals, in which I participated as a volunteer 2) After the survey the team offered pertinent information about available resources, addressing issues noted by the participant during the interview. 3) Educational materials were developed for Missoula's Homeless Shelter staff to help them address communicable diseases and medical emergencies in the shelter setting.

**Summary of Results:** Through this project 60 interviews were conducted. Data from the needs assessment was compiled and can be used by the Outreach Team as a first-step for further community level project development. Education offered to participants ranged from information about the Health Care for the Homeless clinic in Missoula and help making an appointment, to counseling on hospice services. For the Homeless shelter staff, a 26-page medical resource guide was developed including information on communicable diseases, exposure-related conditions, trauma and emergency first aid, and staff health and safety.

**Conclusions:** Even though Missoula has reasonable services for homeless individuals, there are still considerable barriers to accessing healthcare, both inherent in the system, and set by homeless individuals’ own limitations. One possible means for addressing these needs could be through future collaboration of healthcare providers and the Homeless Outreach Team to bring health care to the most vulnerable populations on the streets of Missoula.

371  
**IMPROVING ORAL HEALTH LITERACY AND BREASTFEEDING PRACTICES IN CUT BANK, MONTANA**

Low D, University of Washington School of Medicine, Seattle, WA.

**Purpose of Study:** Over 1/3 of children in Cut Bank live below the poverty line, making access to healthcare very challenging. This is especially true among the Blackfeet Indians and Hutterite colonies, who not only face challenges of poverty, but who also grapple with issues of social exclusion. As such, the Women, Infants and Children (WIC) supplemental nutrition program plays a critical role in Cut Bank, striving to reach these communities and provide a healthcare safety net. Yet, despite WIC’s involvement in Cut Bank, reports suggest that oral health literacy is limited and breastfeeding practices fall markedly short of national recommendations. The purpose of this project is to increase awareness about oral hygiene and breastfeeding practices by partnering with WIC to give educational presentations to WIC clients.

**Methods Used:** Peer reviewed medical literature was consulted to develop effective educational presentations. These presentations were given to WIC clients before and after their scheduled appointments at WIC clinic days in Cut Bank. Each presentation was individualized and lasted 5–10 minutes, focusing on the importance of fluoride use, preventing baby bottle tooth decay, and exclusive breastfeeding for 6 months. As suggested by the literature, the education included an oral presentation, visuals, and physical examples of bottles and toothbrushes, so that WIC clients could learn orally, visually and through practice.

**Summary of Results:** As self-reported by WIC clientele, these presentations increased oral health literacy and knowledge of breastfeeding practices. Additionally, 1/3 of participating women reported that after listening to the presentation, they were newly considering specific behavior changes such as buying fluoride supplements and changing night-time bottle-feeding practices. Whether these changes are implemented is yet to be seen.

**Conclusions:** Multi-method educational forums can be used to encourage better oral health and better breastfeeding practices for WIC women and children in Cut Bank, Montana. However, there is a great need for expanded coverage of this type of education, as many patients, especially those most at risk, often miss their WIC appointments. Therefore, to ensure that these clients receive nutritional supplementation and educational materials, greater outreach is needed.

372  
**VISUAL CONSEQUENCES OF iPAD USE: A PILOT STUDY**

Maducdoc M, Crow W, University of California, Irvine, Irvine, CA.

**Purpose of Study:** The purpose of the study is to quantify the degree of eye symptoms associated with reading text on an iPad compared to a book.

**Methods Used:** 54 students were randomly assigned to two groups (book/iPad). Both groups read text for one hour. Questionnaires were used to determine symptoms.

**Summary of Results:** Mean responses for the control group: eye pain 1.1 (0.3), irritation 1.0(0), eye strain 1.6(0.5), and sensitivity to light 1.1(0.3). Mean response for the iPad group: eye pain 1.5(0.7), irritation 1.6(0.8), eye strain 2.3(1.0), and sensitivity to light 1.5(1.0). Differences in mean were statistically significant (p < 0.05).

**Conclusions:** There were increases in eye pain, irritation, eyestrain and sensitivity to light associated with the iPad group. Reading on iPads may induce increased levels of eye pain, irritation, eyestrain and sensitivity to light.

373  
**EXPERIMENTAL RESEARCH INTO THE INFLUENCE OF YOGA WORKOUTS ON HEART RATE VARIABILITY OF THE MIDDLE AGED AND OLD PEOPLE**

Huang Z1,2, He M1, 1Liaoning Normal University, Dalian, China and 2Changchun Normal University, Changchun, China.

**ABSTRACTS:** Purpose of Study: HRV is one of the non-invasive electrocardiogram monitoring indices and may reflect the regulation of the cardiovascular system by the autonomic nervous system and response to various factors by the same system, which is very significant for detection of cardiovascular diseases and function rehabilitation at present. This research is to analyze and discuss the influence of 32-week Yoga workouts on the autonomic nervous systems of the middle-aged and old females by experiment.

**Methods Used:** 31 middle aged and old females ranging from 50 to 60 years old are selected to do four times per week and 30–40 minutes every time constantly under the instructions of professional Yoga coaches. The time domain indices, the frequency domain indices and non-linear indices of the subjects’ heart rate variability are tested by using the self-generate physiological coherence system before and after experiments.

**Summary of Results:** Through 32-week experiment, standard deviation of all normal RR intervals (SDNN), the root mean of the difference between adjacent normal N-N intervals (RMSSD) and the percent of NN50 in the total
number of NN intervals (PNN50) of the subjects after the experiment is a little higher than that before the experiment with the total power, the power within the high frequency range (HF) and the power within the low frequency range (LF) and normal LF power (LFnorm) as well as the ratio of LF to HF (LF/HF) rising while the power within the ultralow frequency range (VLF) and normal LF power (LFnorm) are down. There is no significant difference (P > 0.05) of the indices before and after the experiment. The stability indices, the adjustment capability indices and the synthetic evaluation indices of the non-linear indices rise significantly (P < 0.05).

Conclusions: The vagus nerve activities in the autonomic nervous system of those having done Yoga workouts are improved, which means Yoga has the functions of adjusting the autonomic nervous systems, in particular improving the vagus nerve activities, however it fails to improve the balance of the sympathetic nerves and vagus nerves. According to the non-linear indices, Yoga workouts may effectively improve the middle-aged and old people's ability to adjust and control bad emotions.

Neonatology - Developmental Biology
Concurrent Session
8:00 AM Saturday, January 25, 2014

374 MECHANISTIC UNDERSTANDING OF T REGULATORY CELL TRAFFICKING IN NORMAL AND PATHOLOGIC PREGNANCIES
Vyas NM, Nguyen TA, Yesayan M, Sneed AL, Kahn DA. David Geffen School of Medicine at University of California, Los Angeles, Los Angeles, CA.

Purpose of Study: Maternal and fetal lymphocytes at the utero-placental interface (UPI) demonstrate unique activation status.

Methods Used: Patients with normal third trimester pregnancies were recruited for sampling of maternal peripheral blood, matching cord-blood, and endometrium at the time of delivery. Lymphocyte populations and their functionality were characterized using flow cytometry and in-vitro suppression assays.

Summary of Results: Maternal lymphocytes isolated from the UPI revealed increased accumulation of CCR6-bearing T regulatory (Treg) cells previously shown to be crucial for the maintenance of normal murine pregnancies. Peripheral Treg cells in women with preeclampsia bore CCR6 at a higher rate than normal. A previously undescribed NK-T cell population bearing CD56, CD3, and CD11b was abundant and secreted the pro-inflammatory cytokine TNF-α. Lastly, increased memory phenotype of fetal Treg cells was observed when the placenta implanted over a previous uterine scar.

Conclusions: This study has proven to be unique in its ability to assess matching maternal-fetal lymphocyte compartments. Women with preeclampsia do not show the activation of NK and T cells in peripheral blood observed in healthy pregnancies. Unique populations of maternal lymphocytes traffic to the UPI in normal pregnancies with the potential to mount in healthy pregnancies. Unique populations of maternal lymphocytes trafficking to the UPI demonstrate unique activation status.

376 MESENCHYMAL STEM CELLS MODIFIED BY SPECIAL TRANSCRIPTION FACTORS TRANSDIFFERENTIATE INTO β-LIKE CELLS
Tang X1,2, Jiang Z1, Li W1, Zhang R1, Zhang X1, Fang L1, Hu L1, Cai S1, 1Anhui University of Science & Technology, Huainan, China; 2Tianjin Medical College, Tainjin, China and 3Jinan University, Guangzhou, China.

Purpose of Study: This study was designed to investigate the mechanisms of the differentiation of mesenchymal stem cells into insulin-producing cells under special transcription factor induction.

Methods Used: This study was designed to efficiently induce the differentiation of the mesenchymal stem cells into insulin-producing islet cells by modifying the expression of pancreatic and duodenal homeobox factor 1 (PDX1) and NKX6 transcription factor related 1 (NKX6.1). The bone marrow mesenchymal stem cells were infected by the recombinant adenoviruses carrying Pdx1 and Nkx6.1 genes, in combination with several cytokines for differentiation. The expression of PDX1, NKX6.1 and insulin and C-peptide in the differentiated bone marrow mesenchymal stem cells were detected by RT-PCR and Western blot. The differentiated bone marrow mesenchymal stem cells were transplanted into the subrenal capsule of diabetic mice, and the cell morphology of the grafts, as well as their secretion of insulin and C-peptide, were examined. The effects of transplantation with the induced cells were also investigated, mainly through measuring the blood glucose levels of the diabetic mice.

Summary of Results: The MSCs induced by recombinant adenovirus of pAdxsi-CMV-PDX1/CMV-NKX6.1 and several cytokines showed positive dithizone staining and significant expression of insulin and Glucose transporter-2, as being revealed by Western blot, immunohistochemical staining and indirect immunofluorescence. Stimulation with different levels of glucose caused different insulin secretion levels at 120.4±109.3 and 3539.8±245.1 mU/L with 5.5 and 25 mmol/L treatments, respectively. More importantly, the transplantation of induced cells recovered the serum glucose in Streptozotocin mice to normal levels.

Conclusions: Co-expression of exogenous PDX1-1 and NKX6.1 efficiently induced the differentiation of bone marrow mesenchymal stem cells into insulin-producing cells. The transplantation of the induced cells restored the blood glucose levels in STZ-induced diabetic mice, providing a new direction for diabetics treatment.
to exostosin-like 3 (EXTL3) and upregulates production of proteins responsible for pancreatic development and islet differentiation. HIP2B has been studied in animal models, adult pancreatic tissue, and an immobilized pancreatic cell line, but has not been evaluated in the developing human fetal pancreas. Fetal pancreatic cell cultures contain significant populations of undifferentiated cells, allowing for further investigation of the effects of HIP2B on human pancreatic cell growth and differentiation. We evaluated the effects of HIP2B on gene expression and protein production of insulin, EXT3 and Neurogenin 3 (Ngn3), a pancreatic transcription factor important in the differentiation of endocrine pancreas.

Methods Used: Fetal pancreatic samples were isolated from 13 to 18 weeks gestation. A portion of each sample was formalin fixed for immunostaining. Primary cell suspensions were created and flow cytometry performed to verify the presence of EXT3L3 receptors. Cells were incubated at 50,000 cells/mL in culture medium containing HIP2B (generously provided by CureDM) from 0 to 500μM. Cells were cultured for 1, 3, or 10 days. RNA was isolated at each time point and qPCR performed.

Summary of Results: Insulin and glucagon staining could be clearly identified in pancreatic islets at all gestations tested. Over 90% of cells expressed EXT3. A dose dependent increase in Ngn3 gene expression was seen in day 1 cultures (p < 0.01, 0 versus 100 and 500μM HIP2B) and day 3 cultures (p < 0.05, 0 versus 100μM) which was not evident at day 10, whereas a dose-dependent increase in insulin gene expression was only seen in day 10 cultures (R2 = 0.49, p < 0.05). No differences were identified in EXT3L3 gene expression at any of the time points.

Conclusions: HIP2B increased gene expression of Ngn3 (within 24 hours of culture), and insulin (after 10 days in culture) in a dose dependent manner. There was no change in EXT3L3 gene expression during the culturing process. We speculate that HIP2B might stimulate pancreatic progenitor cell differentiation, resulting in β-cell growth in mid-trimester human fetal pancreatic endocrine cells.

378 CHRONIC FETAL HYPOXEMIA ATTENUATES GLUCOSE STIMULATED INSULIN SECRETION IN FETAL SHEEP

Benjamin J1, Culpepper C1, Brown L1, Thorn S1, Jonker S2, Limesand S3, Wilkening R1, Hay W2, Rozance P1, 1University of Colorado School of Medicine, Aurora, CO; 2Oregon Health & Science University, Portland, OR and 3University of Arizona, Tucson, AZ.

Purpose of Study: Fetal insulin secretion is stimulated by glucose and inhibited by acute hypoxemia. However, whether chronic fetal hypoxemia inhibits glucose stimulated insulin secretion (GSIS) has not been tested. We hypothesize that fetal anemia will chronically reduce oxygen concentrations and decrease GSIS in the sheep fetus.

Methods Used: Catheters were placed surgically in late gestation singleton fetal sheep. Several days later, they were either bled with isovolumetric saline replacement for an average of 9 days (Anemic, n = 11), or not bled (CON, n = 7). Fetal arterial pH; blood gases; hematocrit; and arterial plasma glucose, insulin, and lactate were measured daily. On the final day, GSIS and glucose potentiated arginine stimulated insulin secretion (GP-ASI) were measured. Pancreatic gene expression was measured by real-time polymerase chain reaction (PCR).

Summary of Results: Fetal arterial oxygen content and hematocrit were 50.4% and 30.9% lower, respectively, in Anemic versus CON (P < 0.005). Arterial plasma glucose concentrations were 15% higher in the Anemic group at the study conclusion (P < 0.05). Fetal arterial pH, PCO2, PO2, hemoglobin-oxygen saturations, lactate and insulin were stable throughout the experiment. During the GSIS study, steady-state glucose concentrations in the Anemic group were 9.6% higher than CON (P < 0.05), but GSIS was lower (P < 0.05), particularly in the early phase (10-15 minutes). There were no differences for GP-ASI between groups. There were no significant differences between groups in gene expression of insulin, glucagon, pancreatic polypeptide, somatostatin, glucokinase, glucose transporter 2 (GLUT2), or pancreatic and duodenal homeobox 1 (PDX-1).

Conclusions: Chronic fetal hypoxemia due to fetal anemia attenuates GSIS. In pregnancies complicated by fetal hypoxemia, such as intrauterine growth restriction, low oxygen concentrations likely contribute directly to β-cell dysfunction. We speculate that improving oxygen levels in these situations could improve insulin secretion.

379 PROLONGED AMINO ACID INFUSION IN INTRAUTERINE GROWTH RESTRICTED FETAL SHEEP DOES NOT REDUCE NET UMBILICAL GLUCOSE UPTAKE RATES

Wai SG, Rozance P, Thorn S, Wilkening R, Hay W, Brown L. University of Colorado School of Medicine, Aurora, CO.

Purpose of Study: Prolonged amino acid (AA) infusion into normally grown, late-gestation fetal sheep increased AA oxidation and decreased net umbilical glucose uptake rates, indicating a shift in substrate oxidation from glucose to AA. Our objective was to determine whether prolonged AA infusion into IUGR fetal sheep decreased net glucose uptake rates from the placenta.

Methods Used: Catheters were placed in IUGR and control (CON) fetuses at day 112–120 of gestation (term 145 days). IUGR fetuses received TrophAmine® to increase plasma AA concentrations 50% above baseline (IUGR-AA, n = 5) or saline (IUGR-sal, n = 6) for 7–14 days. CON animals received saline (n = 7). During the infusions, fetal blood gases, glucose, lactate, insulin, and branched-chain AA (BCAA) were measured. On the final day of infusion, fetal oxygen, glucose, and lactate uptake rates, and body weight and muscle weights were determined.

Summary of Results: Fetal BCAA increased 61% from baseline in IUGR-AA group (p < 0.05). IUGR-AA and IUGR-sal fetuses had lower O2 content (37%) and glucose concentration (26%) compared to CON by the end of the infusion period (p < 0.005), but there was no difference between IUGR groups. Glucose uptake rates (IUGR-AA 15.31 ± 1.17, IUGR-sal 15.77 ± 1.05, CON 20.18 ± 2.08 μmol/kg/min), oxygen uptake rates (IUGR-AA 269.3 ± 0.04, IUGR-sal 270.3 ± 0.01, CON 321.2 ± 0.2 μmol/kg/min), glucose-oxygen quotients (IUGR-AA 0.54 ± 0.03, IUGR-sal 0.55 ± 0.02, CON 0.56 ± 0.02), and lactate production were similar among groups. Fetal weights and biceps femoris weights standardized to lower limb length were lower in both IUGR groups compared to CON (p < 0.05).

Conclusions: Prolonged AA infusion into the IUGR fetus did not affect fetal glucose or oxygen concentrations. Unlike previous studies in normally growing fetuses, we did not observe lower umbilical glucose uptake rates or lower glucose-oxygen quotients. We speculate that exogenous AA in the IUGR fetus are used for purposes other than to maintain oxidative metabolism, such as protein accretion or lactate production. Studies are underway to measure net fetal protein accretion rates and molecular regulation of protein synthesis in skeletal muscle.

Pulmonary and Critical Care II
Concurrent Session
8:00 AM
Saturday, January 25, 2014

380 CRITICAL ILLNESS IN THE INTENSIVE CARE UNIT: DON'T GET TOO OLD AND DON'T GET TOO MUCH INSULIN

Repine JE, Elkins N, Wilson P, Agazio A, Fernandez-Bustamante A, Repine JE. University of Colorado Anschutz Medical Campus, Aurora, CO.

Purpose of Study: Motivated by continuing controversy about the effect of conventional versus intensive insulin therapy on blood glucose levels and the survival of critically ill patients (NEJM 364:1280, 2011), we evaluated the effect of insulin treatment with a simplified, well-controlled rat model used to study the Acute Respiratory Distress Syndrome ("ARDS").

Methods Used: Groups of 3-8 young (3-4 month) and old (12-16 month) Sprague-Dawley rats were infused with cytokines (Interleukin-1 and LPS) that produce an acute respiratory distress syndrome (ARDS) in humans. LPS increased lung neutrophil sequestration and edematous lung injury. Blood glucose levels (glucose) were measured 2hr after cytokine infusion. Lung lavage neutrophil numbers (neutrophils) and lung lavage protein concentrations (proteins) were measured 24hr after cytokine infusion and used as biomarkers of "ARDS".

© 2013 The American Federation for Medical Research.
Summary of Results: While being older or receiving too much insulin that produces hypoglycemia, measuring blood glucose levels and giving insulin nearly continuously and levels (252±28 mg/dl), neutrophils (85±28 x 10⁶), and proteins (7.3±1.1 μg/μl) than young rats. Young rats treated with “conventional” amounts of insulin that produced normoglycemia (131±17 mg/dl) had decreased neutrophils (38±17 x 10⁶) and decreased proteins (0.81±0.30 μg/μl) compared to untreated young rats. However, in contrast, young rats treated with “intensive” amounts of insulin that produced hypoglycemia (72±16 mg/dl) had increased neutrophils (75±16 x 10⁶) and increased proteins (3.5±1.0 μg/μl) compared to both untreated and conventional insulin treated young rats.

Conclusions: Giving the right amount of insulin reduces blood glucose to normoglycemic levels and decreases lung inflammation and injury (“ARDS”) while being older or receiving too much insulin that produces hypoglycemia increases lung inflammation and injury (“ARDS”). Giving the right amount of insulin should be worthwhile but will depend on better ways of serially measuring blood glucose levels and giving insulin nearly continuously and very carefully to these dynamic, critically ill patients.

381
THE MEVALONATE PATHWAY REGULATES EOTAXIN-3 SECRETION FROM HUMAN AIRWAY EPITHELIAL CELLS: A THERAPEUTIC ROLE FOR SIMVASTATIN IN ASTHMA
Sandhu K, Ort S, Wu R, Zeki AA. U.C. Davis School of Medicine, Sacramento, CA.

Purpose of Study: The Th2 inflammatory response is central to human allergic asthma. Interleukin-13 (IL13) and the eotaxins play a central role in airway eosinophilia. Eotaxin-3 in particular is associated with corticosteroid-resistant severe asthma. Statins, which inhibit HMG-CoA reductase in the mevalonolate (MA) pathway, have been shown to reduce eosinophilic airway inflammation in animal models. The effect of statins on this response in human airway epithelium is unknown. We hypothesized that simvastatin inhibits IL13-induced eotaxin-3 expression and protein secretion in human airway epithelial cells by inhibiting the MA pathway.

Methods Used: Human bronchial epithelial (HBE1) cells were grown to 90% confluence in submerged D-media conditions. They were pre-treated with simvastatin (Sim at 1, 5, 10, 20 μM) for up to 72 hours, then stimulated with IL13 (20 ng/mL) for 12 hours to induce eotaxin-3 production. Cells were then harvested for RNA and protein, and cell media were collected for ELISA.

Summary of Results: Sim reduced basal eotaxin-3 mRNA by 37.8% (p=0.0008) and IL13-induced eotaxin-3 mRNA by 58% (p<0.0001). Sim inhibited eotaxin-3 protein secretion by 70% in a MA-dependent manner. Sim ± farnesylpyrophosphate (FPP) and Sim ± geranylgeranylpyrophosphate (GGPP), where FPP and GGPP are downstream metabolites of MA, showed that Sim inhibition of eotaxin-3 secretion was GGPP-dependent and FPP-independent, suggesting a Rho or Rac GTAPase signaling mechanism. Parallel studies using Alamar Blue showed no adverse effects on cell viability at a dose of Sim ≤ 20 μM.

Conclusions: The MA pathway controls airway epithelial eotaxin-3 chemokine expression and extracellular secretion. This is a novel finding showing that the ubiquitous MA pathway, also known as the cholesterol biosynthesis pathway, regulates allergic responses in normal human airway epithelial cells. These results suggest a key role for Sim in mitigating asthmatic allergic responses in human airways. Further research is needed regarding the direct therapeutic potential of statins on the airway compartment.

382
DEVELOPMENT OF A LOW COST ULTRASONIC SPIROMETER
Hallberg CJ, West TE, Olson LE. 1University of Washington, Seattle, WA, 7University of Washington, Seattle, WA and 8Marquette University, Milwaukee, WI.

Purpose of Study: Respiratory illness is a leading cause of death and disability worldwide. Spirometry is an essential tool for the diagnosis and management of respiratory disease. Unfortunately, spirometers are prohibitively expensive in many regions of the world; furthermore, they require daily calibration with costly test equipment. Ultrasonic spirometers do not require regular calibration but are expensive, costing between $1,000 and $2,000. Much of this cost is due to the use of custom computer chips and specialized ultrasonic transducers. The goal of the project was to develop an ultrasonic spirometer, using readily available components, with a target cost of less than $50.

Methods Used: The spirometer flow head was modeled in drafting software and 3D printed in plastic. Two ultrasonic transducers, an operational amplifier, comparator and a microcontroller were selected based on their low cost and availability. A printed circuit board was designed, manufactured and assembled. Ultrasonic pulses were transmitted between the transducers and time of flight was determined by the third zero crossing. Flow rate is proportional to the difference between the upstream and downstream time of flight divided by their product. The flow samples were captured at 500 Hz and integrated to determine volume.

To test flow linearity, compressed air was passed through a rotameter and then through the experimental spirometer. Flow measurement data was collected for nine integer flow rates between 0 and 8 cubic feet per minute. A calculated three-liter syringe was used to evaluate volume accuracy.

Summary of Results: The flow response of the spirometer was linear within the tested range, with a sensitivity of 4.5 mL/Δ4 ns and a noise level of ±7 mL. The mean volume measured with the three-liter syringe was 3.015 L (2.977±0.054 95% CI, n=13) with all trials within 3.5% of 3 L, the range stipulated by the American Thoracic Society guideline for spirometer standardization.

Conclusions: These preliminary results demonstrate the feasibility of producing an ultrasonic spirometer with commercially available components. The cost per device is approximately $40. Pulmonary medicine clinicians and researchers who work in resource-limited settings would welcome such a device.
AN EVALUATION OF THE PHARMACOGENETICS OF INHALED GLUCOCORTICOIDS AND PEDIATRIC ASTHMA CONTROL

Stockmann C1, Fassl B1, Reilly CA1, Nkoy F1, Gaedigk R2, Loader S2, Yost G3, Ward R1, 1University of Utah, Salt Lake City, UT and 2University of Missouri, Kansas City, MO.

Purpose of Study: Inhaled glucocorticoids are a mainstay of therapy in pediatric asthma; however, 30% of children fail to respond. This study assessed the relationship between allelic variations in genes involved in cytochrome P450-mediated glucocorticoid metabolism and pediatric asthma control.

Methods Used: Variability in asthma control scores (ACS) and the connection to genetic variation in drug metabolism was assessed by genotyping ten single nucleotide polymorphisms (SNPs) in CYP3A4, CYP3A5, CYP3A7, and PPARA. Genotype information was compared with ACS (0 = well-controlled to 15 = poorly-controlled), as determined using a validated tool from the National Heart Lung and Blood Institute.

Summary of Results: We recruited 322 asthmatic children who were receiving fluticasone (90%) and beclomethasone (10%). ACS were significantly improved among fluticasone-treated children with the inactivating CYP3A4*22 allele (median 3, range 0-12), as compared to patients without the CYP3A4*22 allele (median 4, range 0-15) (P=0.02). Additionally, for children treated with beclomethasone, the inactivating CYP3A5*3 allele was associated with improved asthma control scores (median 4, range 1-12) when compared to those without the CYP3A5*3 allele (median 10, range 5-13) (P=0.01).

Conclusions: The presence of inactivating SNPs in CYP3A4 and CYP3A5 was associated with improved asthma control for two inhaled glucocorticoids. Identification of these influential genetic loci suggests that it may be possible to develop individualized asthma therapies that improve therapeutic outcomes, minimize adverse effects, and leads to more cost-effective care.

IN VIVO ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION USING ELECTROSPUN POLYCAPROLACTONE

Arshi A1,2, Aron G1,2, Nazemni A2, Yeranosian M1, Petriglino F1,2, Wu B2, McAllister D1,2, 1David Geffen School of Medicine, Los Angeles, CA and 2University of California, Los Angeles, CA.

Purpose of Study: The anterior cruciate ligament (ACL) is critical for the structural stability of the knee and its injury often requires surgical repair. The purpose of this study was to evaluate the suitability of electrospun polycaprolactone (PCL) as a scaffold for ACL reconstruction in an in vivo rodent model.

Methods Used: Electrospun PCL sheets were stacked into scaffolds and used to replace the native ACL in Sprague-Dawley rats using parapatellar arthrotomy. At 2, 6, & 12 weeks post-implantation, rodent limbs were harvested and histological evaluation using H&E was used to assess biological integration and host inflammatory response. Picrosirius red staining was used to examine collagen deposition. Tensile biomechanical testing was performed on newly harvested samples at 12 weeks using an Instron.

Summary of Results: Histological analysis showed two distinct regions of histological architecture: (i) bone tunnel (BT) regions where the construct was surrounded by tibial and femoral bone, and (ii) an intra-articular (IA) region within the knee joint that was comparable to the native ACL. Histological analysis demonstrated an increase in the number of collagen-secreting fibroblasts, new bone formation, and graft bonding by 12 weeks post-implantation, with a transient inflammatory response that peaked at 6 weeks and subsided thereafter. At 12 weeks, the scaffold was populated with robust collagen that covered 71% and 23% of the BT and IA surface areas, respectively (Fig. 1). Biomechanical testing of explanted rodent limbs revealed a three-fold increase in both the failure load and stiffness of the graft at 12 weeks post-implantation relative to pre-implantation PCL grafts.

Conclusions: This study demonstrates that electrospun PCL is biocompatible, supports an aligned collagen matrix, and confers biomechanical strength approaching that of the native ACL. Electrosyn PCL may serve as a potential platform for ligament reconstruction using bioengineered materials.

COMPARATIVE RADIATION EXPOSURE USING STANDARD FLUOROSCOPY VERSUS CONE BEAM CT FOR POSTERIOR INSTRUMENTED FUSION IN ADOLESCENT IDIOPATHIC SCOLIOSIS

Maertens A. University of Washington Medical School, Seattle, WA.

Purpose of Study: The objective of this study was to define the intraoperative radiation exposure during freehand surgical technique with fluoroscopic assistance for placement and confirmation of posterior instrumentation in patients with adolescent idiopathic scoliosis and compare data to published values using intraoperative cone beam CT (CBCT) for similar cases.

Methods Used: A total of 43 idiopathic-like scoliosis cases performed by four staff spine surgeons at our institution were retrospectively reviewed. Radiation exposure (rad-cm²) was recorded intraoperatively for each case. Effective dose was determined using published effective dose to dose-length product conversion factors. Values were compared to previous studies reporting effective doses for similar cases using CBCT intraoperative navigation.

Summary of Results: Calculated effective doses of the 43 idiopathic-like scoliosis procedures performed at our institution using standard fluoroscopy and freehand pedicle screw placement were an average of 0.189 mSv (0.00029-0.953, +/- 0.16711) per case. Average radiation exposure time was 26 seconds (+/- 18s) per case, with an average of 11 vertebral levels fused. The literature reports effective dose for CBCT ranging from 7.29 mSv - 9.72 mSv per case for intraoperative navigation only, and 14.58 mSv - 19.44 mSv per case when CBCT was used for both intraoperative navigation and confirmation of pedicle screw placement.

Conclusions: We have demonstrated that the use of CBCT results in markedly higher radiation exposure during a standard posterior instrumented fusion surgery.
for idiopathic-like scoliosis as compared to the use of standard fluoroscopy. Our study suggests that in the absence of aberrant anatomy, as in trauma or congenital deformity, intraoperative navigation may be unnecessary and will increase the total radiation exposure to the patient. Understanding radiation imparted to patients using standard fluoroscopy versus CBCT is important for assessing the risks and benefits of this technology, especially in the young patient where there is an increased vulnerability for radiation-induced cancer.

TRACHEOSTOMY AT BC CHILDREN’S HOSPITAL: A QUALITY OF CARE 30-YEAR REVIEW

Ogilvie LN, Kozak J, Chiu S, Adderley RJ, Kozak FK. BC Children’s Hospital, Vancouver, BC, Canada and BC Children’s Hospital, Vancouver, BC, Canada.

Purpose of Study: Pediatric tracheostomy has undergone notable changes in frequency and indication over the past 30 years. Frequency of the procedure has recently plateaued after a decline occurred in the 1980’s and 1990’s. The primary indication for tracheostomy has changed to reflect advances in medical care although variation between medical centers is apparent. Complication rates have remained generally consistent with a large reported range. This study investigates the demographics, incidence, indications, length in situ and complications for pediatric tracheostomy at British Columbia Children’s Hospital (BCCH) over a 30-year period.

Methods Used: A retrospective chart review of tracheostomy cases at BCCH from 1982 to 2011 was conducted. Charts were reviewed for demographics, date of tracheostomy, surgery, indication, complications, mortality and date of decannulation. Patients were divided into three 10-year time periods based on date of tracheostomy. Measures for these three groups were then compared to examine changes over time.

Summary of Results: 251 procedures performed on 231 patients (137 males) were reviewed. Mean age at tracheostomy was 3.74 years with 48% of procedures undertaken before the age of one year. Frequency by year declined until the early 2000’s, plateaued, and recently over the last 5 years has begun to increase. Upper airway obstruction remains the most common indication across all three time periods accounting for 33% of procedures. Infection as an indication has declined from 8 cases in the 1980’s to 0 in the 2000’s. The rate of complication across the entire cohort was 19.4%. Decannulation occurred in 63% of patients after a range of 0 to 4463 days of tracheostomy in situ. Tracheostomy related mortality was less than 2.0% of patients.

Conclusions: Upper airway obstruction has remained the most prevalent indication for tracheostomy at BCCH. Infection as an indication has become essentially obsolete. Complication rate at BCCH is within the range previously reported by comparable medical centers. This procedure is associated with a low rate of mortality. Pediatric tracheostomy is considered a safe and effective procedure at BCCH.

REOPERATION AND COMPLICATION RATES FOR THE TREATMENT OF ODONTOID FRACTURES WITH ANTERIOR SCREW FIXATION

McLaugherty F, Mukherjee D, Sarmiento J, McBride D, Patil CG. David Geffen School of Medicine at UCLA, Los Angeles, CA; Cedars-Sinai Medical Center, Los Angeles, CA and Los Angeles County Harbor-UCLA Medical Center, Torrance, CA.

Purpose of Study: Reoperation, complication, and healthcare utilization rates for patients undergoing anterior odontoid screw fixation are limited to small, single-center, retrospective studies.

Methods Used: We queried the MarketScan database for adult patients with odontoid fractures who received anterior odontoid screw fixation. Our analysis revealed complication, reoperation, and mortality rates at up to 2-years postoperatively.

Summary of Results: A total of 221 patients were treated between 2000 and 2009, consisting of 49.3% females with an average age of 67 years. Average index hospitalization was 6.6 days, costing an average of $28,203 dollars, and resulting in a mortality rate of 3.1%. At 90-days postoperatively, 16.2% of patients experienced complications (N=191). Among those with 2-years of postoperative data (N=73), 11.0% and 13.7% required reoperation with posterior C1-C2 fusion at 1- and 2-years post index surgery, respectively. At 2-years post index surgery, patients accrued an additional cost of $10,474 for an additional 4.0 days of hospital treatment, $272 in outpatient emergency department costs, and $3,445 in prescription medication costs.

Conclusions: Anterior odontoid screw fixation appears to have a relatively low 2-year reoperation rate and, given its advantages of preserving cervical motion, should be considered in patients with odontoid fractures that are amenable to surgical treatment.

RISK OF THROMBOSIS WITH CENTRAL VENOUS CATHETER PLACEMENT IN NEONATAL CARDIAC SURGERY PATIENTS

Ibrahim M, Howard-Quijano K, Schwarzenberger J. UCLA David Geffen School of Medicine, Los Angeles, CA.

Purpose of Study: The use of central venous catheters (CVC) is common in critically ill neonates as a lifeeline to ensure administration of medication or fluids, withdrawal of blood for tests, or hemodynamic monitoring. Yet, CVC insertion is the main cause of thrombotic events (TE) in this vulnerable age group (Revel-Vilk et al., 2011). The objective of this study was to analyze the prevalence of CVC-related thrombosis in a population who has undergone cardiac surgery at a weight less than or equal to 5 kilograms (kg) (neonates) as compared to those weighing 5.1 to 10 kg (infants). We hypothesized that neonates will have more frequent TE’s than infants.

Methods Used: This was a retrospective chart review of all neonates and infants with the appropriate weight at the UCLA Ronald Reagan Medical Center who underwent cardiac surgery and required CVC insertion from July 2012 to May 2013. 704 patients were identified for their weight, the location and duration of CVC placement, cardiac diagnosis, and the incidence and location of thrombosis. Statistical analysis was conducted utilizing Fisher’s
exact test, the Student’s-t-test, and the Wilcoxon nonparametric test for multiple comparisons.

Summary of Results: Of the 70 patients, 8/40 (20%) of neonates, but only 1/30 (3.3%) of infants, experienced TEs; this proved to be statistically significant with \( p < 0.05 \). In all TEs, 4/9 (44%) of CVCs were placed in each the internal jugular vein or the femoral vein; 1/9 (11%) of CCVs was placed in the subclavian vein. 7/9 (77%) of TEs occurred at the CVC site (including attempted sites).

Conclusions: Overall, neonates experienced more frequent TEs than infants. These patients are likely more susceptible to TEs due to their underdeveloped clotting mechanisms and small vessel diameters, erythrocytosis from congenital heart disease, and altered coagulation cascades secondary to surgery (Veldman et al.). We plan to compare these findings to the national Society of Thoracic Surgeons’ database and conduct a future prospective study to more definitively describe our results and potentially influence future CVC placement techniques to minimize TEs and the complications that arise from them in neonates.

A PREDICTIVE ANALYTIC APPROACH TO IMPROVE PATIENT HANDOFFS: A RETROSPECTIVE STUDY OF BILIARY COMPLICATIONS AND ACUTE CELLULAR REJECTION EPISODES FOLLOWING LIVER TRANSPLANTATION

Hall SR\(^1\), Hall D\(^2\), Lauer M\(^2\), Reyes J\(^1,2\), Perkins J\(^1,2\). \(^1\)University of Washington, Seattle, WA and \(^2\)University of Washington Medical Center, Seattle, WA.

Purpose of Study: Predictive analytics (PA) is increasingly being used in the delivery of healthcare. Whether predictive analytics can improve patient handoffs between physicians is unknown. This study aims to build predictive models for acute cellular rejection (ACR) episodes and biliary complications after orthotopic liver transplantation (OLT) to improve patient handoffs post-operatively.

Methods Used: Recipient, donor, procurement, and surgical procedure data; post-transplant induction immunosuppressive therapy; and laboratory values for 90 days were collected as predictor variables from 386 OLT patient records transplanted during a 5 year period. Multiple algorithms, based on variable reduction, were used and the best model was chosen. A post-operative and a post-elevated liver function tests (LFTs) risk score. Patient records were assigned to separate risk groups, based on the post-elevated LFTs risk score, for biliary complications and ACR episodes.

Summary of Results: The surgical convenience of a combination tube shunt- cataract extraction/ intraocular lens implantation and a standard tube shunt implantation was not initially different (< 1yr post operation), however late pressure recordings (>1y post operation, 26 eyes) showed a significant decrease in pressure lowering efficacy from 10.34 mmHg to 16.69 mmHg (p < 0.05). The visual improvement, glaucoma drug/drop reduction, and complication rate of simultaneous TS- CE/IOL implantation was each insignificant.

Conclusions: The surgical convenience of a combination tube shunt- cataract extraction/intraocular lens implantation might not be enough to outweigh the decreased efficacy of long-term pressure reduction. Further studies need to be done to determine the nature of ocular surgery interactions and the risks and benefits of simultaneous procedures.

EFFICACY OF TRABECULAR MESHWORK BYPASS TUBE SHUNT IN COMBINATION WITH SIMULTANEOUS ARTIFICIAL INTRAOCULAR LENS IMPLANTATION

Tuong A\(^1\), Francis BA\(^2\). \(^1\)University of California, Irvine School of Medicine, Irvine, CA and \(^2\)Keck School of Medicine, University of Southern California, Los Angeles, CA.

Purpose of Study: To describe the effects of additional simultaneous ocular surgeries on the efficacy of a glaucoma drainage implant by evaluating post-operative intraocular pressure, best corrected visual acuity, glaucoma medications and complication rates. We focus specifically on the efficacy of tube shunt (TS) implantation in combination with cataract extraction (CE); artificial lens (IOL) implantation.

Methods Used: Retrospective chart review of 384 consecutive eyes from 355 consecutive patients who underwent tube shunt drainage implantation done by the ophthalmology faculty of the University of Southern California Doheny Eye Institute. From this data, 55 eyes underwent concurrent TS- CE/ IOL implantation and 55 controls were selected from the data set matched to pre-operation diagnosis. Pre and post-operative outcome measures included intraocular pressure, best corrected visual acuity, number of glaucoma-specific medications/drops, and complication rate (ie hypotony, pupillary membrane, iris-cornea touching, tube-iris touching, peripheral anterior synchiae, corneal edema, and tube erosion) recorded at 1 day, 1 month, 3m, 6m, 1 year, 2y, 3y, etc. as per standard of care.

Summary of Results: The degree of pressure lowering between a simultaneous tube shunt- cataract extraction/ intraocular lens implantation and a standard tube shunt implantation was not initially different (< 1yr post operation), however late pressure recordings (>1y post operation, 26 eyes) showed a significant decrease in pressure lowering efficacy from 10.34 mmHg to 16.69 mmHg (p < 0.05). The visual improvement, glaucoma drug/drop reduction, and complication rate of simultaneous TS- CE/IOL vs. standard TS implantation was each insignificant.

Conclusions: The surgical convenience of a combination tube shunt- cataract extraction/intraocular lens implantation might not be enough to outweigh the decreased efficacy of long-term pressure reduction. Further studies need to be done to determine the nature of ocular surgery interactions and the risks and benefits of simultaneous procedures.

Poster Session III
Behavior and Development

10:00 AM
Saturday, January 25, 2014

PREVALENCE OF SUBSTANCE USE AMONG MOROCCAN ADOLESCENTS AND ITS ASSOCIATION WITH ACADEMIC ACHIEVEMENT

Anderson T\(^1\), Elomari F\(^2\), Salomonsen-Saul S\(^1\), Hoffenberg A\(^1\), Hopfer C\(^1\). \(^1\)University of Colorado Denver, Aurora, CO and \(^2\)Mohammed V University, Rabat, Morocco.

Purpose of Study: Little research has been done on adolescent drug and alcohol use in Arab countries. This study investigates the difference in association of drug and alcohol use on academic performance in male and female adolescents.

Methods Used: Data was gathered using an adapted form of the European School Project on Alcohol and Other Drugs survey administered to 2139 10th-12th graders in 36 urban public high schools in Morocco. Two multiple logistic regressions (one for boys and one for girls) were completed using grade average as a two-part outcome variable and drug use as a four-level categorical independent variable, with father’s education level, mother’s education level, and socioeconomic status as covariates.

Summary of Results: A total of 181 girls (16%) and 390 boys (40%) reported ever having used alcohol, hashish, or psychotropic drugs. Among the girls, drug use in the past 30 days was associated with an adjusted odds ratio (AOR) of 2.62 (95% CI 1.31-5.22) of having average or below average grades, and lifetime use with an AOR of 1.72 (1.07-2.77). The boys who had used in the past 30 days had an AOR of 2.08 (1.33-3.24) of average or below average grades; use in the last 12 months corresponded to an AOR of 1.74 (1.00-3.05). Any previous use with boys and previous 12 month use with girls did not show a statistically significant association with grades.

Conclusions: Drug and alcohol use is widely prevalent among adolescents in Morocco, though the difference in use between genders is substantial. Use in the last 30 days was associated with lower grades among both genders.
ASSESSING EARLY CHILDHOOD NUTRITIONAL PRACTICES IN RURAL UGANDA


Purpose of Study: According to the 2011 Uganda Nutrition Action Plan, 40% of children under 5 are malnourished. Childhood malnutrition was identified as an ongoing problem in the rural village of Nakaseke, Uganda and was an area in need of further exploration. This study was aimed at assessing early childhood nutritional practices in Nakaseke, and to identify barriers to healthy nutritional practices in order to create sustainable interventions.

Methods Used: Data was collected using 7 focus groups with a total of 46 participants including community health workers, village health teams and community members. The interviews were conducted in Luganda using a translator, audio recorded, transcribed, and analyzed for common themes.

Summary of Results: General poverty and lack of knowledge were identified as two major barriers to healthy nutritional practices in the community. Poverty lead to the inability to afford certain nutrition-rich foods and was compounded by lack of family planning resulting in large families. Additionally, early cessation of breastfeeding was common among working mothers, who were often away from their children. A general lack of knowledge contributed to the inappropriate cessation of breastfeeding and the improper introduction of complementary foods, and was due in part to a lack of accessibility to education on nutrition. Suggestions given to improve nutritional practices included increasing accessibility of seminars on nutrition, as well as the use of drummer groups to generate interest and educate the community.

Conclusions: This study identified a continued need for education on nutrition among the community. With a better understanding of current practices and beliefs, we can now collaborate with the community to create sustainable interventions to address their specific needs while taking into account their financial restraints. This represents a first step to improve nutritional practices in the community leading to better childhood developmental and health outcomes.


THE ATTITUDES OF HIGH SCHOOL AND COLLEGE STUDENTS TOWARDS PEER PRESSURE

Totoiu D1, Afghani B2. 1California State University, Fullerton, Fullerton, CA and 2University of California, Irvine School of Medicine, Irvine, CA.

Purpose of Study: The aim of the study was to evaluate the attitudes of high school and college students towards peer pressure.

Methods Used: An anonymous survey containing different questions in regards to peer pressure was distributed to students. The questions asked about the types and methods of peer pressure experienced and the pressures the students succumb to.

Summary of Results: A total of 115 students (64 high school students and 51 college students) took the survey. Of 115, 65 (56%) were females. The students reported that the most common technique used for peer pressure was by friendly request (56% of students) and guilt manipulation (47%). The most common activity given into as a result of peer pressure among both groups was breaking rules (53%). Ten (16%) of 64 high school students, and 19 (37%) of 51 reported smoking because of peer pressure. 14% of high school students and 33% of college students had succumbed to drug use. Skipping school was the most common peer pressure reported (45% of all students) followed by drug or alcohol use (32%) among all students. 33% of high school students and 49% of college students reported that they had lied to their parents. Of all students, 37% reported that peer pressure can sometimes be positive. Majority (65%) of all students reported that people who give into peer pressure have low self-confidence.

Conclusions: Negative peer pressure continues to be prevalent among high schools and college students. More data is needed to determine factors that contribute to succumbing to peer pressure among different populations. Interventions are needed to counter act negative peer pressure.

Poster Session III
Cardiology
10:00 AM
Saturday, January 25, 2014
396

CASE REPORT: SUCCESSFUL TREATMENT, DESPITE A NON-SURGICAL APPROACH, OF SEVERE INFECTIVE ENDOCARDITIS

Boulou P1,2, denk M1-2, 1University of Colorado School of Medicine, Denver, CO and 2Denver Health Medical Center, Denver, CO.

Purpose of Study: Left-sided native valve infections caused by Staphylococcus aureus, in non-intravenous drug users, are associated with mortality rates of 22%-40%, an unacceptably high number that signifies the need for clearer evidence-based treatment guidelines. This report compares treatment strategies, medical vs. surgical, in the context of a patient that presented to our institution with this disease. This investigation involves a thorough analysis of current guidelines put forth by both the American Heart Association and the European Society of Cardiology.

Methods Used: A 60-year-old man with history of Child-Pugh class B cirrhosis was admitted to the hospital with 4 to 5 days of nausea, vomiting, and altered mental status. Following the development of a fever in the intensive care unit and Methicillin Sensitive Staphylococcus aureus (MSSA) bacteremia, a large (15 mm) vegetation was discovered on the anterolateral papillary muscle of the mitral valve by transthoracic echocardiography. Following a thorough multidisciplinary evaluation, the patient was considered to be a poor surgical candidate due to the significant perioperative complications associated with Child-Pugh class B cirrhosis. The patient was treated with 6 weeks IV Nafcillin as an outpatient.

Summary of Results: Transthoracic echo was performed after completion of the 6 weeks of outpatient IV Nafcillin treatment. The previously seen vegetation was no longer appreciated. There was no mitral regurgitation or stenosis. The patient was doing well and denied development of any new cardiac symptoms.

Conclusions: This case report emphasizes that medical management remains an effective alternative to surgery in complicated cases of infective endocarditis, at variance with current guidelines. These guidelines admittedly report that indications for medical vs. surgical treatment remain unclear in situations such as these.

Poster Session III
Developmental Biology
10:00 AM
Saturday, January 25, 2014
397

EMPLOYING APOPTOTIC CELLS TO ACCELERATE GROWTH OF PATIENT SPECIFIC KERATINOCYTES IN SEVERE WOUNDS

Rodriguez S, Bilousova G, Roop D. University of Colorado School of Medicine, Denver, CO.

Purpose of Study: The current state-of-the-art treatment for burn trauma uses cultured epithelium from a non-affected area of skin of the patient to develop large epithelial sheets - a lengthy process that can take 2-3 weeks. If this delay could be drastically reduced and tissue regeneration significantly improved, patient recovery would benefit considerably.

© 2013 The American Federation for Medical Research
Cordycepin induces tumor cell death through ERKs and MTOR-mediated pathway in hepatocellular carcinoma cells

Yang D1, Guo T2, Wang D2, Zhao M1, Teng L1, 2, *Jilin University, Zhuhai, China and 2Jilin University, Changchun, China.

Purpose of Study: Hepatocellular carcinoma (HCC) is the fifth most common cancer in the whole world. Animal studies focus on the anti-hepatocellular carcinoma effects of herbal preparations and nature compounds. Recent studies reported that cordycepin induces apoptosis in human HEK-293 oral cancer cells, breast cancer cells, leukemia and lymphoma cells. Present study was to investigate the anti-hepatocellular carcinoma effects in in vitro and in vivo models.

Methods Used: MTT assay, annexin V/PI staining, crystal violet staining, DCIH-DA staining and JC-1 staining were used to determine the changes of cell viability, apoptosis rate, cell proliferation, reactive oxygen species (ROS) level and mitochondrial apoptotic alternation after cordycepin treatment in both PLC/PRL5 and HepG2 cells. The expression changes of phosphor-mammalian target of rapamycin (P-mTOR), total-mTOR (T-mTOR), phosphor-extracellular signaling-regulated kinase (ERKs) (P-ERKs), total-ERKs (T-ERKs), Cleaved poly (ADP-ribose) polymerase (PARP), PARP, b-cell lymphoma 2 (Bcl-2), and b-cell lymphoma-extra large (Bcl-xL) were determined by western blot. Furthermore, the anti-tumor effects of cordycepin were further confirmed in PLC/PRL5-xenografted nude mice model.

Summary of Results: Cordycepin reduced cell viability, increased the apoptotic rate, inhibited cell proliferation and strikingly enhanced the level of cleaved PARP. Cordycepin caused apoptotic alteration on mitochondrial function and resulted in a reduction of the expression of Bcl-2 and Bcl-xL. Furthermore, cordycepin suppressed the activation of ERKs and mTOR in both PLC/PRL5 and HepG2 cells. Finally, the anti-tumor action of cordycepin was further confirmed in PLC/PRL5-xenografted tumor growth model in mice.

Conclusions: Data demonstrated that cordycepin-mediated anti-hepatocellular carcinoma effects are related to its modulation of the activation of ERKs and mTOR. Our study defines a novel anti-tumor effect of cordycepin and provides a further rational agent for hepatocellular carcinoma treatment.

PERSIMMON INDUCES TUMOR CELL DEATH THROUGH ERK AND MTOR-MEDIATED PATHWAY

Poster Session III
Gastroenterology
10:00 AM
Saturday, January 25, 2014

EXTRAMEDULLARY PLASMACYCTOMA OF THE PANCREAS

Wang J, Liang T, Harris A. *University of British Columbia, Vancouver, BC, Canada.

Case Report: Multiple myeloma is a common type of hematologic malignancy accounting for approximately 10-15% of all cases. While they primarily involve the bone marrow, roughly five percent of these plasma cell tumors occur in other organs. Termied plasmacytomas, they are discrete masses of neoplastic plasma cells that occupy extramedullary soft tissue. The upper respiratory tract and abdominal organs, such as spleen, liver and stomach, are most commonly involved. Pancreatic manifestations of extramedullary plasmacytoma are a rare occurrence, with approximately 25 case reports in the English literature. However, they form an important part of the differential diagnosis in a patient with symptoms of abdominal pain and obstructive jaundice. Here we present a 44-year-old female with pancreatic plasmacyctoma who initially presented to our institution’s Emergency Department with abdominal discomfort and a one-month history of feeling generally unwell. On CT, a large homogeneous mass was identified replacing the entire length of the pancreas as well as a soft tissue component in the peripancreatic region encasing the celiac trunk. This case report aims to highlight the pathophysiology, clinical findings and radiologic approach to this rare but important manifestation of multiple myeloma.

SPATIAL AND TEMPORAL PROTEIN EXPRESSION IN PALATOGENESIS

Poster Session III
Morphogenesis and Malformations
10:00 AM
Saturday, January 25, 2014

CORDYCEPIN INDUCES TUMOR CELL DEATH THROUGH ERKS AND MTOR-MEDIATED PATHWAY IN HEPATOCELLULAR CARCINOMA CELLS

Yang D1, Guo T2, Wang D2, Zhao M1, Teng L1, 2, *Jilin University, Zhuhai, China and 2Jilin University, Changchun, China.

Purpose of Study: Hepatocellular carcinoma (HCC) is the fifth most common cancer in the whole world. Animal studies focus on the anti-hepatocellular carcinoma effects of herbal preparations and nature compounds. Recent studies reported that cordycepin induces apoptosis in human HEK-293 oral cancer cells, breast cancer cells, leukemia and lymphoma cells. Present study was to investigate the anti-hepatocellular carcinoma effects in in vitro and in vivo models.

Methods Used: MTT assay, annexin V/PI staining, crystal violet staining, DCIH-DA staining and JC-1 staining were used to determine the changes of cell viability, apoptosis rate, cell proliferation, reactive oxygen species (ROS) level and mitochondrial apoptotic alternation after cordycepin treatment in both PLC/PRL5 and HepG2 cells. The expression changes of phosphor-mammalian target of rapamycin (P-mTOR), total-mTOR (T-mTOR), phosphor-extracellular signaling-regulated kinase (ERKs) (P-ERKs), total-ERKs (T-ERKs), Cleaved poly (ADP-ribose) polymerase (PARP), PARP, b-cell lymphoma 2 (Bcl-2), and b-cell lymphoma-extra large (Bcl-xL) were determined by western blot. Furthermore, the anti-tumor effects of cordycepin were further confirmed in PLC/PRL5-xenografted nude mice model.

Summary of Results: Cordycepin reduced cell viability, increased the apoptotic rate, inhibited cell proliferation and strikingly enhanced the level of cleaved PARP. Cordycepin caused apoptotic alteration on mitochondrial function and resulted in a reduction of the expression of Bcl-2 and Bcl-xL. Furthermore, cordycepin suppressed the activation of ERKs and mTOR in both PLC/PRL5 and HepG2 cells. Finally, the anti-tumor action of cordycepin was further confirmed in PLC/PRL5-xenografted tumor growth model in mice.

Conclusions: Data demonstrated that cordycepin-mediated anti-hepatocellular carcinoma effects are related to its modulation of the activation of ERKs and mTOR. Our study defines a novel anti-tumor effect of cordycepin and provides a further rational agent for hepatocellular carcinoma treatment.
MEE. In contrast, agrecan is more prevalently expressed in this superficial epithelial layer compared to other regions of the palate. As a result, these two proteins may play distinct roles in the fusion of the MEE and development of the rat palate.

Poster Session III  
Neonatal Pulmonary  
10:00 AM  
Saturday, January 25, 2014

401  
MATERNAL SUPPLEMENTATION WITH 0.1% DHA NORMALIZES THE PPAR-Setd8-H4K20me AXIS IN ADOLESCENT RAT LUNG

German M1, Zou C2, Sainz A2, Wang Y2, Joss-Moore L2, 1University of Utah School of Medicine, Salt Lake City, UT and 2University of Utah, Salt Lake City, UT.

Purpose of Study: Intrauterine growth restriction (IUGR) predisposes to lung disease and abnormal lung development. Normal lung development depends upon the PPARy-Setd8-H4K20me axis. PPARy regulates expression of the enzyme Setd8, which methylates lysine 20 on histone 4 (H4K20me) of target genes, including PPARy itself. We showed that IUGR decreases components of the PPARy-Setd8-H4K20me axis in newborn rat lung (pre-alveolarization). We also showed that activation of PPARy with pharmacologic dose of docosahexaenoic acid (DHA) restores PPARy-Setd8-H4K20me axis in newborn rat lung. However, the effect of IUGR, with or without physiologically relevant doses of DHA, on the PPARy-Setd8-H4K20me axis in adolescent (post-alveolarization) rat lungs is unknown.

Methods Used: IUGR was induced by uterine artery ligation in the rat at day 19 of gestation. Control and IUGR rats received a 0% or a 0.1% DHA diet throughout pregnancy and lactation. At postnatal day 21 rat pup lungs were harvested. PPARy and Setd8 mRNA levels were measured using real-time RT PCR. H4K20me on the PPARy gene was measured using chromatin immunoprecipitation.

Summary of Results: Results are % of 0% DHA diet sex-matched control ± SD, p ≤ 0.05. In female rat lung, IUGR decreased PPARy (34±6%*) and Setd8 (73 ±13%) mRNA levels as well as H4K20me at Exon 4 of the PPARy gene (8±2%*). In male rat lung, IUGR decreased PPARy (68±3%*) and Setd8 (87±6%) mRNA levels. However, in male rat lung, IUGR increased H4K20me at Exon 4 of the PPARy gene (193±30%*). Maternal supplementation with 0.1% DHA normalized Setd8 mRNA levels as well as H4K20me at Exon 4 of the PPARy gene in both female and male rat lungs.

Conclusions: IUGR dysregulates the PPARy-Setd8-H4K20me axis beyond alveolarization, and all changes can be normalized with physiologically relevant levels of DHA. The effects of IUGR on the PPARy-Setd8-H4K20me axis are sex-dependent. In female IUGR rats, decreased PPARy and Setd8 mRNA is associated with increased H4K20me. Alternative chromatin modifications along the PPARy gene in male rat lung may contribute to this dichotomy and warrant further investigation.

402  
ECHOCARDIOGRAPHIC ASSESSMENT OF PULMONARY HYPERTENSION (PH) PREDICTS OUTCOME IN INFANTS WITH CONGENITAL DIAPHRAGMATIC HERNIA (CDH)

Lusk LA1, Wai K2, Moon-Grady AJ3, Keller RL1,3. 1University of California, San Francisco, San Francisco, CA; 2University of California, San Francisco, San Francisco, CA and 3University of California, San Francisco, San Francisco, CA.

ABSTRACTS: Purpose of Study: CDH is associated with significant morbidity and mortality due to lung hypoplasia and PH. Echocardiography can non-invasively assess the severity of PH, although the relationship of persistence of PH and short-term poor outcomes is unknown.

Methods Used: We performed a retrospective cohort study of infants with CDH cared for at UCSF (2002-12). We reviewed medical records for important respiratory outcomes and mortality; infants with other major anomalies were excluded (n=43). Clinical echocardiograms (ECHO) were performed weekly up to 6 wks until PH resolved off support or hospital discharge (DC)/death. They were re-read for this investigation (AMG and KW) to determine severity of persistent PH or resolution. PH severity was determined by a hierarchy of ductus arteriosus level shunt (direction and velocity), interventricular septal position (parasternal short axis view) and TR jet velocity.

Summary of Results: Of 140 infants with ≥1 ECHO, 98 (70%) resolved PH prior to DC. Mean time to resolution was 18d (median 14d, IQR 8.21d). There were no significant differences in time to extubation (13±9 vs. 16±10 d, p=0.11) or proportion DC on supplemental O2 (27% versus 40%, p=0.38) among those with resolution vs. persistence of PH, respectively. Those with persistence of PH had a higher rate of ECMO (26% vs. 4%, p<0.001) and death (59.5% vs. 1%, p=0.001). Persistence of PH (by week) from 14d on demonstrates consistent prediction of poor outcomes, but infants who resolved their PH remained at risk of adverse respiratory outcome (Table).

Conclusions: The majority of infants with CDH resolve PH before DC. However, persistence of PH at 2 wks is associated with substantial pulmonary morbidity and death. Novel therapies for PH and lung hypoplasia in this group could improve short-term outcomes.

403  
ADDITIONAL THERAPIES DO NOT IMPROVE MORTALITY IN PATIENTS WITH CONGENITAL DIAPHRAGMATIC HERNIA

Zalla J1, Yoder B1, Stoddard G2. 1University of Utah, Salt Lake City, UT and 2University of Utah, Salt Lake City, UT.

ABSTRACTS: Purpose of Study: The use of inhaled nitric oxide (iNO), extracorporeal membrane oxygenation (ECMO), epoprostenol and milrinone, in patients with congenital diaphragmatic hernia (CDH) is increasing despite conflicting or no evidence for improvement in mortality. At our institution, iNO was introduced in 2000 (Era2), ECMO in 2003 (Era3), and IV pulmonary vasodilators in 2005 (Era4) in the care of CDH patients. Whether a significant benefit has occurred since incorporating these therapeutic options remains unknown.

Our objective is to determine the time dependent effects on survival of iNO, ECMO, and milrinone/epoprostenol compared to historical controls in the management of infants with CDH at a single center since 1998.

Methods Used: We retrospectively analyzed our CDH database for death prior to discharge across four eras. All live born CDH patients since 1998 were included. Patients were excluded for delayed diagnosis > 24 hours, parents who declined intervention, or severe chromosomal or congenital anomalies. A multivariable Cox regression model was fitted, with Era2, Era3, and Era4 as the primary predictor variables, using Era1 as the referent group.
**Summary of Results:** No significant difference was found across the eras for mortality when controlling for potential confounders including primary repair, gestational age, or additional anomalies. Baseline characteristics across the eras are displayed in the table.

**Conclusions:** Consistent with previous evidence, use of INO and ECMO had no benefit on mortality for CDH. The addition of milrinone and/or epoprostenol provided no apparent benefit on mortality. A randomized controlled trial should be performed to investigate if these outcomes hold true. In a setting of rising health costs and decreased reimbursement, treatments that have no evidenced-based benefit on outcomes should be considered carefully.

---

**404 NEPHROCALCINOSIS IN THE PRETERM INFANT**

Grinsell M1, Chan GM1, Rau C1, Weaver-Lewis K2. 1University of Utah, Salt Lake City, UT and 2Intermountain Medical Center, Murray, UT.

**ABSTRACTS:** Purpose of Study: Nephrocalcinosis (NC) is an uncommon disorder in the preterm infant. However, the new dietary recommendations of higher protein, calcium (Ca), and vitamin D (D) may increase the NC incidence. The aim of this study was to evaluate prematurity associated NC.

**Methods Used:** Forty infants less than 32 weeks gestation or less than 1500 g birth weight were evaluated. All infants were screened with urinalysis after 2 weeks of age for Ca oxalate (CaOx) crystals. Fluid intake, days on parenteral nutrition (PN), feedings, dietary intakes of Ca, D, and protein, blood pressure, serum Ca, phosphate, 25-OH D, urea nitrogen, creatinine, electrolytes, bicarbonate, and alkaline phosphate levels were recorded.

**Summary of Results:** Of the 40 infants, 27 (68%) had a urine for CaOx crystals and a renal ultrasound with NC. Thirteen infants (32%) did not have urinary CaOx crystals or NC and acted as the control group. There were no differences between the 2 groups in gestational age (28.6 ± 2.4 vs 28.0 ± 2.3 wks), birth weight (1071 ± 391 v 1045 ± 247 g), fluid intake, feedings of fortified human milk and preterm formula, blood pressure, or days on PN. There were no differences in Ca, D, and protein intakes from enteral feedings between the groups. However, mean supplemental daily D was higher in the NC group (535 IU v 400 IU, P < 0.04) than controls. Serum Ca (10.1 ± 0.4 v 9.7 ± 0.4 mg/dL, P < 0.005), bicarbonate (26 ± 2.9 v 23 ± 1.4 mm/L, P < 0.001), and 25-OH D (49 ± 23 v 52 ± 17 ng/mL, P < 0.02) levels were higher in the NC group. Serum phosphate, urea nitrogen, creatinine, electrolytes, and alkaline phosphate levels were similar between the groups.

**Conclusions:** Nephrocalcinosis in the preterm infant is associated with higher serum calcium, bicarbonate, and vitamin D levels compared to controls. High vitamin D intakes in the preterm infant may be a risk factor for nephrocalcinosis.

---

**405 THE DEVELOPMENT OF NECROTIZING ENTEROCOLITIS AFTER PACKED RED BLOOD CELL ADMINISTRATION**

Jhun K, Wertheimer F, Barton L, Sardesai S, Ramanathan R. University of Southern California, Los Angeles, CA.

**Purpose of Study:** Necrotizing enterocolitis (NEC) is the most common life-threatening surgical and medical gastrointestinal emergency in the neonatal period. Although many factors have been associated with the development of NEC, only prematurity and a history of feeding are consistently related. Some studies, however, indicate that there may be an association between the administration of packed red blood cell (PRBC) transfusion and the development of NEC. The purpose of this study is to determine if there is an association between the development of NEC within 3 days of PRBC transfusion in neonates at our institution, Los Angeles County-University of Southern California (LAC+USC) Neonatal Intensive Care Unit.

**Methods Used:** After IRB approval, a retrospective chart review was conducted on all neonates with birth weights between 501-1500g admitted to the LAC+USC Neonatal Intensive Care Unit with a first admission from 1994 to 2008. Patients were evaluated for PRBC exposure within 3 days prior to developing NEC. We also studied the relationship between furosemide exposure in the transfusion associated NEC patients.

**Summary of Results:** A total of 1318 charts were reviewed of which 67 patients (5.1%) developed NEC. Fifty-nine of these patients (88%) were exposed to a PRBC transfusion. Necrotizing enterocolitis developed within 3 calendar days after a PRBC transfusion in 34 of the 59 patients (57.6%). Furosemide exposure in these transfusion associated NEC patients occurred in 10 patients (29.4%).

**Conclusions:** There may be an association between the administration of PRBC and the development of NEC. The exposure to furosemide does not appear to increase the risk of development of NEC after PRBC exposure. Further analysis to determine additional factors contributing to the development of NEC after a PRBC transfusion is in progress. Additionally, we hope to determine to what extent a PRBC transfusion is predictive of developing NEC.
**Purpose of Study:** Leadership WalkRounds (WR) are widely used in healthcare organizations to improve patient safety. The relationship between WR and caregiver assessments of patient safety culture, and health care worker burnout is unknown.

**Methods Used:** This cross sectional survey study evaluated the association between receiving feedback about actions taken as a result of WR and health care worker assessments of patient safety culture and burnout across 44 NICUs actively participating in a structured delivery room management quality improvement initiative.

**Summary of Results:** Of 3294 administered surveys, 2073 were returned for an overall response rate of 62.9%. More WR feedback was associated with better safety culture results, and lower burnout rates in the NICUs. Participation in WR and receiving feedback about WR were less common in NICUs than in a benchmarking comparison of adult clinical areas.

**Conclusions:** This study adds to the body of research linking WR to patient safety and organizational outcomes by demonstrating the relationships using both of the most widely used safety culture surveys, including a metric of burnout, and by demonstrating a new method of assessing WR efficacy.
CDH is considered a multifactorial disease, with strong evidence implicating genetic factors. However, as low heritability has been reported in isolated CDH, family-based genetic methods have not been used widely. Our group challenged the dogma that isolated CDH is not familial and showed the role of heritability in the disease (Arrington et al. AJMG 2012). Our research is focused on to identify the pathogenic variants leading to isolated CDH by combining family-based genetic strategies and next generation sequencing.

**Methods Used:** After University of Utah IRB approval, using Utah population database, we identified a family with highly penetrant isolated CDH: 5 affected (a grandfather, a father and two siblings). Patients enrolled after informed consents, medical record reviewed for demographic and clinical data. DNA isolated from blood samples and quantitated with picogreen. Whole exome sequencing performed using Illumina HiSeq platform at University of Utah Microarray and Genomic Analysis Core Facility. The paired-end reads are currently being aligned to the reference human genome build 37 (GRCh37/hg19) using Burrows Wheeler Alignment and Novoalign programs. Sequence variants will be called with Genome Analysis Toolkit

**Summary of Results:**

- Probabilistic search tool that has demonstrated ability to identify deleterious synonymous, stop gain/loss, frameshift insertion/deletion.
- We will use Sequencing Analysis Module in SNP & Variation Suite software (Golden Helix Inc.) which performs similar variant annotation and filter analyses. Finally, we will apply Variant Annotation, Analysis & Search Tool, a sophisticated probabilistic search tool that has demonstrated ability to identify deleterious variants in common, multigenic diseases.

**Summary of Results:**

Unavailable.

**Conclusions:** We anticipate that the combination of our family-based genetic strategies and next generation sequencing will enable us to start unraveling the genetic susceptibilities of isolated CDH.

---

**SLEEP IMPLEMENTATION IN NEONATAL INTENSIVE CARE UNIT (NICU)**

Voos K1, Park N2, Leick-Rude M2, Terreros A2, Larimore P4. 1Children’s Mercy Hospital, Kansas City, MO; 2Children’s Mercy Hospital and Clinics, University of Missouri-Kansas City School of Medicine, Kansas City, MO; 3Children’s Mercy Hospital, Kansas City, MO; 4Children’s Mercy Hospital and Clinics, Kansas City, MO.

**ABSTRACTS: Purpose of Study:** Even with the dramatic decline of SIDS rate over the previous decade of 50%, SIDS remains the leading cause of death in the postnatal period. As well, accidental suffocation and strangulation in bed (ASSB) deaths have quadrupled from 2.8 to 12.5 deaths per 100,000 live births from 1984-2004. In response to these preventable ASSB deaths the American Academy of Pediatrics expanded their previous back to sleep recommendations in 2011 to include a safe sleep environment. The AAP makes specific recommendations to health care professionals to model safe sleep practices in the hospital setting and educate the families of infants on SIDS risk reduction strategies. The objective was to implement a safe sleep program in our NICU.

**Methods Used:** The NICU Safe Sleep policy was revised to include AAP updated recommendations. Educational updates were provided to staff, including electronic communication, inclusion in NICU Baby Bits monthly newsletter, placement on NICU Helpful Hints internal website, and discussion at staff updates. A safe sleep packet with video was created for and shared with families upon infant moving to an open crib. Wearable blankets were implemented to swaddle the infants and prevent use of loose blankets in the crib which pose as a suffocation risk. A safe sleep observation tool was created. Baseline data and post education random observations data was collected and shared with staff. Bed side education continued during observation data collection audits.

**Summary of Results:** At baseline only 10.7% of eligible infants were in a safe sleep environment. After education and reported observation, safe sleep compliance increased to 82% over 1 year.

**Conclusions:** With staff and family education, option of a wearable blanket, and data sharing with staff, safe sleep compliance increased and patient safety improved.

---

**IMPACT OF STANDARDIZED COMMUNICATION TECHNIQUES ON ERRORS DURING NEONATAL RESUSCITATION**

Yamada NK, Fuerch JH, Halamek LP. Packard Children’s Hospital at Stanford, Palo Alto, CA.

**ABSTRACTS: Purpose of Study:** Determine rate and types of errors committed by healthcare professionals during simulated neonatal resuscitation. Assess the effects of standardized communication techniques on reducing those errors.

**Methods Used:** Pilot data was collected by video review of 23 real neonatal resuscitations at our institution from 2003-04. We observed 113 errors in 695 steps indicated by the Neonatal Resuscitation Program (NRP) algorithm, which translates to an error rate of 19.2%.

The intervention is a curriculum to standardize communication during neonatal resuscitation. It is patterned after communication techniques and training manuals used in aviation and air traffic control, and which have decreased error rates in those high-risk fields. These include standard phraseology, prioritization of data that affect algorithm branch points (e.g. heart rate), directed task distribution, and closed-loop communication. This is a prospective, randomized controlled trial currently in progress. Two-person resuscitation teams of one physician or neonatal nurse practitioner and one neonatal nurse are being recruited. Teams are randomized to the Intervention or Control group. All teams will participate in two simulated neonatal resuscitations as follows: Simulation 1, communication training (Intervention) or a placebo educational session (Control), followed by Simulation 2. The scenarios have similar clinical complexity and acuity.

**Summary of Results:** We do not have results to report at this time. We expect to have all scenarios completed by December 2013. Planned Data Analysis: Two NRP instructors blinded to the intervention will review the videotaped
INTROOPERATIVE EPIDURAL METHYLPREDNISOLONE IN PATIENTS WITH MINIMALLY INVASIVE SINGLE-LEVEL LUMBAR DECOMPRESSION: A PROSPECTIVE STUDY

Arnell MJ1, Arita H1,3, Lu DC1,2, 1David Geffen School of Medicine at UCLA, Los Angeles, CA; 2David Geffen School of Medicine at UCLA, Los Angeles, CA and 3David Geffen School of Medicine at UCLA, Los Angeles, CA.

ABSTRACTS: Purpose of Study: Many patients who undergo lumbar disc surgery experience postoperative back and radicular pain, which may delay patient recovery and worsen quality of life. Intraoperative epidural steroid injection (ESI) is used by many surgeons to improve patient outcomes. However, few prospective studies examine its effectiveness, and evidence for long term pain reduction is inconclusive. Studies have demonstrated reduction in short term low back pain, post-operative hospital stay, and use of analgesic medicine. This study aimed to evaluate intraoperative corticosteroid treatment for postoperative improvement in pain and disability outcomes for patients with microdiscectomy, with emphasis on long term follow-up.

Methods Used: 60 patients with lumbar disc herniation or spinal stenosis who presented to Santa Monica Orthopaedic Hospital for minimally invasive single-level lumbar decompression (microdiscectomy) over five months were randomized to receive intraoperative methylprednisolone injection or saline injection in the epidural space at the closure of the standard operative procedure. The patients and analysis team were blinded to the treatment, but the surgeons were not. Post-operative pain level and function were examined using Visual Analog Scale (VAS) and Oswestry Disability Index (ODI) recorded before surgery and at one week, three months, and six months after surgery.

Summary of Results: Data analysis is ongoing to evaluate effectiveness of intraoperative ESI. A significant reduction in negative outcomes may suggest that standardized intraoperative ESI would improve patient well-being in the interval after operation and reduce use of narcotics for pain relief. If evidence shows lack of pain improvement, consideration should be given to minimize excess treatment and cost.

Conclusions: Reduction in postoperative pain may improve patients’ ability to ambulate and complete daily tasks, resulting in improved quality of life. Further areas of study include varying dose of corticosteroid, or combining exercise or postoperative injection with intraoperative corticosteroid for improved pain outcomes.

ROLE OF MYOCILIN IN RECEPTOR ENDOCYTOSIS

Bower T1, Congrove N2, McKay B3. 1University of Arizona College of Medicine, Tucson, AZ and 2University of Arizona College of Medicine, Tucson, AZ.

Purpose of Study: Glaucoma is the second leading cause of blindness in the United States, affecting nearly 2 million people. Mutations in myocilin, a protein of unknown function expressed in many tissues throughout the human body, lead to ocular hypertension and glaucoma. The purpose of this study is to demonstrate myocilin’s participation in receptor endocytosis with GPR143 after ligand stimulation.

Methods Used: COS and MCF7 cells were transfected to express an isoform of myocilin and GPR143. Cell surface biotinylation was used to tag plasma membrane proteins. Receptor endocytosis was initiated through GPR143 stimulation with L-DOPA. Biotinylated proteins, and the cytoplasmic proteins bound to them, were captured using immobilized streptavidin. Myocilin association with biotinylated proteins was determined by western blot analysis. Confocal microscopy was also utilized to visualize myocilin during endocytosis.

Summary of Results: Myocilin associates with an activated GPCR during endocytosis with kinetics similar to arrestin-3. Mutant isoforms of myocilin differ in the interaction with an activated GPCR with P370L exhibiting little interaction and T377M exhibiting late dissociation.

Conclusions: Myocilin associates with transmembrane proteins in a signal transduction regulated process during receptor endocytosis. The receptor endocytosis kinetics of mutant isoforms of myocilin differ dramatically from wildtype and may be important in the pathogenesis of glaucoma in patients with mutations in myocilin.
(DVT) following arthroscopic shoulder surgery as 0.038%. The incidence of PE is even lower, with only case reports published. In each report, an upper or lower extremity DVT led to a PE, and most occurred within three weeks of surgery. We present a unique case report of a patient who developed a PE 41 days post-operatively with no associated extremity DVT.

GK is a 43 year-old right hand dominant female who presented with severe right shoulder pain, weakness and limited overhead motion. After history, physical, radiographic and MR arthrogram examination, she was diagnosed with a partial rotator cuff and biceps tear with acromioclavicular joint osteolysis. She had no risk factors for hypercoagulability. Over a year, GK participated in physical therapy, home exercises and two cortisone injections with no relief. Due to her lack of progress, she elected for surgery. An arthroscopic rotator cuff repair, distal clavicle excision and subpectoralis biceps tenodesis was performed. No complications occurred. She did well until 41 days post-operatively, when she called with sudden right hand swelling and trouble breathing. She also reported flu-like symptoms and stomach pain. There was no calf pain or lower extremity swelling. A statcomputed tomography (CT) angiogram of the chest revealed an acute PE in the right lower lobe. She was admitted to the hematology service and started on therapeutic Xarelto. A right upper extremity venous duplex ultrasound was negative for DVT. In addition, a thorough coagulation work-up was negative for pre-existing risk factors. Her shortness of breath and hand swelling resolved within two days of anti-coagulation therapy, and she completed the normal post-operative rehabilitation course, recovering well from surgery.

We report the first known isolated PE following shoulder arthroscopy. The presentation occurred nearly six weeks post-operatively, and the patient had no risk factors. Signs of acute PE following shoulder surgery include sudden hand swelling, trouble breathing and systemic symptoms. If these occur, there should be a low threshold to order a CT angiogram to evaluate for PE.

**418**

A REAL-TIME DECISION-SUPPORT SYSTEM TO IMPROVE INTRAOPERATIVE COMPLIANCE TO A GLUCOSE MANAGEMENT PROTOCOL

Grunzewig KA1, Peterson GN2, Nair BG2. 1University of Washington School of Medicine, Seattle, WA and 2UW Medical Center, Seattle, WA.

**Purpose of Study:** In a busy operating room environment, compliance to intraoperative glucose management protocol is poor due to difficulties in maintaining vigilance. We investigated whether a real-time decision-support software program, Smart Anesthesia Manager (SAM), could improve compliance with intraoperative glucose management.

**Methods Used:** SAM works in conjunction with an Anesthesia Information Management System to detect issues related to clinical care, and was configured to prompt the anesthesia provider to follow institutional glucose control protocol if a patient required glucose management. SAM generated “pop-up” computer messages to remind providers to make hourly glucose measurements, correct insulin dose adjustments and ensure consistent delivery of 5% Dextrose (DSW) with insulin. Compliance to protocol was compared between 12 months (1242 cases) with no SAM reminders and 7 months (1011 cases) with active reminders. Our study population included non-cardiac, non-transplant surgical patients, who were either diabetic by past medical history, on home insulin or oral hypoglycemic drugs, or had an intraoperative blood glucose value >140mg/dL.

**Summary of Results:** SAM reminders improved compliance to the glucose management protocol from 39.8% to 53.4%, and hourly glucose compliance, correct insulin administration and DSW co-administration doubled. While unexpected, some providers opted to disable SAM decisional support. Comparing cases with SAM disabled to SAM enabled, compliance starting the protocol improved from 29.9% to 77.7%. Providers used SAM for patients with higher BMI (p < 0.001), higher ASA (p = 0.003), and more often for diabetes type 2 patients (p < 0.001) and shorter cases (p < 0.001).

**Conclusions:** This study demonstrates that point-of-care, real-time decision support significantly improves compliance with an intraoperative glucose management protocol.

**419**

HEPATIC FOCAL NODULAR HYPERPLASIA IN CHILDREN POST-ONCOLOGIC THERAPY

Haider AA1, Imagawa DK2. 1University of California, Irvine School of Medicine, Irvine, CA and 2University of California, Irvine, Irvine, CA.

**Purpose of Study:** Focal nodular hyperplasia (FNH) is a benign tumor-like structure found in the liver with ill-defined etiology. When discovered in asymptomatic patients, management usually entails serial imaging to monitor for progression. Further confirmation of diagnosis is needed when patients with previous malignancies present with hepatic lesions. An increased incidence of FNH has been reported in children previously treated for extra-hepatic malignancies. This case series is presented to further understand the pathophysiology of FNH development.

**Methods Used:** Between 2006-2010, we report on four children (male n=2, female n=2) whose age at diagnosis ranged from 5-8 years who developed hepatic FNH after treatment for non-hepatic tumor.

**Summary of Results:** The primary malignancies found in this study are Neuroblastoma (n=3) and Medulloblastoma (n=1). Diagnosis was dependent on the combination of many imaging studies and usually accompanied by a CT guided fine needle aspiration biopsy (excluding Patient 3).

**Conclusions:** Fatty degenerative factors leading to aberrant regeneration may cause FNH. In these patients, chemotherapy agents may cause vascular damage and create a receptive environment for hepatic regeneration leading to FNH. Prospective studies are needed to further delineate the association between chemotherapy and the specific factors involved in the development of FNH.

**420**

THE CORRELATION BETWEEN FACET TROPISM AND DISC DEGENERATION IN THORACIC SPINE

Hobson TE1, Thuiriere M2, Takahashi S1, Wang J1. 1David Geffen School of Medicine at UCLA, Los Angeles, CA and 2University of Southern Florida, Tampa, FL.

**Purpose of Study:** The intervertebral disc and facet joint forms the functional spinal unit, and disc degeneration (DD) and facet joint osteoarthritis play an important role in spinal degeneration. However, there have been no reports that investigate the effect of thoracic facet tropism (FT) on DD.

**Methods Used:** Using kinetic MRI (KMRI) data, thoracic FT, which was defined as a difference of more than one standard deviation (SD) from the mean angle of the facet joints, was investigated in neutral positions. Each segment of thoracic spine was assessed based on the extent of DD (grade I-V) by the Pfirrmann grading system. The facets which were diaphyseal and 140mg/dL.

**Summary of Results:** Of 638 functional spinal units in 58 subjects, 345 functional spinal units (54.1%) were examined. There was no difference of the facet angle according to DD grade (P=0.696). The prevalence of FT was 39.1%. In facet symmetry group, the proportion of DD grade was 23.8% in grade I, 38.1% in grade II, 30.0% in grade III, and 8.1% in grade IV, while the proportion in the FT group was 22.2%, 43.0%, 29.6%, and

<table>
<thead>
<tr>
<th>TABLE 1. Compliance Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>Intervention</td>
</tr>
<tr>
<td>Intervention SAM-on</td>
</tr>
<tr>
<td>Intervention SAM-off</td>
</tr>
</tbody>
</table>

*p < 0.001 (chi-squared test) Adjusted for duration, age, ASA, procedure type and diabetes.
52.0%, respectively. No significant difference was observed between DD and FT (P=0.384).

Conclusions: No significant correlation was observed between thoracic FT and DD.

421

DOES GELATIN-THROMBIN MATRIX TISSUE SEALANT ALTER RISK OF PELVIC ABSCESS IN PATIENTS UNDERGOING GYNECOLOGIC SURGERY?

Jarrett M1, Behbakht K2, Anderson C2, Frank DN3, Vázquez-Torres A4, McCollister BD5. 1University of Colorado Health Sciences Center, Aurora, CO; 2University of Colorado Health Sciences Center, Aurora, CO and 3University of Colorado Health Sciences Center, Aurora, CO.

Purpose of Study: Retrospective review of institutional data indicates intraoperative use of gelatin-thrombin matrix tissue sealant is an independent predictor of pelvic abscess and post-operative infection in hysterectomies. We propose further investigations to test whether this is a property unique to gelatin-thrombin matrix tissue sealants as opposed to other topical hemostatic agents.

Methods Used: Samples of hemostatic agents will be transported from the operating room and plated on culture media to establish sterility. PCR quantification of bacterial 16S rRNA in samples will be carried out. The second arm of the study includes inoculating topical hemostatic agents with common pathogens involved in pelvic abscess to compare colony formation. The final aspect entails inoculating topical hemostatic agents in culture with patient swabs taken from the vaginal cuff during hysterectomy procedures to assess for growth of pathogens. Women ages 18-85yr undergoing abdominal and laparoscopic hysterectomies will be included. Medical and demographic data will be collected to track clinical outcomes.

Total aerobic and anaerobic colony counts and PCR quantification of bacterial 16S rRNA in samples provide outcome measures. Plates producing >5,000 CFUs will be categorized as "contaminated". Pathogens will be identified using common laboratory techniques. Clinical outcomes following hysterectomies will be tracked to assess for pelvic abscess, defined as an encapsulated collection of fluid in the pelvis as identified on medical imaging, manual vaginal exam consistent with vaginal cuff infection, and fever (>38°C) or leukocytosis (11.109/lt). Summary of Results: Thus far, 13 samples of various hemostatic agents collected displayed no colony formation in culture. 10 DNA extractions from samples have been performed in preparation for PCR quantification of bacterial 16S rRNA.

Conclusions: All samples of topical hemostatic agents collected thus far exhibit no colony formation when plated in culture.

422

MANAGEMENT OF BIRTH RELATED BRACHIAL PLEXUS INJURIES

Neufeld M1,2, Verchere C1,2, Bucevcska M2, 1University of British Columbia, Vancouver, BC, Canada; 2BC Children’s Hospital, Vancouver, BC, Canada and 3BC Children’s Hospital, Vancouver, BC, Canada.

Purpose of Study: There is a lack of literature available to describe algorithms used in the management of Birth Related Brachial Plexus Injuries (BRBPI) in Canada. Capturing these algorithms will facilitate collaboration and research among these centres. The purpose of this study is:

1. To identify and compare Canadian centres’ algorithms in managing patients with BRBPI and methods of data collection.
2. To initiate the creation of a nationwide study group that can collaborate in the care and research of BRBPI.

Methods Used: A survey was conducted with health care teams at Canadian pediatric health centres that treat BRBPI. The data collected included source of referral, age of initial presentation, follow-up schedule, scoring systems used, physiotherapy and occupational therapy routines, and indications for surgery, splinting, casting and Botox injections. The clinical indications for radiological imaging and nerve conduction studies were also identified. The survey gathered details regarding the centre’s data collection and research involvement. The findings were then summarized by using descriptive statistics and tables.

Summary of Results: Out of the 9 centres contacted, 8 centres responded. Many similarities were seen among the centres. There was consensus that the ideal referral criterion was any BRBPI. The ideal age to first see a patient was within the first 4 weeks of life at most centres. Plastic surgeons and occupational therapists were both routinely involved in BRBPI care and most centres found it would be helpful to have more dedicated personnel involved in their BRBPI clinics. Classification of BRBPI at each of the centres was done using the Active Movement Scale assessment tool. The most variation was seen with regards to follow-up schedule and indications for interventions. All centres demonstrated an interest in being a part of a BRBPI study group.

Conclusions: BRBPI are managed similarly across Canada. A BRBPI treatment algorithm can now be contemplated on the basis of the consensual survey responses. There is also considerable interest in the development of a BRBPI study group among Canadian centres. A future direction from this study will be the establishment of such a group.

423

SHORT-TERM PHYSICAL INACTIVITY IMPAIRS VASCULAR FUNCTION

Nosova E1,2, Yen P3, Chong K3,4, Alley H3, Conte MS1, Stock EO5, Owens CD6,4, Grenon S2,3, 1UCSF, San Francisco, CA; 2Veterans Affairs Medical Center/UCSF, San Francisco, CA; 3UCSF, San Francisco, CA; 4UCSF, San Francisco, CA and 6Veterans Affairs Medical Center, San Francisco, CA.

Purpose of Study: Sedentarism, or physical inactivity, is an independent risk factor for cardiovascular diseases. Mechanisms thought to be involved include insulin resistance, dyslipidemia, hypertension, and increased inflammation. It is unknown whether changes in vascular and endothelial function also contribute to increased risk. We hypothesized that a short-term exposure to sedentarism would lead to vascular dysfunction and promote inflammation.

Methods Used: Five healthy subjects (4 males and 1 female) underwent 5 days of strict bed rest (BR) to simulate physical inactivity. Measurements of vascular function (flow-mediated brachial and femoral artery vasodilation [FMD]) to evaluate endothelial function; arterial tonometry to assess arterial resistance [AR]) and inflammation were made before BR, during (days 1, 3, 5) and after 2 recovery days. Subjects adhered to an isocaloric diet.

Summary of Results: BR led to significant decreases in FMD (Braekahl: 11 ± 3% pre-BR vs. 9 ± 2% post-BR, P<0.04; Femoral: 4 ± 5% vs. 2 ± 1%, P<0.04). Peripheral and central augmentation indices increased with BR (Peripheral: 44 ± 11 vs. 52 ± 14, P=0.01; Central: -4 ± 9 vs. ± 5 ± 11, P=0.03). Diastolic blood pressure (DBP) increased (58 ± 7 mmHg vs. 62 ± 7 mmHg, P=0.02), while neither systolic blood pressure nor heart rate changed. No significant changes in inflammatory biomarkers were observed. After 2 recovery days, FMD appeared to improve from post-BR values but did not fully return to baseline.

Conclusions: Acute exposure to sedentarism leads to a decrease in endothelial function and increases in AR and DBP. These changes are not coupled with changes in inflammatory biomarkers. We speculate that inactivity promotes a vascular "deconditioning" state characterized by arterial stiffening and increased basal arterial tone, leading to a weakened endothelial response and diminished vasodilation. These findings are especially relevant to sedentary individuals and hospitalized patients, suggesting that mobility should be encouraged to prevent deterioration of vascular function.

424

LOS ANGELES COUNTY TOTAL HIP AND KNEE PATIENTS ARE MORE ENGAGED IN THEIR HEALTH BEHAVIOR

Pham C, Andrawis J, Tsuchida G, Saini P, Kwong L, David Geffen School of Medicine, Los Angeles, CA.

Purpose of Study: 1) To analyze patient activation in patients undergoing total hip or knee arthroplasty in a distinct population and 2) investigate whether individuals within this population have lower patient activation. This unique population is primarily composed of patients from Los Angeles County who are socioeconomically challenged.
Methods Used: In this prospective study, we enrolled patients undergoing primary hip or knee arthroplasty. Patient activation was assessed preoperatively and correlated with baseline evaluations of demographic information and selected outcome measured to determine possible relationships with recovery after surgery. The patient activation measurement (PAM) is a patient-completed 13-item questionnaire that addresses key psychological factors and personal competencies.

Statistical analysis was conducted to compare the disability and functional status as a function of patient activation. Linear regression models were used to test the association between patient activation and functional recovery over time. We looked at the intensity of current pain, disability, and physical and mental health compared with patient activation. Statistical significance was assessed using a α level of 0.05.

Summary of Results: PAM scores did not follow a normal distribution with mean score of 76.4 (SD 20.6). There were no significant differences among quartile groups with respect to sex, age, insurance coverage, and ethnicity. Individuals born in the United States showed predictive PAM compared to individuals born in a foreign country (P = 0.018). Employed individuals were more likely to have higher physical health scores (P = 0.027). PAM scores were correlated with higher mental health scores.

Conclusions: Higher PAM suggests that this unique patient population constrained by socioeconomic limitations were more likely to engage in adaptive health behavior leading to higher patient activation measurement.

425

TRAUMATIC POSTERIOR SPONDYLOLISTHESIS L5/S1
Robbins M, Mallon Z, Patel R, Roberto R, Gupta M, Klineberg E. UC Davis, School of Medicine, Sacramento, CA.

Case Report: A 23 year-old female presented with back pain status post high speed motor vehicle accident. She was a restrained rear seat passenger (wearing both lap and shoulder belts) without loss of consciousness, and was able to self-extricate from the vehicle. On arrival to the ED, she complained of back pain with tingling in the buttocks and posterior thighs. A CT scan was obtained, but she was initially discharged home. Two hours later, upon final read of her CT scan which demonstrated retrolisthesis of L5 on S1 with a small anterior fracture along the endplate of L5/S1 and narrowing of the disc space, she was called back to the ED. She complained of worsening radicular symptoms and pain with ambulation. A subsequent MRI demonstrated disruption of the posterior ligamentous complex and disc disruption (Fig 1) with a collection of fluid in her facet joints. Traumatic posterior L5/S1 spondylolisthesis was confirmed, and compression of the neurological structures was causing radicular symptoms.

The patient was brought to the operating room. Hemorrhage with edema in the soft tissues was present. There was complete transverse disruption of the posterior midline fascia due to tension failure of the posterior structures. The surgical dissection was completed from the spinous processes to the posterior midline fascia due to tension failure of the posterior structures. The patient tolerated the procedure without complications.

Postoperatively she had a favorable outcome with complete resolution of her radicular symptoms. She was fully ambulatory upon discharge without neurological deficits.

MRI showing L5-S1 retrolisthesis, interspinous ligament injury and disc herniation with narrowing of the spinal canal.

426

BENEFICIAL EFFECTS OF PREOPERATIVE STATINS ON CARDIAC SURGERY PATIENTS

Purpose of Study: The use of preoperative statins among cardiac surgery patients has been shown to decrease both postoperative renal complications and infection rates. Yet statin use is not part of the quality measures for this group of high-risk patients. The aim of this study was to investigate whether preoperative statin therapy leads to improved outcomes in cardiac surgery patients.

Methods Used: A retrospective review of an institutional database was done to identify adults who underwent cardiac surgery at our institution from 2008 to 2013. The primary endpoint was survival to discharge. We developed a multivariate logistic regression model adjusting for the following risk factors: surgical indication, age, gender, BMI, preoperative CHF, previous MI, preoperative renal failure, cross-clamp time, smoking history, and preoperative beta-blocker use. Additional secondary outcome measures were also examined, as seen below.

Summary of Results: 2099 patients met inclusion criteria. In-hospital mortality was 2.58% and postoperative renal failure was 2.33%. Preoperative statin therapy was associated with lower odds of prolonged ventilation (OR = 0.69, P = 0.004), decreased total length of stay (OR = 0.37, P < 0.001), and a decrease in the incidence of reoperation (OR = 0.55, P = 0.022). A decrease was noted in the incidence of postoperative renal failure, though there were not enough total events to reach statistical significance.

Conclusions: These results indicate that preoperative statins in high-risk patients (i.e. requiring cardiac surgery) were associated with significant improvement in several postoperative outcomes, including duration of mechanical ventilation, hospital length of stay, and the need for acute reoperation.

These results suggest that the administration of preoperative statins may substantially improve outcomes in cardiac surgery patients and randomized trials are indicated.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Pre-Operative Statin OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital Mortality</td>
<td>0.66 (0.35-1.25)</td>
<td>0.204</td>
</tr>
<tr>
<td>Atrial Filtration</td>
<td>1.04 (0.77-1.36)</td>
<td>0.87</td>
</tr>
<tr>
<td>Prolonged Vent Time (&gt;24hrs)</td>
<td>0.65 (0.49-0.87)</td>
<td>0.004*</td>
</tr>
<tr>
<td>Reoperation</td>
<td>0.55 (0.33-0.92)</td>
<td>0.022*</td>
</tr>
<tr>
<td>Post-op Renal Failure</td>
<td>0.53 (0.28-1.02)</td>
<td>0.058</td>
</tr>
<tr>
<td>Total ICU Hours</td>
<td>0.96 (0.73-1.23)</td>
<td>0.74</td>
</tr>
<tr>
<td>Length of Hospital Stay</td>
<td>0.37 (0.21-0.66) /&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

**= STATISTICALLY SIGNIFICANT

Adolescent Medicine and General Pediatrics III
Concurrent Session
11:00 AM
Saturday, January 25, 2014

427

UNIVERSITY OF NEW MEXICO BREASTFEEDING PROJECT: RATES KNOWLEDGE AND ATTITUDES, BARRIERS AND SUPPORT
Sebesta EA, McGough-Maduena A. University of New Mexico, Albuquerque, NM.

Purpose of Study: The AAP recommends that babies be breastfed exclusively for 6 months and for at least 12 months total. The aims of this pilot study are to develop first week and follow up breastfeeding surveys, recruit
DEVELOPING A CLINICAL PATHWAY TO IMPROVE SCHOOL-BASED HEALTH CARE OF ADOLESCENT SUBSTANCE ABUSE

Ramos M1, Stoltzfus W3, Sharff M1, Condon T2.

SUMMARY OF RESULTS: Two surveys and a script for an open-ended interview were created. An ethnically diverse convenience sample was recruited. Most mothers reported a high level of confidence in their ability to breastfeed and the intent to exclusively breastfeed for 6 months and 12 months total. Many women believed they should not breastfeed if they had a fever or if they were angry, sad, or upset. Mothers were most aware of the short-term health benefits for mothers and babies and the nutritional benefits for babies. Less than half were aware of long-term health benefits for themselves or their babies. Mothers who were breastfed or had close friends who breastfed were more likely to still be breastfeeding at 2 months. Seventy-five percent of mothers felt supported by physicians to achieve their breastfeeding goals versus 95% by nurses.

CONCLUSIONS: In this pilot study, we were able to recruit an ethnically diverse group of New Mexican mothers. Mothers reported breastfeeding goals consistent with the AAP recommendations. Support for mothers who were not breastfed or who do not have friends who breastfed is needed. Breastfeeding education should include the safety of breastfeeding when a mother is ill and regardless of her mood as well as the long-term benefits to both mothers and babies. Training of physicians and mid-level providers to provide effective breastfeeding support is needed.

SCHOOL-BASED HEALTH CARE OF ADOLESCENT DEVELOPING A CLINICAL PATHWAY TO IMPROVE

Methods Used: Surveys evaluating mothers’ attitudes, knowledge, and support for and barriers, utilizing existing CDC questionnaires, the Breastfeeding Self-Efficacy Scale-Short Form (Dennis, C. 2003), and additional questions, were created. A script to guide investigators during an interview was created to better explore maternal beliefs, barriers and supports, and potential interventions. Mothers of newborns born at UNMH were recruited while they were on the Mother-Baby Unit or in the Newborn Clinic.

Purpose of Study: To improve substance abuse screening at SBHCs, we defined SA as use of tobacco, alcohol or other drugs. SA was identified through the SBHC nurse intake process. Pediatricians complete a brief assessment, and if the pediatrician identifies risk, the youth is referred for further evaluation.

SUMMARY OF RESULTS: Based on the survey results, the multidisciplinary team began to identify the barriers to implementing the clinical pathway. The team met 10 times to develop the clinical pathway. The team included pediatricians, nurses, behavioral health therapists, and frontline SBHC staff.

CONCLUSIONS: The team identified many areas for improvement including providers not using the clinical guideline, lack of available resources and little knowledge about the specific needs of the adolescent population. Learning about new resources and creating a plan to address these barriers were the next steps for our team.

428

BREAKING THROUGH TO AT-RISK YOUTH: REFLECTIONS OF PEDIATRIC RESIDENTS MENTORING GIRLS AT AN URBAN HIGH SCHOOL IN FRESNO, CA

Shilahkhtinsitava K1, Azin A1, Farrell A1 Kretzmer R1, Kinman R1,2

SUMMARY OF RESULTS: In this pilot study, we were able to recruit an ethnically diverse group of New Mexican mothers. Mothers reported breastfeeding goals consistent with the AAP recommendations. Support for mothers who were not breastfed or who do not have friends who breastfed is needed. Breastfeeding education should include the safety of breastfeeding when a mother is ill and regardless of her mood as well as the long-term benefits to both mothers and babies. Training of physicians and mid-level providers to provide effective breastfeeding support is needed.

Purpose of Study: Pediatricians are expected to care for patients from birth to 21 years old. Yet many pediatricians feel ill-equipped to handle the challenges of the adolescent patient. Although many physicians may be able to identify with the high-achieving adolescent patient as a result of their own teenage experiences, interacting with high-risk urban teenage patients requires a unique set of skills. Adolescent medicine and community pediatrics are two required rotations within the pediatric residency program where pediatric residents can develop these abilities.

Methods Used: We instituted a recent curricular change in these two rotations in order to help meet these needs. Residents in the UCSF-Fresno Pediatric Residency Program now rotate weekly at a large urban high school in Fresno, working with a small group of female high school students (16-26 students, grades 9-12) identified as being at extremely high risk for dropping out. Students are members of the Work’s Alliance an elective course where students work to develop personal behavior and academic skills that will enable them to achieve success not only in the classroom, but also in their personal lives. The goal of this project is for the students themselves to produce a monthly interactive lunchtime education session in which they educate other students at this school on health topics of interest to this adolescent population.

CONCLUSIONS: Other valuable lessons have been learned by both residents and attending physicians as a result of this process. These include the following: 1) Students are more involved when they have direct ownership of their project and choose their own topic, 2) Students would rather work in one large group, rather than several small groups, 3) Although projects can change 3 times in 3 weeks, an effective presentation can still be produced in one week, 4) Students respond best to projects with immediate gratification, 5) Interactive sessions are more productive than lectures.

430

SKELETAL MUSCLE SPASTICITY RESULTS FROM SATELLITE CELL DEFICIENCY

Lyuasyuk V1, McKay B1, Dayanidhi S1, Chambers H2, Lieber RL1, UCSF, San Francisco, CA, 1UCSF, San Francisco, CA and 2Children’s Hospital Oakland, Oakland, CA

SUMMARY OF RESULTS: Topics thus far have included teenage pregnancy and obesity with project presentations including a teen pregnancy "Game of Life" and a demonstration of the amount of sugar in commonly consumed beverages.

CONCLUSIONS: However, other valuable lessons have been learned by both residents and attending physicians as a result of this process. These include the following: 1) Students are more involved when they have direct ownership of their project and choose their own topic, 2) Students would rather work in one large group, rather than several small groups, 3) Although projects can change 3 times in 3 weeks, an effective presentation can still be produced in one week, 4) Students respond best to projects with immediate gratification, 5) Interactive sessions are more productive than lectures.

© 2013 The American Federation for Medical Research
Conclusions: Quantification of satellite cells in situ demonstrated drastically decreased satellite cell number in spastic muscle compared to normal. This is important because the number of satellite cells is supposed to increase after muscle injury. Abnormally small numbers of satellite cells in cerebral muscle might be responsible for its limited ability to regenerate and grow. This limitation in longitudinal growth may be responsible for contractures that children with cerebral palsy develop. This possible novel mechanism opens new opportunities for the development of novel cerebral palsy treatments.

Methods Used: Blood samples from healthy non-pregnant (n=130) and pregnant women at 16 weeks gestation (n=181) living in Vancouver were used. Plasma was isolated to perform analysis of choline and its metabolites (betaine and dimethylglycine) using liquid chromatography-mass spectrometry. Buffy coats were isolated to perform genotyping for SNPs in genes involved in choline metabolism using Sequenom.

Summary of Results: Preliminary results showed a significant difference (p=0.018) in the plasma betaine concentrations of non-pregnant women; specifically, women of Chinese descent were found to have significantly higher plasma betaine concentration. The plasma choline, betaine, and dimethylglycine concentrations of pregnant women of Chinese descent were significantly higher than those of their Caucasian counterparts (p=0.008, 0.001, and 0.003, respectively).

Conclusions: Based on preliminary results, plasma betaine concentration was significantly higher in healthy non-pregnant women of Chinese descent. Plasma choline, betaine, and dimethylglycine concentrations were also significantly higher in healthy pregnant women of Chinese descent. These preliminary findings may highlight possible ethnic differences in choline deficiency risk. The next steps in this study will be to determine whether the ethnic differences noted above can be explained by SNPs in genes involved in choline metabolism and not by differences in diet.

TABLE 1. Outcomes of Patients Developing Moderate Pericardial Effusion

<table>
<thead>
<tr>
<th>Outcome</th>
<th>n=33</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericardial effusion resolves w/o intervention</td>
<td>26/33 (78.8%)</td>
</tr>
<tr>
<td>Mean time to resolution (days)</td>
<td>160.2 ± 121.4</td>
</tr>
<tr>
<td>Pericardial effusion persists w/o intervention</td>
<td>3/33 (9.1%)</td>
</tr>
<tr>
<td>Pericardial effusion Worsening Requiring Intervention</td>
<td>4/33 (12.1%)</td>
</tr>
<tr>
<td>Number of patients undergoing pericardiocentesis</td>
<td>3/4 (75.5%)</td>
</tr>
<tr>
<td>Number of patients undergoing pericardial window</td>
<td>1/4 (25.0%)</td>
</tr>
</tbody>
</table>

Summary of Results: We found 33 (11.3%) heart transplant patients who had developed moderate pericardial effusion within the first 6 months post-transplant. The average time to detection of pericardial effusion was 22.4 ± 18.4 days. In follow up, 78.8 % had resolution of the pericardial effusion, 9.1% had no change (at 1 year follow up), and 12.1% had worsening of pericardial effusion requiring either pericardiocentesis or pericardial window placement (see table). All patients were treated with diuretics to reduce the effect of the pericardial effusion.

Conclusions: The development of moderate pericardial effusion after heart transplantation resolves in a majority of cases and therefore does not necessarily require invasive intervention. However, close follow up is advised.
DO REDO HEART TRANSPLANT PATIENTS HAVE AN INCREASED RISK OF ANTIBODY DEVELOPMENT?

Aquino A, Yu Z, Liou F, Hamilton M, Kobashigawa J. Cedars-Sinai Medical Center, Los Angeles, CA.

Purpose of Study: Redo heart transplant patients may have higher levels of circulating antibodies due to the fact that they have been exposed to a foreign graft. In addition, these patients may have had additional blood transfusions which may have also contributed towards the development of circulating antibodies. It is not clear whether patients undergoing redo heart transplants are more sensitized compared to primary heart transplant recipients. Furthermore, it is not clear as to whether redo heart transplant patients have a higher tendency to develop more circulating antibodies following their second heart transplant surgery. These antibodies have been associated with poor post-transplant outcomes including survival and the development of cardiac allograft vasculopathy (CAV).

Methods Used: Between 2006 and 2012, we assessed 15 heart transplant patients who have undergone redo heart transplant compared to 215 in the same era who have undergone primary heart transplant surgery and had 0% panel reactive antibodies (PRA) pre-transplant. Post-transplant, the development of de novo circulating antibodies was obtained for the first year after transplantation (defined as PRA > 0% at any time point). 3 year actuarial survival and freedom from cardiac allograft vasculopathy (CAV) were determined for both groups. First year freedom from antibody mediated rejection and cellular rejection was also assessed.

Summary of Results: Post-transplant, there was no difference between the two groups in the percentage of patients developing de novo circulating antibodies within the first year. Survival and freedom from CAV at 3 years post-transplant were comparable between the two groups. Freedom from antibody-mediated cellular rejection and cellular rejection was also comparable between the two groups.

Conclusions: Redo heart transplant patients did not have a greater tendency to develop more antibodies post-transplant.

---

DOSE CONVERSION FACTOR BETWEEN CYCLOSPORINE AND TACROLINUX IN PEDIATRIC HEART TRANSPLANT PATIENTS

Notaro E1, Brown L2, Albers E3, Law S3, Kemna M3. 1University of Washington, Seattle, WA; 2University of Washington, Seattle, WA and 3Seattle Children’s Hospital, Seattle, WA.

Purpose of Study: We examine the relationship between cyclosporine (CyA) and tacrolimus (TAC) dosing in the pediatric heart transplant patients, seeking a conversion factor between calcineurin inhibitors (CNIs) that accounts for patients’ individual differences in drug metabolism and may provide more accurate dosing than the traditional mg/kg guidelines.

Methods Used: Retrospective study of 59 CNI conversions in 57 patients ≤ 18 yo. Conversion factor was defined as patients’ stable 24-hour CyA dose divided by stable 24-hour TAC dose. Prediction accuracy of conversion factor was assessed using leave-one-out cross-validation.

Summary of Results: Stable CyA dose strongly correlated with stable TAC dose (r=0.81). The geometric mean of conversion factors was 60 for the children < 2 yo and 42 for children ≥ 2 yo. Using conversion factors had lower individual effects compared to patients with baseline heart rate greater than 100 beats per minute. Several disease states have demonstrated that sinus tachycardia may result in long-term poor outcome in patients with severe heart failure and with severe coronary artery disease. Recent studies have also suggested that faster heart rates in heart transplant patients may also be associated with poor outcome. For this reason, we reviewed our heart transplant patients with baseline heart rate greater than 100 beats per minute who were treated with beta blockade versus those patients with heart rate greater than 100 who were not treated with beta blockade. All patients in this study were treated with beta blockade for hypertension and not for chronic rejection.

Conclusions: Beta blocker therapy for patients with sinus tachycardia greater than 90 beats per minute in heart transplant recipients appears to have no beneficial effect for long-term outcome. There may not be a gain to beta-blocker therapy slow a fast heart rate after heart transplantation.

---

BETA BLOCKERS TO LOWER HEART RATE AFTER HEART TRANSPLANTATION MAY NOT BE BENEFICIAL

Parikh A, Yu Z, Liou F, Hamilton M, Kobashigawa J. Cedars-Sinai Medical Center, Los Angeles, CA.

Purpose of Study: Heart transplant patients are known to be denervated, which results in a higher resting heart rate usually between 90-110 beats per minute. Several disease states have demonstrated that sinus tachycardia results in long-term poor outcome in patients with severe heart failure and with severe coronary artery disease. Recent studies have also suggested that faster heart rates in heart transplant patients may also be associated with poor outcome. For this reason, we reviewed our heart transplant patients with baseline heart rate greater than 100 beats per minute who were treated with beta blockade versus those patients with heart rate greater than 100 who were not treated with beta blockade. All patients in this study were treated with beta blockade for hypertension and not for chronic rejection.

Methods Used: Between 2001 and 2011, we reviewed 41 heart transplant patients who were treated for hypertension with beta blockers post-transplant and included only those patients with baseline heart rate greater than 90 beats per minute. Controls matched for age, sex, time from transplant, and hypertension served as 2:1 controls. End points included subsequent 3 year survival, freedom from cardiac allograft vasculopathy (CAV), and freedom from non-fatal major adverse cardiac events (NF-MACE).

Summary of Results: Patient started to take beta blockers after an average of 1.4 ± 1.1 years post heart transplant. The average length of patient on beta blockers is 3.2 ± 1.3 years. For the beta blocker group, pretreatment heart rate was 102 ± 11 bpm and decreased to 87 ± 12 bpm with beta blocker treatment. Those heart transplant patients treated with beta blockade had neither increase in long-term poor outcome nor greater freedom from CAV and NF-MACE compared to the control group.

Conclusions: Beta blocker therapy for patients with sinus tachycardia greater than 90 beats per minute in heart transplant recipients appears to have no beneficial effect for long-term outcome. There may not be a gain to beta-blocker therapy to slow a fast heart rate after heart transplantation.
**CYLEX SCORES FOR AFRICAN AMERICANS VS. CAUCASIANS: IS THERE A DIFFERENCE?**


**Purpose of Study:** African Americans undergoing heart transplantation have been reported to have increased rejection episodes. This may be due to a difference in their metabolism of immunosuppression medications, specifically by CYP3A enzyme activity, compared to Caucasians. Currently, immunosuppression is measured by therapeutic drug levels. The Cylex score offers the ability to assess immunoresponsiveness to medication dosing and trough levels. It is not clear whether African Americans have greater immunoresponsiveness to similar trough level immunosuppression compared to Caucasians, which may be the reason for the increase in rejection episodes.

**Methods Used:** Between 2008 and 2012, we evaluated 225 heart transplant patients and divided them into African Americans and Caucasians. At 1, 3, and 6 months after transplant, Cylex scores, tacrolimus doses and trough levels were compared between groups.

**Summary of Results:** African American group had a trend towards a higher Cylex score at month 1 but became similar to Caucasian group at later follow up.Tacrolimus doses were significantly higher in the African American group. However, the trough levels were numerically lower throughout the first year compared to the Caucasian group (see table). There was no difference in 1 year freedom from cellular or antibody-mediated rejection between the two groups.

**Conclusions:** African Americans appear to have a greater metabolism of tacrolimus resulting in numerically lower trough levels despite higher dosing. This manifests in a higher Cylex score suggesting that they are less immunosuppressed. In the study there did not appear to be an increase in rejection rates; however, numbers are small. This increased metabolism of immunosuppression medications may be a reason for the previous report that African American had higher rejection rate.

**Health Care Research III: Novel Diagnostics and Therapies**

Concurrent Session

11:00 AM  
Saturday, January 25, 2014

**LONGITUDINAL DEVELOPMENT OF OBESITY IN THE POST FONTAN POPULATION**

Wellnitz KA1, Fineeman JR2, Harris I3, Radman M1. 1UCSF San Francisco, CA and 2UCSF San Francisco, CA.

**Purpose of Study:** An elevated body mass index (BMI) in childhood is a significant independent risk factor for cardiovascular disease and may pose an additional risk to children and adults with congenital heart disease after palliation. While previous cross-sectional studies estimate that 16% of children status post Fontan palliation were either overweight (OW) or obese (OB), little is known about the longitudinal changes in BMI after surgery and to what extent development of obesity contributes to disease burden. The objective of this study is to determine the prevalence of OW and OB at time of Fontan palliative surgery, to track longitudinal changes in BMI after surgery, and ultimately to determine whether factors such as pre-operative BMI, ethnicity, and pre-operative heart defect are associated with later development of OW or OB.

**Methods Used:** A retrospective chart review was done of 100 patients undergoing Fontan palliation between 1974 and 2012. Demographic data including gender, ethnicity, and pre-operative heart defect were recorded. Height, weight, and BMI were obtained at time of Fontan and on a yearly basis post-surgery. Children’s BMI percentiles and Z scores were calculated using an online program based on the US Centers for Disease Control (CDC) growth charts. CDC definitions of OB and OW were used.

**Summary of Results:** Of the 100 patients, 54% were male and 46% were female. Median age at Fontan was 4.9 years. Most common underlying diagnostis necessitating Fontan was tricuspid atresia. At time of Fontan palliation, 12.9% (9) were OB or OW (n=70). At 5, 10, and 15 years post Fontan, 39.1%, 44.4%, and 55.6% of patients were either OB or OW (respectively, 9 of 23, 4 of 9, and 5 of 9). At 20 years post Fontan, 66.7% of patients were OB or OW (4 of 6). While the prevalence of OB and OW at time of Fontan was almost one third of that in US children (12.9% vs 30%), by twenty years post-Fontan/adulthood, the percentage of post-Fontan palliation patients who were OB or OW was almost identical to the general US adult population (66.7% vs 69.2%).

**Conclusions:** A large percentage of patients status post Fontan palliation go on to become OB or OW. Further study is needed to delineate the risk factors for development of obesity in this population and its affect on cardiovascular function.

**MAGGOT THERAPY IS IMPROVING WOUND CARE IN RESOURCE-LIMITED POPULATIONS**

Rosen S1,2, Mirabzadeh A3, Ladani M3, Sharifi S2, Mashayekhi M4, Azema M5, Imani B2, Sherman R1. 1University of Colorado School of Medicine, Aurora, CO; 2Iranian Research Organization for Science and Technology, Tehran, Islamic Republic of Iran and 3BioTherapeutics, Education & Research Foundation, Irvine, CA.

**Purpose of Study:** The need for improved wound care is a global issue of increasing importance in patients’ quality of life due to the rising rate of diabetes and aging global population. Too often patients face the difficult choice of amputation or death from eventual infection and necrosis of their wound. Maggot debridement therapy (MDT) has long been used with promising results; however, MDT is overlooked by many Western practitioners who instead treat chronic wounds with expensive dressings, antibiotics and surgery. Despite these advanced methods, wound healing still often fails, resulting in 100,000 amputations per year in the U.S., alone. Patients in countries with limited resources are more susceptible to amputation from insufficient wound care. In this study, we sought to evaluate the effectiveness of MDT in a country with limited resources.

**Methods Used:** The use of MDT was studied in wounds that failed conventional care at three hospitals in Tehran, Iran. Primary outcomes were recorded, including time to debridement and wound healing, demographic factors, wound characteristics, underlying medical conditions, and treatment attitudes. Data was analyzed by Student t-test and ANOVA.

**Summary of Results:** A total of 29 wounds in 28 patients were treated with MDT. Most (55%) of the wounds were ischemic, neuropathic, or mixed-pathology foot ulcers in diabetic patients. At least thirteen (45%) were believed to require amputation or radical resection. After maggot therapy, all wounds were completely debrided; none required amputation, grafts, or advanced interventions. Osteomyelitis was present in all cases prior to maggot therapy but appears to have been eradicated without recurrence after at least two years of follow-up. The most common adverse events were bad odor and wound pain. All patients and therapists were pleased with their overall experience.

**Conclusions:** MDT can provide advanced wound care, even in patients who have failed conventional therapy and in resource-limited areas of the world. In Iran, the safety and efficacy was good enough that many patients and doctors now demand the treatment.
THE EFFECT OF TRADITIONAL CHINESE MEDICINE ON CHEMOTOXICITY AMONG ETHNICALLY DIVERSE BREAST CANCER SURVIVORS

Tam E1, Ergas IJ2, Roh JM2, Kwan ML2, Kushi LH2. 1 UCLA, Los Angeles, CA and 2 Kaiser Permanente, Oakland, CA.

Purpose of Study: This study aims to examine oral Traditional Chinese Medicine (TCM) and its effects on chemotoxicity in recently diagnosed breast cancer survivors.

Methods Used: The study is a prospective cohort study of 1,765 women diagnosed with invasive breast cancer in the Kaiser Permanente Northern California Medical Care Program from 2006-2009. Participants completed a complementary and alternative medicine survey at approximately 8-months post-diagnosis to examine the types of TCM used in conjunction with chemotherapy. The TCMs include astragalus root, black cohosh, dandelion, garlic, ginger, ginseng, and reishi mushroom. Selected chemotoxicity include nephrologic, cardiovascular, gastrointestinal, infectious, and hematologic conditions. Seven selected herbal supplements were examined.

Summary of Results: Participants who took ginger (p=0.027) and garlic (p=0.029) were associated with having lower incidence of low white blood cell counts. Additionally, participants who took ginger (p=0.0244) and dandelion (p=0.0355) were associated with having lower incidence of requiring blood transfusion. Interestingly, ginger was not found to be associated with chemotherapy-induced gastrointestinal conditions.

Conclusions: Patients of underprivileged background tend to have higher incidence of cancer, but have poorer cancer outcomes. TCM products such as ginger and garlic are easy to obtain, cheap to buy, and possible alternatives to combat chemotherapy side effects for breast cancer survivors.

EXPERIMENTAL RESEARCH INTO THE INFLUENCE OF DIFFERENT EXERCISES OF ANKLES ON INTRAVENOUS BLOOD REFLUX IN LOWER EXTREMITIES

Wang X. Yanshan University, Qinhuangdao, China.

Purpose of Study: When the toes and instep are bent and the feet are turning around, the ankle joints affect the instep and toe muscle group and digital flexor muscle group, causing the intravenous blood in lower extremities to reflux. In this paper, color Doppler ultrasound testing is used to compare the dynamic parameters of intravenous blood reflux of lower extremities including active and passive ones for their change characteristics, and to provide objective scientific basis for effectively improving the intravenous blood flowing speed of lower extremities and preventing venous thrombosis in the lower extremities.

Methods Used: The color Doppler ultrasound method is used to test the peak and mean flowing speed of femoral intravenous blood while the veins of 12 healthy adults are in rest or the ankles do different exercises. The exercises are: foot bending and stretching, inward and outward turning, turning around of feet. Ultrasound testing: Testing related ultrasound parameters of four veins (Common Femoral Veins, superficial femoral vein, deep femoral vein to popliteal vein) for the change of intravenous blood flowing of lower extremities before and after the three exercises.

Summary of Results: Foot bending and stretching and inward and outward turning can only improve the intravenous blood flowing slightly, and the turning-around has better effects than the other two with its peak speed up by 32.4% and mean speed up by 34.1%. The turning-around can increase the peak intravenous blood speed by 42.1% and 33.2%, and the mean intravenous blood flowing speed by 39.8% and 33.3% higher than the bending and stretching, and inward and outward turning. The turning around of ankles can promote the femoral intravenous blood flowing best, and may accelerate blood flowing, significantly increase the blood flow (p<.01) and increase the peak speed by 70.1% and the mean speed by 70.4%.

Conclusions: Foot bending and stretching, inward and outward turning, and turning around of feet is practically significant for preventing slow blood flowing, pooling of blood and intravenous thrombus. The effect of foot turning around is the best, simple and easy to promote, practical.

HIERARCHICAL REPRESENTATIONS FOR LUNG NODULE DETECTION IN CHEST COMPUTER TOMOGRAPHY WITH DEEP NETWORKS

Zheng H1, Chan J1, Li F3, Ying H3, Zhang M2, Kenji S3. 1 Xi’an University of Technology, Xi’an, China; 2 Xi’an Jiaotong University, Xi’an, China; *University of Chicago, Chicago, IL, and *Aichi Prefectural University, Nagakute, Japan.

Purpose of Study: Lung cancer accounts for the most cancer related deaths around the world. Chest Computer tomography (CT) is the most commonly used diagnosis technique for detection of pulmonary nodules in routinely examination. However, it should be noticed that despite much effort being devoted to, lung CAD systems remain an ongoing research topic. With this in mind, this paper describes a new method for Lung Nodule detection in Chest CT.

Methods Used: In this study, we propose a novel representation automatically through unsupervised feature learning with deep neural networks, where a Convolutional Restricted Boltzmann Machine (CRBM) with real valued visible input nodes v and binary valued hidden nodes h is utilized. In our study, we trained the deep CRBMs with up to two layers of CRBMs. After constructing a convolutional deep neural, we perform inference of the whole network in a feed forward manner.

Summary of Results: For our experiments, 827 images from 24 cases from Xi’an Jiaotong University Hospital, we obtained the CT image file in the DICOM (Digital Imaging and Communication in Medicine) format. File size was adjusted for processing time and disk space by using the XV image viewer.

Conclusions: The resultant image matrix was 512×512 with 1 byte/pixel, and the total size was 256 kb. Our experiments show that there are 2 false negative results in 43 true nodules, which were verified by a chest radiologist. Therefore, we had a 96% nodule detection sensitivity, which was very good when compared with existing methods for lung nodule detection rely on feature representations given by hand-crafted image descriptors.

Acknowledgments: This work is partially supported by a grant from the National Natural Science Foundation of China (No.61072151), the Nature Science Foundation of Shanshi Education Department (No.2013JK1136), the Nature Science Foundation of Science Department of PeiLin count at Xi’an and the Nature Creative Science Program of Xi’an University of Technology (No.116-211107).

INTERIM RESULTS: AN INNOVATIVE COMBINATION OF EXCIMER LASER, CLOBETASOL SPRAY, AND CALCITRIOL OINTMENT FOR THE TREATMENT OF PSORIASIS


Purpose of Study: Psoriasis is a chronic inflammatory dermatosis that is estimated to affect 2-3% of the US population. The therapeutic approach may be determined based on the distribution of psoriasis such that localized disease is managed with topical agents and targeted UV therapy, while biologic agents are usually reserved for generalized disease. The excimer laser is a targeted treatment modality indicated for localized psoriasis that allows selective irradiation of affected skin, resulting in less photodamage compared to traditional whole body phototherapy. The use of laser in combination with topical therapy has never been studied in generalized psoriasis. In this study, we aim to improve the excimer laser efficacy with clobetasol spray and calcitriol ointment for the treatment of generalized psoriasis.

Methods Used: Patients with plaque psoriasis involving 10-30% body surface area were recruited for this 12-week study. All patients underwent twice weekly treatments with the XTRAC® Velocity 308nm excimer laser until week 6 and thereafter as needed if <75% improvement in Psoriasis Area Severity Index (PASI). The 12-week study period is divided into three 4-week treatment periods in which the patients supplemented laser treatment with twice daily dosing of topical agents, including clobetasol spray (weeks 1-4), calcitriol ointment (weeks 5-8), or both clobetasol and calcitriol (weeks 9-12). The primary endpoint was the percentage of patients achieving ≥75% reduction in PASI (PASI-75) at week 12.

Summary of Results: To date, a total of 21 patients have completed the protocol. At week 12, 76% of patients (16/21) achieved PASI-75 with an average of 15 laser treatments. The treatments were well tolerated with the most commonly reported side effects of pruritis, burning, and superficial blistering.
Conclusions: This is the first ever study investigating the treatment of generalized psoriasis with excimer laser in combination with clobetasol and calcitriol. At week 12, 76% of patients achieved PASI-75, which is superior to the efficacy of biologic medications without the internal risks of systemic therapy. While the excimer laser is usually reserved for localized psoriasis, the results of this study demonstrate its utility in generalized psoriasis when supplemented with topical therapy.

THE PSYCHOSOCIAL AND OCCUPATIONAL STATUS OF PATIENTS AFTER TREATMENT OF GENERALIZED PSORIASIS WITH A BIOLOGIC USTEKINUMAB: INTERIM RESULTS


Purpose of Study: Psoriasis is a common chronic skin disease associated with several comorbidities including psoriatic arthritis. Patients with psoriasis often experience psychosocial and occupational difficulties due to the visible and uncomfortable nature of their disease. In addition to measuring physical efficacy of treatment, it is critical to evaluate quality of life in this population. This study aims to prospectively assess the effect of ustekinumab treatment on generalized psoriasis, with an emphasis on the psychosocial and occupational well-being of patients measured by multiple validated psychometric instruments pre and post treatment.

Methods Used: Patients received 36 weeks of ustekinumab therapy and were assessed every 4 weeks for psoriasis severity and quality of life. Psoriasis severity was measured using the Psoriasis Area and Severity Index (PASI). Quality of life was assessed using the Dermatology Life Quality Index (DLQI), Psychological General Well Being (PGWB), Work Productivity and Activity Impairment (WPAI), and Psoriasis Quality of Life-12 items (PQOL-12).

Summary of Results: This study plans to include 35 patients, 16 of which have completed the study. The interim data illustrates that pre-treatment, patients with psoriasis suffer intense negative psychological impact comparable to untreated congestive heart failure, diabetes, breast cancer, and COPD based on PGWB. After 9 months of treatment with ustekinumab, patients experienced improved psychological status so that their scores were similar to the general public. For those subjects who achieved a ≥75% improvement in PASI, overall work impairment and activity impairment due to psoriasis improved 23% and 30% respectively. Marked improvement was also seen in DLQI and PQOL-12 with ustekinumab treatment.

Conclusions: These results reveal that untreated psoriasis negatively impacts psychosocial well being as much as untreated major medical conditions. With effective therapy, the psychological well being of patients with psoriasis can improve greatly demonstrating that appropriately aggressive and effective intervention by dermatologists is critically indicated.

Hematology and Oncology II
Concurrent Session
11:00 AM
Saturday, January 25, 2014

445

SIFTING THROUGH IT ALL: THE QUALITY OF ONLINE RESOURCES FOR OVARIAN CANCER PATIENTS

Yu 1, Inglesew 2.
1 University of British Columbia, Vancouver, BC, Canada and 2 BC Cancer Agency, Surrey, BC, Canada

Purpose of Study: Ovarian cancer is the most fatal gynecological cancer, with the majority of patients diagnosed at an advanced stage. Online information can serve as an important tool for patients to learn about their condition in a timely manner. To date, there have been no published studies assessing the quality of ovarian cancer websites. Our aim is to comprehensively evaluate the quality of these resources.

Methods Used: A previously validated website evaluation tool was used to analyze the quality of online ovarian cancer resources. The term “ovarian cancer” was used to retrieve hits from Google, Dogpile and Yippy. A “top 100” website list was compiled using pre-specified inclusion and exclusion criteria. Websites were evaluated regarding administration, accountability, authorship, organization, readability, content and accuracy. Inter-rater reliability was confirmed via kappa statistics and results were analyzed via descriptive statistics.

Summary of Results: Over 1300 websites were retrieved from the 3 search engines. Of the top 100, 77% disclosed ownership, sponsorship and/or advertising. There were significant deficiencies in attribution; author(s), their affiliations and credentials were only identified in 38%, 28% and 34% of websites, respectively. Sources were cited in 43% of websites, with only 30% referencing ≥ 3 reputable sources. Over half (55%) of websites were last updated over 4 years ago or not at all. The Flesch-Kincaid Grade Level Readability scores ranged from 6 to 15, with an average grade level of 10.6. Most websites described the symptoms and diagnosis of ovarian cancer (97%, 94%) but nearly half did not cover prognosis (56%). While most websites contained accurate information, those that presented prognostic information often cited inaccurate figures.

Conclusions: Although there are many websites with ovarian cancer patient information, there are deficits in the information and the sites. While most websites contain accurate information and identify ownership, very few cite reputable sources, identify authors or include prognostic details. The average grade level for readability is high and may not be appropriate for the general population. Overall, the quality of ovarian internet resources is variable, underscoring the need to develop new resources and address information gaps during the patient-physician encounter.

446

CIRCULATING TUMOR CELL (CTC) COUNTS AND CTC TELOMERASE ACTIVITY (TA) ARE PROGNOSTIC OF OVERALL SURVIVAL (OS) IN SWOG S0421: DOCETAXEL +/- ATRASENTAN FOR METASTATIC CASTRATION RESISTANT PROSTATE CANCER (mCRPC)

Goldkorn A 1,2, Vogelzang N 2, Fink L 2, Ely B 2, Quinn D 2, Tangen C 2, Tai YC 2, Twardowski P 2, Van Velthuizen P 2, Agarwal N 2, Carducci M 2, Monk J 2, Garzotto M 2, Mack P 2, Lara P 2, Higano C 2, Hussain M 2, Cote R 2, Thompson I 2, University of Southern California, Los Angeles, CA and Southwest Oncology Group, San Antonio, TX.

Purpose of Study: CTCs are promising biomarkers in mCRPC, and telomerase activity (TA) is a recognized cancer marker. In this Phase 3 trial we analyzed CTCs using 2 methods: CellSearch for fixed cell enumeration, and a novel Parylene-C slot filter for live CTC capture and TA measurement.

Methods Used: Blood samples (7.5 ml) were drawn at baseline (d1) & pre-cycle 2 (d2) of Rx for CellSearch CTC enumeration and for filter live CTC capture and TA measurement by qPCR-based telomeric repeat amplification. The association between OS and TA overall and within subgroups was assessed.

Summary of Results: Samples were obtained from 263 men. Median d1 CTC count was 5, and there was a significant difference in OS for d1 CTC < vs. ≥5, hazard ratio (HR) 2.92 (p <0.001) after adjustment for other factors. D1 CTC and OS had ROC AUC of 0.781. Rise in CTC count from d1 to d2 was associated with longer OS, HR 0.45 (p=0.012); adjusting for risk factors. For TA, men with baseline CTC ≥5 (41% of cohort) who had high CTC TA had HR 1.14 (p<0.005) for OS after adjustment for other factors including CTC counts.

Conclusions: Day 1 CTC counts and d1 to d2 CTC dynamics were prognostic of OS after risk factor adjustment in this first and largest phase 3 docetaxel-based prospective CTC study to date. In men with CTC counts ≥5, TA from cells live-captured on a new slot filter constitutes the first CTC-derived biomarker prognostic of OS in a prospective clinical trial.

447

PLASMIN MEDIATED KALLISTAIN GENE EXPRESSION BY ELECTROPORATION IN VIVO FOR TREATMENT OF NCI-H446 SUBCUTANEOUS XENOGRAFT TUMOR

Jia D, Huang X, Zhang C, Feng J, Zou J, Diao Y, Huaqiao University, Quanzhou, China

Purpose of Study: To investigate the inhibitory effect of electroporation mediated plasmid DNA encoding kallistatin (KAL) on NCI-H446 xenograft tumor growth.
Methods Used: Xenograft tumor was induced by subcutaneous injection of 5 × 106 NCI-H446 cells into the right flank of BALB/c nude mice. Seven days later, naked plasmid pEGFP or pKAL was injected by intramuscular electrottransfer into the tibialis anterior of nude mice (n = 6 for each group). We electrotransferred with 60 V, 10 ms pulse width, 12 pulse times, the longitudinal electric field direction, plasmid concentration of 1.0 mg/ml/100 g dose volume which were the best electroporation conditions our group explored. Tumor growth was measured by calipers in two dimensions. Tumor volume was calculated according to the formula \( V = 0.52 \times a \times b^2 \), where a and b are the largest and smallest diameters, respectively. Tumor angiogenesis was determined with tumor microvessel density (MVD) by CD34 immunohistochemistry. Tumor cell migration and proliferation was assessed by E-cadherin and Ki-67 staining. Tumor cell apoptosis was assessed by TUNEL method.

Summary of Results: Intramuscular injection of pKAL inhibited tumor growth in the treatment group by 85% (71 ± 33 mm³) at d 42 compared to d 42 compared to the pEGFP control group (486 ± 187 mm³). Microvessel density was significantly inhibited in tumor tissues treated with pKAL. The cellular proliferation (Ki-67 positive cells) also decreased in tumors compared with the pEGFP control group.

Conclusions: Plasmid plasmid KAL gene expression by intramuscular electrottransfer can inhibit the growth of subcutaneous xenograft tumor by reducing angiogenesis and proliferation of tumor cells. This strategy may provide a promising anti-angiogenesis-based approach to the treatment of metastatic lung cancer.

Acknowledgments: This study was supported by the National Science Foundation of China (No. 30873591, 81271691, 81371669); Program for International S&T Cooperation Projects of China (No. 2011DFG33320).

**ANALYSIS OF OUTCOMES FOR SURGICAL RESECTION AND RADIOTHERAPY IN PATIENTS WITH INTRACRANIAL PAPILLARY MENINGIOMA**

Chung L,1 Thill K,1 Ung N,1 Gopen Q,2 Yang I,1 1University of California Los Angeles, Los Angeles, CA and 2University of California Los Angeles, Los Angeles, CA.

Purpose of Study: Meningioma is one of the most common central nervous system tumors. While most are benign, papillary meningioma (PM) is an aggressive subtype characterized by higher rates of recurrence and extracranial metastasis. Due to the rarity of this malignant disease, studies examining the relationship between specific treatments and clinical outcomes are limited. Gross total resection (GTR) is considered the standard treatment; however, when GTR is not feasible, subtotal resection (STR) followed by radiotherapy (RT) has been an alternative. This study investigated the clinical outcomes and recurrence rates of PM patients who underwent GTR, STR alone, or STR followed by RT.

Methods Used: A comprehensive review of the literature was conducted to identify patients diagnosed with PM. Clinical data were aggregated for each patient and the outcome of each patient was measured by recurrence, as reported in the literature. Patient data lacking extent of resection, follow-up, or recurrence information were excluded. Patients were grouped into those who received GTR, STR alone, or STR followed by RT for statistical analysis.

Summary of Results: Patients who underwent GTR alone had a mean age of 35.1 years and mean follow-up of 51.1 months. Of these GTR patients, 58.3% experienced recurrence. Patients who received STR followed by RT had a mean age of 21.8 years and a mean follow-up of 42.3 months. Among these, a higher recurrence rate of 75% was observed. Patients who received STR alone had a mean age of 41.3 years and mean follow-up of 19 months, with 100% experiencing recurrence.

Conclusions: PM is a rare, but aggressive subtype of meningioma. However, data is limited due to the scarcity of available cases. Our research suggests that patients receiving GTR clearly exhibited a lower recurrence rate compared to patients who received either STR or STR with RT. Therefore, these results support GTR as the treatment of choice. Furthermore, our data show that when GTR was not feasible, STR with RT as an adjuvant treatment was associated with lower rates of recurrence compared to STR alone. Future studies with larger sample sizes are needed to further elucidate the optimal treatment for this rare disease.

**INVESTIGATING THE REGULATION OF miR-21 IN PANCREATIC CANCER TUMOR-ASSOCIATED FIBROBLASTS**

Bikhchandani M, Toste P, Donahue T. UCLA David Geffen School of Medicine, Los Angeles, CA.

Purpose of Study: The dense tumor-associated stroma (TAS) is a defining feature of pancreatic ductal adenocarcinoma (PDAC). Activated tumor-associated fibroblasts (TAFs) are the major components of the TAS and contribute to disease progression and treatment resistance. Increased MiR-21 expression in PDAC TAFs correlates with worse survival, higher rates of lymph node metastasis, and increased invasion by tumor cells. Signal transducer and activator of transcription 3 (STAT3) and AP1 transcription factors are the best characterized regulators of miR-21 expression. We explored the regulation of miR-21 in PDAC TAFs by inhibiting STAT3 signaling and the MAP kinase pathway, which is the major regulator of AP1 transcription factors.

Methods Used: Human PDAC TAF cell lines were cultured either in the presence of a MEK inhibitor (U0126 or PD0325901), a STAT3 inhibitor (Stattic), or DMSO control. MiR-21 levels were assessed by qRT-PCR. Expression of total STAT3, phospho-STAT3, total ERK, and phospho-ERK was assessed by Western blotting.

Summary of Results: MiR-21 expression was unchanged after Stattic treatment for 24, 48 and 72 h. Western blotting confirmed successful STAT3 inhibition as evidenced by a significant decrease in phospho-STAT3. MiR-21 expression also did not change with inhibition of the MAP kinase signaling pathway at 24 and 48 hours even though Western blotting demonstrated decreased phospho-ERK, confirming effective MEK inhibition. Interestingly, α-smooth muscle actin expression (α-SMA), a marker of TAF activation, was decreased significantly with STAT3 inhibition at 24 and 48 hours while levels of phospho-ERK were increased.

Conclusions: Our results indicate that neither STAT3 nor the MAP kinase/AP1 pathway individually regulates miR-21 expression in PDAC TAFs. We did demonstrate that STAT3 signaling may be important for TAF activation as evidenced by decreased α-SMA following Stattic treatment. The increase in phospho-ERK observed after STAT3 inhibition may reflect a synergistic mechanism between the MAP kinase pathway and STAT3 signaling to regulate miR-21 expression levels. We plan to explore this potential relationship by evaluating miR-21 expression after simultaneous STAT3 and MAPK inhibition.

**INHIBITING MONOPOLAR SPINDLE 1 KINASE SUPPRESSES COLONY FORMATION IN MEDULLOBLASTOMA CELLS**

Ng JH,1 Harris P2, Venkataraman S2, Balakrishnan F, Vibhakar R.2 1University of Colorado School of Medicine, Aurora, CO and 2Children’s Hospital Colorado, University of Colorado Denver, Aurora, CO.

Purpose of Study: Medulloblastoma is the most common malignant pediatric brain tumor with less than optimal outcomes. Current therapies include cytotoxic drugs and radiation that target rapidly growing cells. These therapies are associated with significant long-term morbidity including neurocognitive defects and secondary tumors. Therefore, there is a critical need for medulloblastoma therapies that selectively target tumor cell populations.

The Vibhakar laboratory has recently identified several kinases involved in the G2/M cell cycle checkpoint to influence medulloblastoma cell viability. Among these is the Mps1 kinase. Mps1 is involved in chromosomal segregation during mitosis and overexpression of Mps1 is associated with aneuploidy. Studies have shown that inhibiting Mps1 induces abnormal chromosome segregation and apoptosis in breast cancer and osteosarcoma. Despite the abnormal overexpression of Mps1 in some medulloblastomas, the effect of Mps1 inhibition on medulloblastoma tumor cell growth has yet to be evaluated.

Methods Used: Expression of Mps1 mRNA and protein in medulloblastoma tumor lines was evaluated using qRT-PCR and Western blot. To investigate the therapeutic efficacy of inhibiting Mps1, we used a clinically relevant inhibitor of Mps1 (NMS-P715). We performed cell proliferation and colony formation assays using well-characterized medulloblastoma cell lines.

Summary of Results: Expression of Mps1 mRNA was up to 150 times more elevated in all medulloblastoma tumor lines as compared to normal...
cerebellum. Inhibition of Mps1 significantly decreased the colony-forming ability of medulloblastoma cells.

Conclusions: These analyses suggest that targeting Mps1 via small molecule inhibitors may be a valuable approach in medulloblastoma therapy.

Immunology and Hematology

Concurrent Session

11:00 AM

Saturday, January 25, 2014

451

SNAPC1 MEDIATES SUSCEPTIBILITY TO MYCOBACTERIAL INFECTION IN ZEBRAFISH

Levite S1,2, Berg R1,2, Cameron J1, Ray J1, Tobin D2, Moons C3, Ramakrishnan L1,2.

1University of Washington, Seattle, WA and 2University of Washington, Seattle, WA.

Purpose of Study: Mycobacterium tuberculosis (Mtb) infection in humans manifests in a phenotypic range, from resistance to progressive and severe disease. A model studying underlying mechanisms was developed using zebrafish and Mycobacterium marinum (Mm), a genetic relative of Mtb. Our lab previously carried out a forward genetic screen to identify mutants with differential susceptibility to Mm. Molecular mapping of a hypersusceptible mutant identified a mutation in a subunit of the SNAP complex (SNAPc). SNAPc regulates expression of small regulatory RNAs and RNA Polymerase II-mediated transcription. We investigated the mechanism by which this subunit of SNAPc regulates susceptibility to mycobacterial infection.

Methods Used: This study used a variety of cell and molecular methods including morpholino oligonucleotides (MOs) to disrupt gene function, RT-PCR to assess transcript abundance, HRM-PCR for genotyping mutants, visualization with dyes (Neutral Red, Acridine Orange, Sytox), fluorescence and confocal microscopy. Several transgenic zebrafish lines were used in the characterization of hematopoietic compartments.

Summary of Results: Zebrafish larvae lacking SNAPc function display hypersusceptibility to Mm, evidenced by overall bacterial load and distinct extracellular bacterial growth (P<0.01). Investigations using transgenic zebrafish revealed an increase in the number of blast-like macrophages in snapc mutants (P<0.01), while the abundance of cells derived from other hematopoietic lineages is relatively unaffected. Macrophages are classically understood to be the main cell type involved in the pathogenesis of mycobacterial infection. Acridine Orange staining revealed decreased apoptosis in snapc mutants (P<0.01). Recent studies investigating the action of SNAPc revealed a role in the cellular response to retinoic acid, which promotes the differentiation of macrophages and also promotes apoptosis. We are currently testing this model in our system.

Conclusions: To date no study has identified a role for the central transcriptional complex SNAPc in immunity. The retinoic acid mechanism we implicated presents a novel way to investigate the role of cell death and differentiation in mediating the cellular response to mycobacteria.

452

PYROSEQUENCING AS AN ESSENTIAL TOOL TO DETECT POLYMORPHISMS IN FCRIIIa RECEPTOR (CD16) FOR PATIENTS UNDERGOING IMMUNOTHERAPY

Shirley B1, Gale J2, Khalili P3, Wilson B1, Vassel M3, Winter S1, Matlawaska-Wasowska K2,4,1 University of New Mexico, Albuquerque, NM, 2University of New Mexico, Albuquerque, NM and 4University of New Mexico, Albuquerque, NM.

Purpose of Study: Surface specific antigens expressed on the cell membrane of hematopoietic cells are an attractive target for antibody mediated immunotherapy in hematologic malignances or autoimmune diseases. Monoclonal antibodies (mAb) involve various mechanisms to eliminate abnormal cells, including antibody dependent cell mediated cytotoxicity (ADCC) and phagocytosis (ADCP) mediat ed by immune effector cells such as NK cells and macrophages bearing FcγRIIA (CD16) receptor. Previous studies reported that clinical efficacy of mAbs can be linked to the single nucleotide polymorphism found at position 559 in cDNA of the gene encoding CD16. This allelic polymorphism generates the following allotypes: VN/VN or FF at amino acid position 158 and can affect binding of mAbs and immune cell effector function. CD16-mediated binding is most efficient with the VN genotype, and least efficient with the FF genotype, leading to a range of efficacy in mAb-mediated targeted therapies. Currently, many patients are not screened for CD16 heterozygosity. Nevertheless there is a clear need for a diagnostic assay that will allow estimating polymorphisms in patients undergoing therapy with mAb utilizing ADCC/ADCP. Here we hypothesized that the pyrosequencing might improve screening for polymorphisms of human CD16 receptor.

Methods Used: We studied 42 normal human subjects for the incidence of V/V, F/V and F/F CD16 polymorphisms using pyrosequencing technologies and compared them to qPCR and nested PCR-based allele-specific restriction assay.

Summary of Results: Compared to pyrosequencing, nested PCR-based allele-specific restriction assay and qPCR were relatively insensitive, not specific and were generating inconsistent results.

Conclusions: Since the efficacy of the mAb-based targeted immunotherapy may be highly dependent upon the CD16 polymorphism in a given individual, we propose that pyrosequencing of the CD16 receptor be routinely evaluated in all patients. Such practices might prevent patients from randomizing to receive targeted therapies to those hematological malignancies or autoimmune diseases that have little or no therapeutic potential.

453

MECHANISM OF REGULATION OF INFLAMMATORY ARTHRITIS BY TRANSCRIPTION FACTOR AhR

Kaur GP1, Sarkar S2, 1 U Az College of Medicine, Tucson, AZ and 2 U AZ College of Medicine, Tucson, AZ.

Purpose of Study: AhR is a transcription factor expressed in all vertebrate cells, playing a critical role in the regulation of cellular enzymatic reactions. Studies have shown that AhR plays a critical role in the regulation of key players of autoimmune inflammation, including the cytokine TNFalpha. This cytokine plays an indispensable role in collagen induced arthritis (CIA) and rheumatoid arthritis. The expression of AhR is upregulated during arthritis and AhR knock-out mice develop reduced incidence of arthritis, suggesting that AhR plays a pathogenic role in CIA, although the mechanism is unknown. The aim of this study is to elucidate the effect of AhR activation on the TNFalpha production on immune cells from mice with arthritis in comparison to naïve mice.

Methods Used: 8-10 week old male DBA/1 mice were immunized with collagen and CFA for the induction of CIA. Mice were clinically scored for arthritis (scale of 1-4, with 4 being the most severe arthritis). Mice with scores of 4 were euthanized and spleens harvested. Single cell suspensions of splenocytes were cultured with AhR agonist (FICZ). Supernatants were collected for analysis of TNF-alpha. naïve mice remained unimmunized; splenocytes were similarly cultured for analysis by ELISA. The levels of cytokines induced/suppressed by AhR agonist/antagonist in arthritic mice were compared to naïve mice. P values <0.05 were considered to be statistically significant.

Summary of Results: In naïve mice, TNFalpha with an agonist was upregulated at lower concentrations. In arthritic mice, TNFalpha with agonist was upregulated at higher concentrations. The trends were apparent, however, the results (naïve: P=0.1, arthritic P=0.2) were not significant.

Conclusions: Based on the results form the naïve and arthritic mice, TNFalpha may be induced at a lower concentration, as there is no inflammatory state. In arthritic mice, it may be induced at a higher concentration, as inflammation is already present. This needs to be further explored in order to elucidate a clearer pattern of induction.
GENERATION OF A HUMAN T-CELL RECEPTOR CELL LINE TO EVALUATE INFLUENZA PEPTIDE PRESENTATION

Machkovech H1, Bloom J2, 1University of Washington, Seattle, WA and 2Fred Hutchinson Cancer Research Center, Seattle, WA.

Purpose of Study: Cytotoxic T Lymphocytes (CTLs) recognize internal proteins of influenza and kill infected cells. Virally infected cells present viral epitope via major histocompatibility complex (MHC) class I, which is recognized by the T-cell receptor (TCR). It has previously been shown that influenza has evolved CTL-escape mutations to the influenza nucleoprotein (NP) epitope comprised of amino acids 383-391. The aim of this project is to clone a human TCR specific to NP epitope 383-391 and an IL-2 reporter into a Jurkat cell line. This T-cell line will allow us to determine the amount of epitope presented by cells infected with mutant viruses by measuring IL-2 reporter activation. This assay will be a valuable tool to interrogate influenza evolution.

Methods Used: The lentiviral backbone plasmid pHAGE2-eF1a-ZsGreen-TCR was constructed as follows: RNA was isolated and reverse transcribed from a human T-cell clone containing a TCR specific to epitope NP 383-391. The TCR α and β chains were PCR-amplified and ligated into the pHAGE2 backbone with ZsGreen using In-Fusion cloning (Clonetech). Lentivirus containing pHAGE2-eF1a-ZsGreen-TCR was produced by HEK293T cells and used to transduce CD8+ Jurkat cells lacking an endogenous TCR. At 72 hours post-transduction, flow cytometry for CD8 and ZsGreen was performed. The pHAGE2-IL2-mCherry lentiviral backbone plasmid contains the IL-2 promoter sequence followed by mCherry. This plasmid will allow us to assay the degree of T-cell activation by measuring mCherry fluorescence. It is being constructed in the manner described above.

Summary of Results: Flow cytometry of Jurkat cells for ZsGreen and CD8 surface expression, which is only expressed on the surface with a properly folded TCR, confirmed TCR expression and protein folding. Transduced cells were 82.5% double positive whereas mock transduced cells were 0.07% double positive.

Conclusions: These results indicate that a high level of TCR is being expressed on the cell surface of Jurkat cells. Future work will be aimed at construction and integration of the IL-2 reporter into the Jurkat cell line. The Jurkat cell line will be used to assay influenza antigen presented by infected cells, ultimately allowing us to study the effect of viral mutations on MHC presentation.

IMPROVING STABILITY OF THE LIPASE IMMOBILIZED IN AMINO-FUNCTIONALIZED MESOPOROUS SBA-15 WITH CROSS-LINKING METHOD

Zhao C1, Li Y2, Jiang L1, Gao B1,2, 1Jilin University, Zhaohai, China and 2Jilin University, Changchun, China.

Purpose of Study: In order to promote the stability of the immobilized enzyme better and expand the immobilized enzyme applications in pharmaceutical industry, we use cross-linking methods to introduce the cross-linking sites between enzymes and mesoporous materials with glutaraldehyde as coupling agent. We also study the stability of covalent immobilized lipase with glutaraldehyde as coupling agent. We also study the stability of covalent immobilized lipase with glutaraldehyde as coupling agent.

Methods Used: We use ethanol as a pore-expanding agent in this experiment, and synthesize the SBA-15 to immobilize the lipase with amino-modified. NH2-SBA-15 was suspended in 5.0 ml of glutaraldehyde solution for 2 h under stirring. Lipase solution in 50 mM PBS buffer (pH = 7.0) was added into solid. Hydrolysis of olive oil was used to assay the activity of the immobilized lipase and the free lipase. The lipase-solid samples prepared above were suspended by stirring in 5 ml of PBS buffer solution (pH = 7.0) for 1 h. The solution left over the solid was again tested using the Bradford assay to indicate the amount of lipase that had leaked from the solids.

Summary of Results: The immobilized lipase exhibits higher stability than the free lipase. The immobilized lipase preserves about 80% of its original activity, while the free lipase is practically inactivated for 5h of incubation at 50degree centigrade.

The results show the leaking behavior of lipase in SBA-15 and -NH2 group SBA-15. Over 30% of lipase supported in SBA-15 is found to leak out after being washed 5 times. However, NH2-SBA-15 has a wide range of retention of lipase. The samples, NH2-SBA-15, stand out in the leaking test, with only 1% of leaking being recorded in each case.

Conclusions: The functionalization of the internal surface of SBA-15 permits lipase immobilization by using glutaraldehyde as coupling agent. Not only was the activity of immobilized lipase maintained but also the stability was considerably enhanced compared with that of free lipase. Retention up to 99% of the lipase is observed in most favorable cases. Using covalent cross-linking method to immobilize lipase has certain prospect in industrial production.

OPTIMIZATION OF ULTRASOUND-ASSISTED EXTRACTION CONDITIONS OF POLYSACCHARIDES FROM TRICHOLOMA MATSUTAKE MYCELIUM USING RESPONSE SURFACE METHODOLOGY AND PRELIMINARY STUDY ON ITS ANTIOXIDATIVE EFFECT

Wang Y1,2, Li Q1, Xie J1, Tong L1,2, 1Jilin University, Changchun, China and 2Zhejiang College of Jilin University, Zhaohai, China.

Purpose of Study: Tricholoma matsutake is a high economic value fungi. As reported previously, its polysaccharides possess various pharmacological activities. Our present research aims to using response surface analysis methodology (RSM) to optimize ultrasound-assisted extraction conditions of polysaccharides in Tricholoma matsutake mycelium. Additionally, preliminary study on its antioxidative effect will be performed.

Methods Used: Firstly, single-factor experiment was performed to investigate the influence of water-solid ratio, extraction time and ultrasonic power on the water extraction of polysaccharide. Based on the results, the experiments were arranged according to Box-Behnken central composite experiment design. RSM was applied to analyze the effect of casual factors on the yield of T. matsutake polysaccharides. Furthermore, by using pyrogallol autoxidation and Fenton system, the antioxidative effects of polysaccharides in Tricholoma matsutake mycelium on oxygen and hydroxyl radical were studied.

Summary of Results: The results showed that the optimum ultrasound-assisted extraction condition for T. matsutake polysaccharides was as follows: extraction time 223 s, ultrasonic power 427W and ratio of water to solid 69.7:1 (mL:g). The predicted best extraction yield raw was polysaccharides 14.52%, comparatively, its actual extraction yield was 14.33% , with relative error 1.29%. Moreover, data revealed that Tmatsutake polysaccharides possess 19.32% and 88.24% inhibitory effects on oxygen and hydroxyl radical respectively.

Conclusions: Our present findings suggest that RSM was an accurate and reliable method applied to optimize the ultrasound-assisted extraction of polysaccharides in Tricholoma matsutake mycelium. T. matsutake polysaccharides significantly suppressed oxygen and hydroxyl radical.
Conclusions: Comparing the 2011-12 and 2012-13 seasons, although the use of hypertonic nebulized saline increased and the use of steroids and albuterol decreased in infants hospitalized with RSV, the length of hospitalization or oxygen requirement was not affected significantly. Large studies are needed to compare the effect of different nebulized solutions in treatment of infants hospitalized with RSV.

TABLE 1. Comparison of Patient Characteristics and Treatments for RSV: 2011-12 vs. 2012-13 Seasons

<table>
<thead>
<tr>
<th>Season/ Characteristics</th>
<th>2011-2012</th>
<th>2012-2013</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (%)</td>
<td>5.4</td>
<td>6.0</td>
<td>0.56</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>4</td>
<td>4</td>
<td>0.89</td>
</tr>
<tr>
<td>Oxygen Requirement (%)</td>
<td>10.0</td>
<td>10.0</td>
<td>0.96</td>
</tr>
</tbody>
</table>

Conclusions: We describe characteristics of neonates who were admitted with invasive HSV infection over a thirteen year period. It is important for the clinicians to be vigilant in recognizing the various characteristic features of invasive HSV infection so therapy is instituted as soon as possible.

TABLE 1. Characteristics of Invasive HSV Infection in Neonates, 1999 to 2012

<table>
<thead>
<tr>
<th>Patient</th>
<th>Admitted Due to</th>
<th>Fever</th>
<th>Seizures</th>
<th>Weight</th>
<th>Admission</th>
<th>NICU</th>
<th>CSF</th>
<th>HSV-PCR</th>
<th>Viral Culture</th>
<th>HPAV</th>
<th>HSV Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>NA</td>
<td>Neg</td>
<td>Positive IgM</td>
<td>IgG</td>
<td>Positive IgM and IgG</td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>HSV-2 Positive</td>
<td>ND</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>14</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>HSV-2 Positive</td>
<td>ND</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>HSV-2 Positive</td>
<td>Neg</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>19</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>HSV-2 Positive</td>
<td>Neg</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>20</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Bldg</td>
<td>HSV-2 Positive</td>
<td>Neg</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>35</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>HSV-2 Positive</td>
<td>ND</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>35</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>HSV-2 Positive</td>
<td>ND</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
</tr>
</tbody>
</table>

ND= Not Done, Abnl=Abnormal, Nl=Normal, Pos=Positive, Neg=Negative

SEXUAL RISK BEHAVIORS AND SUBSTANCE USE AMONG GAY AND NOT GAY-IDENTIFIED YMSM WHO USE GRINDR

Conclusions: GI and NGI YMSM on GRINDR in Los Angeles appear to have important differences in HIV risk behaviors. As public health interventions target gay-focused online social networks, it is important to recognize that populations using the media are not homogeneous. In particular, NGI MSM populations continue to represent an important bridge population between male and female sex partners for HIV transmission.

TABLE 1. Characteristics of Invasive HSV Infection in Neonates, 1999 to 2012

<table>
<thead>
<tr>
<th>Number of Infections</th>
<th>HSV Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Positive IgM and IgG</td>
</tr>
<tr>
<td>2</td>
<td>Positive IgM and IgG</td>
</tr>
<tr>
<td>3</td>
<td>Positive IgM and IgG</td>
</tr>
<tr>
<td>4</td>
<td>Positive IgM and IgG</td>
</tr>
<tr>
<td>5</td>
<td>Positive IgM and IgG</td>
</tr>
<tr>
<td>6</td>
<td>Positive IgM and IgG</td>
</tr>
<tr>
<td>7</td>
<td>Positive IgM and IgG</td>
</tr>
<tr>
<td>8</td>
<td>Positive IgM and IgG</td>
</tr>
</tbody>
</table>
and immunological studies suggest that infection with the Lyme disease spirochete Borrelia burgdorferi could be transferred from person to person via intimate human contact without a tick vector (Harvey and Salvato, Med Hypotheses 2003;60:742; Stricker et al, J Investig Med 2004;52:S151). Detecting viable spirochetes in vaginal and seminal secretions would provide additional evidence to support this hypothesis.

Methods Used: Three North American patients with a history of Lyme disease, one male and two female, were selected for the study after informed consent was obtained. Serological testing for B. burgdorferi was performed on all three subjects. Blood and semen or vaginal secretions were used to inoculate BSK-H medium for Borrelia culture. Motile spirochetes were detected in culture supernatant. Light and dark field microscopy, and immunohistochemical staining for further characterization. Polymerase chain reaction (PCR) testing was performed by two independent laboratories for specific identification of the cultured isolates. Positive and negative controls for immunohistochemical staining and PCR were performed in all experiments.

Summary of Results: Serum antibodies to B. burgdorferi were detected in all three patients. Motile spirochetes were observed in culture fluid inoculated with blood and genital secretions from the three subjects. Morphological features of spirochetes were confirmed by Dieterle staining, SEM and immunohistochemical staining of culture concentrates. PCR testing confirmed that the spirochetes isolated from blood and genital secretions were strains of B. burgdorferi, and PCR subtyping indicated that the strains were B. burgdorferi sensu stricto.

Conclusions: The culture of viable B. burgdorferi in genital secretions suggests that Lyme disease could be transmitted by intimate contact from person to person.

461
COTTON FEVER: A SELF-LIMITING SYNDROME IN IVDA
Ramirez MD, Marsh B. UCSD Medical Center; Hillcrest, CA.

Case Report: Cotton fever, a post-injection complication familiar to many IV drug users, has been poorly described in medical literature. It is a self-limited, sepsis-like syndrome that affects users after they inject heroin reclaimed from previously used cotton filters. The exact cause remains unclear, but it has been postulated that reuse of cotton filters leads to fiber breakdown and subsequent injection of fiber particles. A 19-year-old female, presented with subjective fevers, chills, abdominal pain, vomiting, and weakness of 2 days duration. Her symptoms began abruptly after her last IV heroin injection during which she had reused 10-day-old cotton filters. Upon presentation, the patient was febrile to 100°F, diaphoretic, and tachycardiac. She had a blood pressure of 101/69, respiratory rate of 18, and oxygen saturation of 98%. Her physical exam was significant for severe abdominal tenderness. Labs revealed a WBC count of 34k with 69% neutrophils and 29% bands. Her liver function tests were elevated with alkaline phosphatase 192, ALT 115, AST 107, and total bilirubin 1.7. EKG revealed sinus tachycardiac with no abnormal signs, and a transcutaneous echocardiogram was negative for any valvular abnormalities or vegetations. CT scan of the abdomen showed slight enlargement of the liver with periportal edema with a small amount of ascites. Two sets of blood cultures were obtained and the patient was empirically started on IV Vancomycin and Zosyn for suspected sepsis. She was fluid resuscitated with 4L normal saline and admitted to the medicine ward. Within 8 hours of admission, the patient’s heart rate and temperature normalized, her strength returned, and her abdominal pain resolved. This case demonstrates the importance of obtaining a thorough history regarding the drug habits and practices of patients with a history of IV drug use. One diagnostic difficulty lies in differentiating the relatively benign course of cotton fever from more critical infectious diseases, such as sepsis, endocarditis, or abscesses. A detailed understanding of common techniques used by recreational IV drug users can help prepare physicians to make this distinction. Admission to short-term observational units rather than medicine units may improve patient outcomes, provide better patient-centered care, decrease hospital costs, and limit unnecessary, invasive diagnostic studies.

462
SHINGLES VACCINE AWARENESS: EDUCATING SENIOR CITIZENS AND CAREGIVERS IN POWELL, WYOMING
Michelle Ju UW SOM, Seattle, WA
Ju M. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Almost 1 out of 3 people in America will develop shingles during their lifetime. Adults 60+ years of age are more likely to get shingles, experience severe pain from the disease, and also have postherpetic neuralgia. Powell is a town with 16.6% of its population over 65 years of age (vs. 12.4% in Wyoming), which indicates that its population may be more affected by shingles. The goals of this project were:

1. To provide information on the early signs and symptoms of shingles, contagiousness, and treatment recommendations;
2. To inform seniors about the shingles vaccine; and
3. To encourage vaccination by providing accurate information regarding costs and benefits.

Methods Used: Interviews were conducted with clinicians, public health officials, and senior services directors to identify shingles and shingles vaccination as health issues in the community. A literature review was conducted to provide evidence-based facts on shingles vaccination guidelines, vaccine effectiveness and risks, and cost-effectiveness of the shingles vaccine. Senior facilities staff was consulted to determine the best methods for educating their senior populations. Educational sessions were scheduled with all four of the facilities in Powell providing services targeted specifically to seniors. A pamphlet was developed outlining the signs/symptoms of shingles and the “who, what, when, where, and how” of shingles vaccination.

Summary of Results: These educational sessions addressed shingles and the shingles vaccine with a total of 60 seniors and 10 caregivers. A formal talk was given at each of these sessions, followed by informal question-answer time and discussion. Information was well-received and cleared up misconceptions surrounding shingles recurrence, contagiousness, and vaccine recommendations. A pamphlet was provided to each attendee. This pamphlet was also added to the health resource room of 3 facilities and adopted by the Park County Public Health office for use in shingles vaccine education.

Conclusions: Shingles is a disease that significantly affects the senior population, and vaccination has been proven to be effective in reducing disease burden and improving quality of life. Providing accurate information to seniors and their caregivers empowers this group to make informed decisions regarding their health and wellbeing.

Neonatology - General IV
Concurrent Session
11:00 AM
Saturday, January 25, 2014

463
SPLENCHIC TISSUE OXYGENATION IN PRETERM INFANTS WITH SIGNIFICANT ANEMIA: OBSERVATIONS UNDER NEAR INFRARED SPECTROSCOPY
Braski K, Yost CC, Baserga M. University of Utah, Salt Lake City, UT.

Purpose of Study: Necrotizing Enterocolitis (NEC) in very low birth weight (VLBW) infants can result in significant morbidity and/or mortality. Among risks factors, an association between elective red blood cell transfusions and the development of NEC has been proposed. However, lower hematocrit (Hct) levels have also been associated with increased risk of NEC. Near Infrared Spectroscopy (NIRS) is a non-invasive technique used to assess cerebral and splanchic tissue oxygenation. Previous studies using NIRS have shown increased splanchic oxygenation during enteral feeds in VLBW infants without anemia. In the present study we hypothesized that significant anemia in VLBW will be associated with lack of increased splanchic oxygenation during enteral feedings, a time of higher metabolic demands.

Methods Used: VLBW infants were included who were prescribed enteral feedings. Splanchic tissue oxygenation was measured with 3D-NIRS, which combines 3 wavelengths (680, 770, 850 nm) and measures the concentration of reduced (Hb) and oxidized (HbO2) hemoglobin. Data was collected at baseline, before enteral feeding, and during enteral feeding. The following parameters were collected: baseline oxygen saturation (SvO2), arterial oxygen saturation (SaO2), and venous oxygen saturation (SvO2v). Results were compared to expected values of 65-75% for SvO2, 95-100% for SaO2, and 40-50% for SvO2v.

Summary of Results:

Baseline Premeal Postmeal p-value
CSO2 mean ± s.d. 0.754±0.11 0.726±0.08 0.1
Splanchnic TOI, mean ± s.d. 48.29±7.37 47.01±5.71 0.25
Brain TOI, mean ± s.d. 64.25±5.85 64.75±3.50 0.4
SURVIVAL AND OUTCOMES OF 23 WEEKS GESTATION INFANTS OVER TIME

Wang K1,2, Barton L1,2. "Keck School of Medicine of USC, Los Angeles, CA and 2LAC+USC Medical Center, Los Angeles, CA.

Purpose of Study: Decisions to resuscitate extremely premature infants are controversial. The 23-week gestational age (GA) is regarded as the “gray area” for routine resuscitation by most neonatologists in the US, as decisions are made based on expected outcomes and parents’ wishes. This retrospective study of 23-week GA neonates over the last two decades found improved survival and pre- and postnatal factors associated with this improved survival.

Methods Used: All 23-week GA inborn neonates at LAC+USC Medical Center from January 1, 1994 through June 30, 2013 were examined by retrospective chart review. Survival rates were analyzed by GA and various maternal and infant characteristics. Significant short-term outcomes of survivors were also assessed for improvements before and after 2010. We used t-test, chi-square, and Fisher’s exact tests for analysis with p < 0.05 considered significant.

Summary of Results: Ninety-nine patients fulfilled the inclusion criteria, 34 for data analysis. Ninety-nine percent were GA ≤ 32 weeks) infants using advanced neuroimaging techniques. We have encountered multiple challenges in neuroimaging which require action to avoid adverse effects on study feasibility and are presented here.

Methods Used: This is a prospective, longitudinal study of very preterm children at 4, 9, and 18-22 months. Subjects are imaged during natural sleep. No sedation is used. Anticipated scan time is 50 minutes once the child is asleep and total visit time 2 hours to allow time to get to sleep.

Summary of Results: 36 infants have qualified for inclusion. Of these, 13 families have expressed interest. To date, 6 families have been scheduled and 4 have been seen for their 4 month study visit. The feasibility of scheduling nighttime scans has caused some limitation in scheduling further infants as attendants and MRI technicians must come in after hours to perform these specialized scans. One family no-showed; one family cancelled. Both lived out of town. Of the 4 scans performed to date, 2 have been successful on the first attempt. One of these took >3 hours due to multiple infant awakenings during the scanning procedure. The other 2 scans were unsuccessful due to 1) infant awakenings; 2) attempting the during the infant’s regular daytime naptime without infant sleep. Of the two scans repeated a second time, both were unsuccessful due to infant awakenings and were successful on the third attempt.

Conclusions: Multiple interventions may be necessary including 1) obtaining detailed information regarding the infant’s schedule, and supporting families to replicate that at the study visit. Supplying things like infant bath facilities and supplies, mattresses with bedding and food for parents may aid this; 2) evening scans should be performed preferentially; 3) increasing travel allotments; 4) hiring a dedicated MRI operator; 5) further investigation into the processes used prior to and during successful scans may inform other necessary interventions. Such interventions may ensure appropriate budgeting, timely completion, and family satisfaction.

### TABLE 2. Survival of 23 week GA infants (1994-2013)

<table>
<thead>
<tr>
<th>GA (weeks)</th>
<th>% Survival</th>
<th>% Survival</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 32</td>
<td>23%</td>
<td>23%</td>
<td>0.653</td>
</tr>
<tr>
<td>33-36</td>
<td>23%</td>
<td>23%</td>
<td>0.0002</td>
</tr>
<tr>
<td>Birth weight &lt;500g</td>
<td>23%</td>
<td>23%</td>
<td>0.235</td>
</tr>
<tr>
<td>Birth weight ≥500g</td>
<td>23%</td>
<td>23%</td>
<td>0.297</td>
</tr>
</tbody>
</table>

Conclusions: Over time, 23-week gestation neonates have improved survival in our unit. Antenatal steroids, GA by day, and BW played important parts in survival. We speculate that changes in our resuscitation policy of less invasive ventilation in the delivery room and more aggressive resuscitation may have contributed to the increased survival and decreased morbidity.

### OUTCOMES OF EXTREMELY PRETERM INFANTS AFTER DELIVERY ROOM CARDIOPULMONARY RESUSCITATION

Handley S1, Sun Y1, Wyckoff M2, Lee H3. "University of California, San Francisco, San Francisco, CA; 2University of Texas Southwestern Medical Center, Dallas, TX and 3Stanford University, Palo Alto, CA.

Purpose of Study: To describe the association between delivery room cardiopulmonary resuscitation (DR-CPR), defined as chest compressions and/or epinephrine, and short-term outcomes of extremely preterm infants.

Methods Used: This was a population-based cohort study of the California Perinatal Quality Care Collaborative. Inclusion criteria: gestational age 22 + 0/7 to 27 +6/7 weeks and birth between January 2005 and December 2011. Exclusion criteria: severe congenital anomalies, congenital viral infections, and palliative care defined as lack of ventilator support and death. The primary outcome was death before hospital discharge. Secondary outcomes included sepsis, intraventricular hemorrhage (IVH), and necrotizing enterocolitis. Analysis was stratified by gestational age and compared those who did or did not
receive DR-CPR. Multivariate logistic regression models accounted for gestational age, birth weight, gender, multiple gestation and antenatal steroids.

Summary of Results: There were 14,160 infants; 12,483 did not receive DR-CPR and 820 received DR-CPR. Significant characteristics of infants who received DR-CPR were gestational age (24.9 vs 25.4 weeks), birth weight (768.9g vs 819.5g), antenatal steroids (69% vs 78%) and chorioamnionitis (9% vs 6%). Associations differed by gestational age. In infants 22-23+6/7 weeks DR-CPR was associated with increased surgical intervention for necrotizing enterocolitis (OR 2.53, CI 1.00-6.43), but no difference in mortality or IVH. In infants 24-25+6/7 weeks DR-CPR was associated with grade 3 or 4 IVH (OR 1.37, CI 1.06-1.76), but no difference in mortality. In infants 26-27+6/7 weeks DR-CPR was associated with death in the first 12 hours of life (OR 2.52, CI 1.24-5.14), early onset sepsis (OR 2.44, CI 1.38-4.31), grade 3 or 4 IVH (1.90, CI 1.38-2.64), and death prior to hospital discharge (OR 1.76, CI 1.25-2.47).

Conclusions: Although the population who received DR-CPR was younger, smaller and likely sicker, infants who received DR-CPR did not have better outcomes after DR-CPR. These findings support previous reports of DR-CPR and associations with mortality and impaired neurodevelopment. Differences in outcomes by gestational age may have implications for prenatal counseling in extremely preterm infants.

HISTONE MODIFICATIONS ARE ALTERED IN THE RENAL CORTEX OF VENTILATED PRETERM LAMBS
Blair A, Staub E, Dong L, Dahl MJ, Albertine K. University of Utah, Salt Lake City, UT.

Purpose of Study: Histone covalent modifications impact regulation of gene expression. Changes in these modifications are triggered by abrupt shifts in environment, such as preterm birth and mechanical ventilation (MV). Long-term impairments in the lung and brain in ventilated preterm lambs are related to epigenetic modifications. We hypothesized that ventilation of preterm lambs affects histone modifications in kidneys.

Methods Used: Preterm lambs were delivered at ~130d (~29wk human) gestation, intubated, given surfactant and caffeine. They were ventilated by invasively or non-invasively. HFD was associated with death in the first 12 hours of life (OR 2.52, CI 1.24-5.14), early onset sepsis (OR 2.44, CI 1.38-4.31), grade 3 or 4 IVH (1.90, CI 1.38-2.64), and death prior to hospital discharge (OR 1.76, CI 1.25-2.47).

Conclusions: Although the population who received DR-CPR was younger, smaller and likely sicker, infants who received DR-CPR did not have better outcomes after DR-CPR. These findings support previous reports of DR-CPR and associations with mortality and impaired neurodevelopment. Differences in outcomes by gestational age may have implications for prenatal counseling in extremely preterm infants.
oxidative stress and inflammation. We also observed significantly different cytokine responses in cortex vs. hippocampus. These results demonstrated a novel mechanism by which NAC protects against blood-brain barrier dysfunction under conditions of systemic inflammation, and can provide insight on the relationships between systemic inflammation and Alzheimer’s disease. Thus, we sought to characterize the disruption of the BBB by lipopolysaccharide (LPS)-induced inflammation.

Methods Used: We measured disruption induced at different concentrations of LPS injected, the effect of multiple injections of LPS over a twenty-four hour period, and whether the antioxidant NAC and or the prostaglandin inhibitor indomethacin could block BBB disruption. LPS was administered 3 times (3 mg/kg) over a twenty-four hour period. Animals were assessed four hours after the last injection (28 h after the first injection). A total of 225 mice were used in this study-90 were used to assess the regional disruption of the BBB, 90 for assessing whether the anti-oxidant NAC prevented disruption of the BBB, and 45 for assessing whether the anti-inflammatory agent indomethacin prevented disruption. We assessed disruption by injectorecording radioactively labeled with 14C and determining its penetration of the BBB twenty minutes later.

Summary of Results: 1) Only the highest dose of LPS disrupted the BBB (p<0.05); 2) LPS disrupted the BBB in most but not all regions of the brain (p<0.05); 3) The anti-oxidant NAC did not protect the BBB from LPS-induced disruption but the anti-inflammatory indomethacin had a protective effect (Indomethacin: p<0.0001).

Conclusions: The BBB disruption was protected by prostaglandin inhibition but not by antioxidant administration. Thus, we conclude that indomethacin has protective effects against inflammation-induced disruption of the BBB.

470

DISSECTING THE EFFECT OF NOVEL BASAL GANGLIA-PREFRONTAL CORTICAL PROJECTIONS IN SCHIZOPHRENIC PATHOPHYSIOLOGY

Duggan NM1, Saunders A2, Sabatini BL2. 1University of Washington School of Medicine, Seattle, WA and 2Harvard Medical School, Howard Hughes Medical Institute, Boston, MA.

Purpose of Study: Schizophrenia is a debilitating mental illness, yet underlying pathophysiology remains unclear. One prominent model suggests hyperactivation of dopamine 2 receptors (D2R) drives disease. While major Schizophrenic functional deficits are observed in prefrontal cortical (PFC) architecture and gene expression, the major D2R expressing cells are inhibitory indirect pathway medium spiny projection neurons (iMSNs) of the basal ganglia striatum. Overactive dopamine signaling is predicted to inhibit iMSN activity. Traditional anatomy suggests iMSNs interact with the PFC only indirectly, yet canonical intervening regions between striatum iMSNs and the PFC show only mild deficits in disease. Thus it is unclear how D2R hyperactivation influences cortical dysfunction. Recent work revealed a cryptic neuronal projection connecting iMSNs from the basal ganglia globus pallidus (GP) directly to the PFC. Here we test whether chronic pharmacogenetic hyperactivation of this novel projection system is sufficient to drive canonical changes in GABA synthesis gene expression observed in Schizophrenia.

Methods Used: Adult site-specific IRES-Cre mice (n=8) were intracranially injected with a rAAV carrying double floxed inverted designer receptor (hM3D-mCherry) transgenes into the striatum. A designer ligand (cno, 1mg/kg) was subcutaneously administered twice daily to littermate pups (n=4) to mimic iMSN dysregulation, with saline injections into age-matched controls (n=4). Cortical expression of GABA synthesis genes (GAD1 and GAD2) were analyzed by fluorescence in situ hybridization. Expression levels were quantified by fluorescence microscopy and analyzed using Image J software.

Summary of Results: No significant difference in cortical GAD1 gene expression was observed between the two injection conditions. A slight elevation of GAD2 expression was found in cno-injected mice (p=0.03). Differences were observed in control GADPH expression (p=0.02).

Conclusions: Preliminary data suggests novel direct GP-PFC projections are likely not the primary circuitry involved in Schizophrenic pathophysiology. Further exploration of additional cell types comprising these projections is necessary to determine their potential involvement in disease.

471

INTRANASAL ADMINISTRATION AS A ROUTE FOR DRUG DELIVERY TO THE BRAIN: EVIDENCE FOR A UNIQUE PATHWAY FOR ALBUMIN

Falcone JA1, Salameh TS1,2, Banks WA1,4,5, Puget Sound, Seattle, WA; 1U of Washington School of Med, Seattle, WA; 2U of Washington School of Med, Seattle, WA and 4U of Washington School of Med, Seattle, WA.

Purpose of Study: Intranasal (IN) administration has emerged as a method of drug delivery that circumvents the blood-brain barrier, a major impediment to the pharmacological treatment of neurodegenerative disease. Serum albumin, used as a carrier, increases the half-life of therapeutics, and several drug-albumin binding strategies exist. Here, we investigate the potential of albumin in the context of IN administration. We examine the time course and regional distribution of albumin uptake in the brain, as well as mechanisms whereby this occurs.

Methods Used: I-125 labeled albumin (I-Alb) was administered IN in adult mice. In a time course study, brains were collected 5min-6hr after IN-Alb administration. Brains were dissected into 11 regions which were read in a gamma counter. Saturability of albumin uptake was examined by IN coadministration of labeled and unlabeled albumin and gamma counting four regions after 30min. Lastly, phenylendiamine oxide (PAO), filipin, LY294002, or phorbol 12-myristate 13-acetate (PMA) were given IN 30min before I-Alb, and four regions were gamma counted 30min later.

Summary of Results: All regions show I-Alb uptake at 5min, after which various patterns emerge. In many regions I-Alb is highest at 5min and gradually decreases, while others plateau through 1-2hr. A few show distinct peaks—noteably striatum, midbrain, and hypothalamus. Highest levels are seen in olfactory bulb, striatum, and midbrain. Coadministration of unlabeled albumin decreases I-Alb uptake in the whole brain (p=0.0173), indicating a saturable mechanism. PAO and PMA were able to modify I-Alb uptake: PAO decreased I-Alb in subcortical structures (p = 0.0021) while whole brain (p=0.0139), while PMA increased I-Alb in cortex (p=0.0157).

Conclusions: After IN administration, albumin reaches all parts of the brain with variable regional uptake, unique from that seen for other substances in the literature. The mechanism is both saturable and pharmacologically modifiable. These experiments might therefore indicate an active pathway of brain uptake unique to albumin, and support albumin’s potential in the development of intranasal therapeutics for the treatment of neurodegenerative diseases.

472

APAMIN IMPROVES LEARNING AND MEMORY IN ANGELMAN SYNDROME MICE

Claus C. Coll. of Osteopathic Medicine, Western Univ., Pomona, CA.

Purpose of Study: The maternally deleted Ube3a gene is responsible for the learning and memory deficits associated with Angelman syndrome. This gene is responsible for coding E6-AF, an E3 ligase protein, involved in the ubiquitin-mediated protein degradation pathway. It has been hypothesized that this pathway contributes to the removal of SK2 channels, Ca2+ activated K+ channels that control action potentials, specifically after hyperpolarization. Thus, the accumulation of SK2 channels in the postsynaptic membrane may be responsible for the learning and memory impairments found in Angelman syndrome. We tested this by injecting the drug Apanin, which blocks SK2 channels, in Ube3a deficient mice hoping to see some recovery of learning deficits.

Methods Used: Wild-type and mutant mice were randomly selected to receive the drug Apanin or the Vehicle (saline) injection. After 4 days of habituation, each mouse received shocks paired with a tone. The following day (day 2) the mouse received no shock or tone. On day 3, the tactile, olfactory, and visual cues in the box were removed but the tone played for 3 min preceded by a 3 minute period of silence. Graders assessed the behavior of each mouse every 10 s and observed the mouse as either “freezing” or “non-freezing”. Freezing rates were calculated as a percentage of number of freezes over number of observations.

Summary of Results: Day 2, with the contextual cues showed a higher (p=0.0136) total freezing rate (FR) of mutant mice who received Apanin.
(MT-A) than those who received saline (MT-V) during the full 4 minutes. No other significant difference between the 4 groups were observed over the same 4 minutes. However, during the third minute, MT-A showed a significantly higher FR than WT-A (p < .005) as well as MT-V (p < .01). During the first minute, WT-V mice showed a higher freezing rate (p < .005) than mutant mice who also received saline. On day 3, during the min 2 of silence MT-A showed a higher FR (p < .005) than WT-A while during the first min of the tone WT-A mice froze at much higher rate (p < .01) than WT-V.

**Conclusions:** Overall, we noted a significant recovery of learning impairment in Ube3a+/− mice after Apanin treatment especially in day 2 suggesting that lack of Ube3a could account for the deregulation of SK2 degradation, and the resulting impairment in synaptic plasticity and cognitive function in Angelman Syndrome.

**474**

**HIF-1α IS A REGULATOR OF POSTNATAL OLIGODENDROCYTE DEVELOPMENT**

Messier A, Wang R, Li L, Cunningham L. ¹University of New Mexico, Albuquerque, NM and ²University of New Mexico, Albuquerque, NM.

**Purpose of Study:** Preterm birth is associated with neurodevelopmental disability due to white matter injury. White matter damage may be caused by disrupted postnatal oligodendrocyte (OL) development. Hypoxia inducible factor-1α (HIF-1α), stabilized in hypoxic conditions, is a prominent transcription factor that regulates neural stem cell (NSC) development in the adult subventricular zone (SVZ). As oligodendrogenesis occurs during the third trimester, in hypoxic conditions, HIF-1α may be critical to OL development from the NSC niche. The exact role of HIF-1α in oligodendrogenesis, and how it may be disrupted by preterm birth is unknown.

**Methods Used:** To investigate the role of HIF-1α in OL development from NSCs, we induced yellow fluorescent protein (YFP) expression in nestin+ NSCs and their progeny by administering tamoxifen on postnatal day 3 (P3) to nestin-CreERT2;R26-YFP;HIF1-α wt/wt wild type mice (WT) and induced concomitant bi-allelic HIF-1α deletion in nestin-CreERT2;R26-YFP;HIF1-α fl/fl conditional HIF-1α knockout mice (HIF-1α iKO). Mice were sacrificed at P16 and P50, and YFP+ cells were immunophenotyped and quantified, in the SVZ and corpus callosum, using cell specific markers for OLs, OL progenitor cells (OPCs), astrocytes, and neuroblasts.

**Summary of Results:** At P50, there is a significant reduction in the percentage of YFP+ OLs in HIF-1α iKO mice in the corpus callosum (43.02% vs 32.02%, p < 0.001), and the SVZ (20.1% vs 10.5%, p < 0.001). OL maturational state is preserved between HIF-1α iKO and WT mice with no difference in OPC or mature OL composition in the SVZ or CC at either time point. However, the percentage of DCX+/YFP+ neuroblast lineage demonstrates a significant interaction between age and genotype (p=0.0186) in the HIF-1α iKO mice at P50. The observed decrease in percentage of DCX+/YFP+ cells at P50 numerically mirrors the decrease in YFP+ OLs at same time point, suggesting a reciprocal switch in fate from a glial to neuronal lineage.

**Conclusions:** HIF-1α appears to play a critical role in supporting OL development from the postnatal NSC niche, and its deletion may result in a lineage fate switch, pushing NSCs to a neuronal lineage. In humans, premature birth exposes the developing brain to increased oxygen concentrations, which may impede HIF-1α expression and thus OL development.