Cardiovascular I
Concurrent Session

12:30 PM
Thursday, January 24, 2013

1

ADVANCES IN HEART TRANSPLANTATION ACROSS THE MilLENNIUM

Tittle M, Raffel M, Osborne A, Hamilton M, Kobashigawa J. Cedars-Sinai Heart Institute, Los Angeles, CA.

Purpose of Study: Since the first heart transplant in 1967, significant advances have been made in perioperative care and immunosuppression which have led to improved outcomes, establishing cardiac transplantation as the preferred treatment for appropriate patients with end-stage heart disease. In recent years, this has allowed sicker patients (on ventricular assist devices) to be considered for this therapy. It is not established whether this has adversely impacted post-transplant outcomes. We reviewed morbidity and mortality following cardiac transplantation in 3 contemporaneous eras straddling the millennium.

Methods Used: We evaluated 1058 patients between 1995 and 2009 and divided them by era of transplantation (Era 1 1995-1999 = 422 pts, Era 2 2000-2004 = 333 pts and Era 3 2005-2009 = 303 pts). We assessed 5-year actuarial survival, 5-year freedom from cardiac allograft vasculopathy (CAV), 5-year freedom from Non-Fatal Major Adverse Cardiac Events (NF-MACE, defined as myocardial infarction, heart failure, need for percutaneous cardiac intervention, stroke) and 1-year freedom from any treated rejection.

Summary of Results: 5-year survival, 5-year freedom from CAV and 1-year freedom from any-treated rejection were all significantly greater in the most recent era (Era 3) compared to earlier periods. NF-MACE remained relatively unchanged through the eras.

Conclusions: Outcomes after heart transplantation continue to improve despite an expansion of the procedure to involve sicker patients (on ventricular assist devices). In the recent era, this has allowed sicker patients (on ventricular assist devices) to be considered for this therapy. It is not established whether this has adversely impacted post-transplant outcomes. We reviewed morbidity and mortality following cardiac transplantation in 3 contemporaneous eras straddling the millennium.

2

ABNORMAL SINOTRIAL NODE PACEMAKING ACTIVITY OF ATRIAL-SPECIFIC SODIUM-CALCIUM EXCHANGER KNOCKOUT MICE

Goldstein ZM1, Torrente A2, Lamp ST2, Zhang R2, Chyu K2, Philipson KD3, Goldhaber JJ1, 2. David Geffen School of Medicine at UCLA, Los Angeles, CA and 3 Cedars Sinai Heart Institute, Los Angeles, CA.

Purpose of Study: The sodium-calcium exchanger (NCX) is the dominant calcium (Ca) efflux mechanism in cardiac cells, and is hypothesized to be a critical component of sinoatrial node (SAN) pacemaker activity. Thus it is surprising that atrial-specific NCX knockout (KO) mice live into adulthood. However, these mice have lower heart rates than wildtype (WT) mice, and no P waves on surface electrocardiogram, suggesting abnormal SAN pacemaking activity. To test the hypothesis that NCX is required for initiation of pacemaking in SAN, we examined the pacemaking activity of atrial-specific NCX1 KO mice through optical voltage mapping.

Methods Used: We isolated the right and left atrium and the SAN and placed it on the bottom of an imaging chamber coated with Sylgard and stretched by pinning the atria. We loaded the tissue with the voltage-sensitive indicator di-4-anepps for 40 minutes and performed optical voltage mapping on a 400 diode mapping system (WoTech Instruments, H469-V Photodiode Array). Data were recorded using custom software programmed in IDL 6.1 (ITT Exelis, McLean,VA).

Summary of Results: In the WT, there was an organized and rapid spread of depolarization from the SAN to both atria, with the points of initiation clustered within a small area. The leading pacemaker region in KO was poorly defined, with multiple initiation points involved in the depolarization. The depolarization spread more slowly throughout the preparation and the SAN did not reliably depolarize the atria. The beta agonist isoproterenol (ISO,100mM) increased depolarization frequency of initiation points in both WT and KO, but didn’t increase the success of atrial depolarization in the KO.

Conclusions: The inability of KO mice to depolarize the atria could explain the lack of P waves on ECG. However, these mice have lower heart rates than wildtype (WT) mice, and are more irregular than WT. This suggests that a rudimentary but disorganized spontaneous depolarization mechanism can function in SAN cells despite the lack of NCX. Thus NCX appears to be required for organized pacemaker activity in mouse SAN.

3

INTRAUTERINE GROWTH RESTRICTION AFFECTS EXPRESSION OF VEGF AND ITS RECEPTORS IN A MODEL AND GENDER SPECIFIC MANNER IN THE RAT HEART

Kaza E, Callaway CW, Kaza AK, Zalla J, Joss-Moore L, Lane RH. University of Utah School of Medicine, Salt Lake City, UT.

Purpose of Study: Intrauterine growth restriction (IUGR) results from multiple etiologies including maternal tobacco exposure (MTS) or surgically-induced IUGR (sIUGR). Although there is a known association between IUGR and postnatal cardiovascular disease, mechanisms of molecular pathogenesis of cardiovascular disease are poorly understood. Inadequate capillary growth impairs myocardial function and may contribute to heart failure. A key mediator of myocardial perfusion and capillary development is Vascular Endothelial Growth Factor (VEGF) and its receptors VEGFR-1 and VEGFR-2. We hypothesized that both MTS and sIUGR would decrease VEGF mRNA variants and VEGF receptors in right ventricular (RV) myocardium in a gender specific manner.

Methods Used: IUGR was induced in pregnant rats either by surgical ligation of the uterine arteries on day e19 of gestation (sIUGR) or maternal tobacco smoke exposure at day e11 of gestation (MTS). Myocardial RV tissue (female and male) was harvested at day 21. Real-time RTPCR was performed to measure mRNA expression of VEGF variants (120, 164, 188), VEGFR-1 and VEGFR-2. We hypothesized that both MTS and sIUGR would decrease VEGF mRNA variants and VEGF receptors in right ventricular (RV) myocardium in a gender specific manner.

Summary of Results: Results are relative to age and sex-matched controls. In male RV, MTS significantly decreased mRNA expression of VEGF variants 120 (64%), 164 (85%), 188 (72%), VEGFR-1 (76%) and VEGFR-2 (77%) while sIUGR did not show any difference in VEGF receptor expression. In female, MTS did not show any significant changes. *p<0.05

Conclusions: We conclude that MTS decreases expression of all VEGF variants in male RV myocardium, with no change in female RV. We further noted that MTS decreases VEGF Receptor expression in both male and female RV myocardium. While IUGR generally impairs cardiovascular health, we speculate that mechanisms of heart disease may be specific to the cause of IUGR. These results are important as strategies aimed at up-regulating VEGF and its receptors may be useful in maintaining capillary growth and preventing heart failure.
Long-Term Tacrolimus Has Significant Renal Benefit Over Cyclosporine in Heart Transplantation

Kim Y, Rafei M, Osborne A, Yabuno J, Hamilton M, Kobashigawa J. Cedars-Sinai Heart Institute, Los Angeles, CA.

Purpose of Study: The use of calcineurin inhibitors, including cyclosporine and tacrolimus, have decreased rejection after heart transplantation. However, these agents have significant side effects particularly in renal insufficiency and its partner of hypertension. Short term randomized trials have shown differences between these two drugs in that tacrolimus may have less nephrotoxicity and hypertensive tendencies. There are no studies looking at long term outcome of these specific medications in terms of 5 year end points of renal insufficiency and blood pressure defined as number of blood pressure medications.

Methods Used: Between 1994 and 2007, we evaluated 499 heart transplant patients and divided them into those initiated on cyclosporine and tacrolimus immunosuppression and maintained for 5 years. Serum creatinine and the number of blood pressure medications at annual visits were recorded between these 2 groups and assessed by student t-test.

Summary of Results: 5-year outcomes revealed that tacrolimus had significantly lower serum creatinine compared to those patients treated with cyclosporine (1.70 ± 1.32 vs 1.32 ± 1.06, p=0.01). Both cyclosporine levels and tacrolimus levels were maintained in the predefined target range throughout the study. However, the average number of blood pressure medications were comparable between the groups.

Conclusions: Long term use of tacrolimus appears to have benefit over cyclosporine in terms of maintenance of renal function but number of blood pressure medications are comparable between groups.

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<thead>
<tr>
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<th>Cyclosporine</th>
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<td>Baseline Creatinine (mg/dL)</td>
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<td>116</td>
<td>0.39 ± 0.95</td>
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Tacrolimus-induced diabetes leads to more diabetic complications after heart transplantation

Ngan A, Rafei M, Osborne A, Hamilton M, Kobashigawa J. Cedars-Sinai Heart Institute, Los Angeles, CA.

Purpose of Study: Immunosuppression after heart transplant (tx) has revolved around cyclosporine (CsA) and tacrolimus (TAC) as the main immunosuppressive agents. Both CsA and TAC are diabetogenic, however, TAC, is much more so in clinical practice. It is not clear whether TAC-based immunosuppressive agents. Both CsA and TAC are diabetogenic, however, TAC is much more so in clinical practice. It is not clear whether TAC-based immunosuppression may have outcome benefit as TAC-based immunosuppression developed more complications of diabetes within 5 years after heart tx (neuropathy and retinopathy). Average serum creatinine on TAC was initially lower compared to those patients treated with CsA versus those treated with TAC at the time of heart tx. 5 year outcomes revealed that tacrolimus had significantly lower serum creatinine compared to those patients treated with cyclosporine (1.70 ± 1.32 vs 1.32 ± 1.06, p=0.01). Both cyclosporine levels and tacrolimus levels were maintained in the predefined target range throughout the study. However, the average number of blood pressure medications were comparable between the groups.

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Diabetic Complications after Heart Transplant

Ngan A, Rafiei M, Osborne A, Hamilton M, Kobashigawa J. Cedars-Sinai Heart Institute, Los Angeles, CA.

Purpose of Study: The use of calcineurin inhibitors, including cyclosporine and tacrolimus, have decreased rejection after heart transplantation. However, these agents have significant side effects particularly in renal insufficiency and its partner of hypertension. Short term randomized trials have shown differences between these two drugs in that tacrolimus may have less nephrotoxicity and hypertensive tendencies. There are no studies looking at long term outcome of these specific medications in terms of 5 year end points of renal insufficiency and blood pressure defined as number of blood pressure medications.

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FEASIBILITY OF PULSE OXIMETRY SCREENING FOR CRITICAL CONGENITAL HEART DISEASE AT 2600 FEET ELEVATION

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Purpose of Study: Pulse oximetry has been shown to be an effective screening tool for detecting Critical Congenital Heart Disease (CCHD) at sea level, but the ability to utilize current recommended protocols at cities of elevation is unknown (Kemper AR, Mahle WT, Martin GR et al. Strategies for implementing screening for critical congenital heart disease. Pediatrics. 2011;128:e1259-67). Higher elevations may result in decreased pulse oximetry readings leading to a high false positive rate when screening for CCHD. The primary aim of this project was to evaluate the feasibility of implementing a current pulse oximetry screening protocol at a city of modest elevation, with a specific focus on the false positive screening rate.

Methods Used: The study was conducted at the University of Arizona Medical Center in Tucson, Arizona, at an elevation of 2600 feet above sea level. Pulse oximetry screening was performed with a sensor on the right hand (pre-ductal) and either foot (post-ductal) after 24 hours of life. A positive screen was defined as: 1) oxygen saturation level <90%, 2) oxygen saturation <95% on 3 separate measures, or 3) >3% decrease in oxygen saturation between the right hand and foot on 3 measures one hour apart. A positive screen resulted in a pediatric cardiologist evaluation and echocardiogram.

Summary of Results: A total of 595 newborns were screened over a period of 6 months in 2012. The pre-ductal oxygen saturation ranged from 92%-100% (mean 98.59%) and the post-ductal oxygen saturation ranged from 94%-100% (mean 98.58%). Two patients were excluded secondary to protocol violations. Two patients had positive screens and both had a normal pediatric echocardiogram, with the exception of right-to-left shunting across a patent foramen ovale. Of those patients, one required antibiotics and a 7-day hospitalization for suspected sepsis. The false positive rate was 2/593 or 0.34% (specificity 99.66%).

Conclusions: The recent pulse oximetry screening protocol for CCHD proposed by Kemper et al. is feasible at an elevation of 2600 feet with a low false positive rate of 2.04%. We do not recommend adjustments to the protocol for elevations of 2600 feet or less. Future studies at higher elevations are required.

COMPLETE BLOOD COUNT PROFILE, ATOPY, EOSINOPHILIA AND RISK OF REJECTION IN PEDIATRIC HEART TRANSPLANT RECIPIENTS

Arbon K1, Albers E2, Law S1,2, Kemna M1,2, Law W1,2. 1University of Washington School of Medicine, Seattle, WA and 2Seattle Children’s Hospital, Seattle, WA.

Purpose of Study: Heart transplantation is a valuable therapy for treating pediatric end-stage heart disease, but allograft rejection and the long-term effects of immunosuppression remain significant clinical challenges. Pediatric recipients, particularly infants, are known to have less rejection episodes compared to teenagers and adults. Atopic conditions are also prevalent in pediatric recipients, especially infants. We hypothesize that the expression of an allergic phenotype (Th2 cell driven) is a marker of immunologic dominance over Th1 cells, which are linked to organ rejection. We assessed whether an allergic phenotype is protective of rejection.

Methods Used: This single-center, longitudinal, retrospective study included heart transplant patients (n =86) followed from 1994-2011. Post-transplant, biannual Complete Blood Counts were extracted from the medical records. Atopic conditions, rejection episodes, sensitization history, and other clinical characteristics were collected to perform analysis of risk factors for rejection.

Summary of Results: Of the study patients, 38 (44.2%) had at least 1 acute cellular rejection (ACR) while 11 (12.8%) had antibody mediated rejection (AMR). 49 patients (56.3%) had an atomic condition. All patients with AMR had median absolute eosinophil counts < 400 cells/μM (p=0.059), a literature value indicating eosinophilia. Presence of anti-HLA antibodies before and after transplant, low white cell, lymphocyte, neutrophil, and eosinophil counts were associated with AMR, but in the multivariable analysis, only presence of pre-transplant anti-HLA-A antibodies (p=0.049) and eosinophil count (p=0.102) approached significance. For ACR, eosinophil count (p=0.071) and female sex (p=0.082) neared significance and were independent risk factors in the logistic regression analysis (p=0.053 and 0.016, respectively). Atopic conditions or transplant at a young age were not protective of rejection.

Conclusions: This pilot study is the first to associate eosinophilia with freedom from rejection in pediatric heart transplantation. Identifying a marker for low rejection risk may allow reduction in immunosuppression. Whether an elevated eosinophil count is involved in the mechanism or simply a cellular biomarker requires future investigation.

Endocrinology and Metabolism I

Concurrent Session 12:30 PM Thursday, January 24, 2013

9

NITRIC OXIDE-MEDIATED CONTROL OF VASCULAR MITOCHONDRIAL DYNAMICS IN VIVO

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Purpose of Study: Mitochondrial dysfunction has emerged as a risk factor for vascular disease. Mitochondrial integrity is crucial for management of reactive oxygen species, calcium homeostasis, and vascular contractility. Nitric oxide (NO) is an upstream regulator of mitochondrial biogenesis; previous work in our lab has shown a significant decrease in mitochondrial electron transport chain (ETC) complexes in the aorta of endothelial Nitric Oxide Synthase (eNOS) knock-out mice. The role of NO in mitochondrial turnover dynamics, including fission/fusion and autophagy remains largely unexplored. We hypothesized that interference with NO generation would result in perturbation of mitochondrial dynamics.

Methods Used: To test this hypothesis, we examined the effect of short term (3-day) inhibition of NO generation by all Nitric Oxide Synthase (NOS) on mitochondrial biogenesis, fission/fusion, and autophagy in the aortas of 12-week-old male Sprague-Dawley rats. Intraperitoneal injection of 50mg/kg/day of L-NitroArginine Methyl Ester (L-NAME) or vehicle was done once a day for 3 days and the aortas harvested 24 hours following the last injection (n=10 per group). Western blot analysis was done for senti-markers of mitochondrial biogenesis (ETC Complexes, VDAC1, SIRT1, PGC1α, pCREB) and autophagy proteins (Beclin1, LC3b, p62, Bnip3).

Summary of Results: Acute NOS inhibition significantly decreased mitochondrial ETC (p=0.035) as well as VDAC1 (p=0.0023) and CREB (p=0.0129). SirT1 and PGC1α content were unchanged. Mitochondrial fusion proteins decreased significantly (OPA1 p=0.0011, Mitofusin p=0.0002, Mitofusin2 p=0.0027), while mitochondrial fission proteins increased significantly (Fis1 p=0.043, DRP1 p=0.0023) in L-NAME treated rats compared to vehicle. Autophagy markers were largely unchanged, though BNIP3 did show a mild decrease in response to NOS inhibition (p=0.0485).

Conclusions: Acute NOS inhibition resulted in decreased vascular mitochondrial biogenesis, increased fission and decreased fusion proteins with a minimal effect on autophagy profiles. This research suggests a new role for NOS in maintenance of vascular mitochondrial dynamics and strengthens the evidence for eNOS as a therapeutic target.

10

AN INCREASED COMPLEMENT OF NATURAL KILLER T CELLS CONTRIBUTES TO METABOLIC DYSFUNCTION AND Atherosclerosis in OBESE MICE

Subramanian S1, Turner M1, Ding Y1, Kim J1, Buckner J2, O’Brien KD2, Chait A1, Reardon C3, Getz G3. 1University of Washington, Seattle, WA and 2Benaroya Research Institute, Seattle, WA and 3University of Chicago, Chicago, IL.

Purpose of Study: Obesity is a chronic inflammatory state characterized by adipose tissue immune cell infiltration. While macrophages are a key...
player, current evidence also implicates T lymphocytes in adipose inflammation. Natural killer T (NKT) cells are a specialized lymphocyte subset expressing natural killer cell and T cell receptors that uniquely bridge the innate and adaptive immune systems. NKT cells recognize lipid antigens through specific cell surface markers. In obesity, decreased tissue NKT cell numbers has been demonstrated. However, the role of NKT cells in adipose inflammation continues to be inconclusive and contradictory. We hypothesized that the presence of an excess complement of iNKT cells might worsen metabolic abnormalities in obesity.

Methods Used: We utilized the Vα14 transgenic (Vα14Tg) mice which has increased numbers of NKT cells, on a LDL receptor deficient (Ldlr−/−) background. We confirmed the presence of increased NKT cells in these mice by flow cytometry. Vα14TgLdlr−/− mice and control Ldlr−/− were placed on a high fat diet (HFD) for 16 weeks. Effects on body weight, dyslipidemia, insulin resistance, visceral adipose tissue macrophage accumulation, and atherosclerosis were evaluated.

Summary of Results: Vα14TgLdlr−/− mice gained 25% more weight on HFD compared to littermate controls and also had increased fat mass on body composition analysis. Hypertriglyceridemia and hypercholesterolemia developed in the transgenic mice compared to controls. Transgenic mice also developed hyperinsulinemia and insulin resistance. Increased macrophage F4/80, monocyte chemotactic gene expression and Mac2 immunostaining suggested worsened adipose inflammation. Increased hepatic triglyceride accumulation and inflammation were also observed in the transgenic mice. Currently, these mice had increased atherosclerotic lesion area on en face lesion analysis.

Conclusions: Thus, Vα14TgLdlr−/− mice had significantly worsened metabolic features of obesity. These results suggest that the relationship of NKT cells in metabolism is complex and that an excess of these immunological cells is not sufficient to beneficially modify metabolic abnormalities associated with obesity.

11 HEPATIC RESPONSE TO REDUCED MATERNAL GLUCOSE SUPPLY IN FETAL SHEEP


Purpose of Study: Fetal hepatic glucose production is normally absent until just prior to birth. However, sheep models of reduced maternal glucose supply, maternal fasting, and intrauterine growth restriction (IUGR) have measured fetal glucose production using whole-body glucose metabolism. The rate of hepatic glucose production in response to reduced maternal glucose supply. We hypothesized that reduced maternal glucose supply to the fetus will lead to activation of fetal hepatic glucose production.

Methods Used: Late gestation fetal sheep (n=4) had catheters surgically placed in the abdominal aorta, umbilical vein, and left hepatic vein to measure glucose, lactate and oxygen concentrations. Fetal arterial and umbilical vein samples were used to calculate umbilical (net fetal) uptake rates. Hepatic vein samples were compared to umbilical vein samples to measure hepatic uptake/output. First, a basal metabolic study was performed. Then a maternal insulin infusion was initiated to reduce maternal and fetal glucose concentrations by 50%. Fetal metabolic studies were repeated after 1 (d1) and 5 (d5) days of reduced maternal insulin infusion.

Summary of Results: Maternal insulin infusion decreased fetal umbilical glucose uptake and glucose concentrations by 50% on d1 and d5 compared to basal (P<0.05). During the basal period, there was net hepatic uptake of glucose and by d5 there was net hepatic output of glucose (P<0.05). During the basal period, there was net fetal and hepatic uptake of lactate which both decreased on d1 and d5 (P<0.05). Fetal oxygen uptake rates were similar at all the time points (P=0.8).

Conclusions: Reduced maternal glucose supply resulted in fetal hypoglycemia and increased hepatic glucose output by d5. Interestingly, hepatic lactate uptake decreased during hypoglycemia, suggesting that other carbon substrates (glucose, fatty acids, pyruvate, or glycogen) are being used for hepatic glucose output. Additional studies are underway to test the role of substrates and hormones in regulating fetal hepatic glucose output. These findings are important for understanding the development of hepatic glucose output in response to reduced maternal glucose supply and in other cases of fetal nutrient restriction, including IUGR.

12 DOES SHORT TERM VITAMIN C REDUCE CARDIOVASCULAR RISK IN DIABETES?

Durán-Valdez E1, Gutierrez A2, Schade DS1.1. UNM, Albuquerque, NM and 2.University of Texas Health Sciences Center at Houston, Houston, TX.

Purpose of Study: Vitamin C is a powerful antioxidant, potentially useful in the prevention of atherosclerosis. However, the mechanism(s) of vitamin C’s antiatherosclerotic effects in vivo are unresolved and clinical trials have been conflicting. Therefore, we performed 32 studies in a randomized, crossover, dose-response trial in eight volunteers with type 2 diabetes mellitus to determine the effects of vitamin C on serum vitamin C levels, lipids, and standard markers of atherosclerotic risk.

Methods Used: Well-controlled, type 2 volunteers received, in randomized order for 2-week periods, each of the following: (1) no vitamin C, (2) low-dose vitamin C (250 mg/d), (3) medium-dose vitamin C (500 mg/d), and (4) high-dose vitamin C (1000 mg/d). A high caloric content, carbohydrate/fat meal was ingested during each study arm to enhance oxidative stress. Serum vitamin C levels and atherosclerotic risk factors including hyperlipidemia, hyperglycemia, and high density lipoprotein were measured. Surrogate markers of oxidative stress, inflammation, and hypercoagulability were also determined.

Summary of Results: Compared to placebo, serum vitamin C levels increased significantly at all dosages. Vitamin C increased total cholesterol, non-HDL cholesterol, triglycerides, high density lipoprotein, and low density lipoprotein were measured. Surrogate markers of oxidative stress, inflammation, and hypercoagulability were also determined.

Conclusions: In conclusion, these data suggest that vitamin C, if indeed it does have antithrombotic effects, does not express them through the traditional pathways that are identifiable by established surrogate markers of risk. Before any additional large scale clinical trials with vitamin C are undertaken, an antithrombotic mechanism should be identified.

13 VARIABILITY IN BODY FAT DEPOTS AMONG PEOPLE WITH TYPE 2 DIABETES: EFFECT OF WEIGHT LOSS

Almazdo JP, Nelson RH, Miles JM. Mayo Clinic, Rochester, MN.

Purpose of Study: During weight gain, it has been suggested that upper body fat expands by increasing adipocyte size, whereas lower body fat expands by increasing adipocyte number. Previous studies have shown marked variability (~60%) in the size of body fat depots in young people, with lower variability in the elderly (~35%) and no difference in variability between lower body fat and upper body fat.

Methods Used: We studied 13 people with type 2 diabetes (9 men and 4 women, age 52±2 years, BMI 34±1 kg/m², hemoglobin A1c 7.9±0.3%) at baseline and after an approximate 14% weight loss induced by an intensive 5-month lifestyle intervention consisting of calorie restriction and near-daily aerobic exercise. Regional and total body fat was determined with dual energy x-ray absorptiometry and single-slice CT imaging.

Summary of Results: BMI decreased to 29.2±1.1 kg/m² and hemoglobin A1c decreased to 6.3±0.2% (both p<0.001). Leg and trunk fat mass decreased from 10.0±0.9 to 7.7±0.9 kg and from 25.4±1.2 to 17.8±1.6 kg (both p<0.001). Trunk:leg fat ratio decreased from 2.7±0.2 to 2.5±0.2 (p<0.05), indicating a preferential loss of upper body fat. Visceral and upper body subcutaneous fat area decreased from 328±18 to 208±22 cm² and from 264±31 to 187±25 cm², both p<0.001. At baseline the inter-subject variability in the size of the leg fat depot was greater than trunk fat (coefficient of variation 32.5% vs 17.0%, p<0.05) and increased after weight loss to 43.0 and 31.8%, respectively, p=NS. Baseline variability in abdominal subcutaneous fat as determined by CT was greater than that of visceral fat (42.8% vs 19.7%, p=0.05). Variability of visceral fat mass increased after weight loss to 37.3%, but did not change for abdominal subcutaneous fat (38.9%, p=NS vs visceral fat).

Conclusions: Thus, the present study indicates that in people with type 2 diabetes there is greater variability in the size of the leg fat depot compared with trunk fat. This may be due to a greater and more variable ability of leg fat to expand, although further studies are needed to test this hypothesis.
ACANTHOSIS NIGRICANS SCORING AS A PREDICTOR OF IMPAIRED GLUCOSE TOLERANCE AND DIABETES IN OBESE CHILDREN AND ADOLESCENTS

Nuyen B,1 Gamst A2, Franklin S,2 Schwimmer J,2 University of California, San Diego, La Jolla, CA and 4 University of California, San Diego, La Jolla, CA.

Purpose of Study: The identification of obese children and adolescents with type 2 diabetes is an important clinical problem. The prevailing approach relies upon application of body mass index (BMI) to determine whether or not to test fasting glucose. However, despite the association between obesity and type 2 diabetes, BMI has a low specificity for type 2 diabetes. Therefore, we sought to improve upon current identification strategies by using acanthosis nigricans (AN) scoring as a potentially more robust clinical tool. The study aim was to assess AN score as a predictor of diabetes, impaired fasting glucose, and hyperinsulinemia in obese youth.

Methods Used: We studied obese children between 8 and 19 years of age. AN scoring was performed at the neck, and severity was graded 0-4. Fasting glucose and insulin were measured. Logistic regression was used to assess the association between AN score and diabetes, impaired fasting glucose, and hyperinsulinemia.

Summary of Results: 411 obese children between 8 and 19 years of age were enrolled; the mean BMI was 33.4±7, with mean BMI Z-score of 1.4±3.9. There was a significant positive association between AN score and glucose (r = 0.249, p < 0.001) and between AN score and the log transformation of insulin (r = 0.601, p < 0.001). First controlling for age, sex, race and ethnicity, and the log transformations of weight percentile and height percentile, AN score was a significant predictor of diabetes (OR = 2.1 [1.4, 3.9]; p = 0.001). AN score was also a significant predictor of impaired fasting glucose and hyperinsulinemia.

Conclusions: After controlling for BMI and other clinically important variables, AN score was a significant and clinically relevant predictor of hyperinsulinemia, impaired fasting glucose, and diabetes. We found that for every one unit increase in AN score, the odds of having diabetes doubled. AN scoring is simple to perform, is inexpensive, and holds promise as a tool to more effectively target screening for type 2 diabetes in children.

Health Care Research 1
Concurrent Session
12:30 PM Thursday, January 24, 2013

NATIONAL STUDY OF PRIMARY CARE-TREATABLE EMERGENCY DEPARTMENT VISITS AS INDICATORS OF LIMITED ACCESS TO CARE

Pakurpól P, Ginde AA. University of Colorado School of Medicine, Centennial, CO.

Purpose of Study: Some authors have hypothesized that the trend towards increased emergency department (ED) utilization is driven by individuals who substitute ED care for outpatient primary care. Many of these prior studies are limited by sample size, short time courses, or narrow geographic representation. This study utilizes a national sample to assess the proportion of ED visits that may have been treatable by other primary care providers according to payer type over a 13 year period, and assess potential markers of limited access to care such as visit time.

Methods Used: A retrospective secondary analysis of the National Hospital Ambulatory Medical Care Survey (NHAMCS) from 1997 to 2010. Utilizing the New York University Emergency Department (NYU ED) algorithm, ED visits are classified as either primary care-treatable (PCT) or ED necessary (EDN) based on the primary diagnosis ICD-9 code. Multivariate regression is utilized to evaluate associations between exposure to Private Insurance, Medicaid, Medicare Self Pay or Other, adjusted for age, race, gender, and geographic region. Associations between the time of the visit, including During Regular Business Hours and Outside Regular Business Hours, are also evaluated.

Summary of Results: In the unadjusted crude analysis, of 241,167 visits classified as PCT or EDN, payment by Medicare was associated with fewer PCT visits compared to payment by private insurance (52.48% Medicare vs 67.15% Private Insurance), while payment by Medicaid (72.58%) and Self-Payment (71.54%) were associated with more PCT visits compared with payment by private insurance. In the adjusted crude analysis, visits occurring after Normal Business Hours were associated with increased PCT visits.

Conclusions: This study is among the first to characterize primary care-treatable visits to the ED in a national sample based on payer type and time of visit.

UNDERSTANDING AND OVERCOMING BARRIERS TO OFFICE-BASED PHYSICIANS’ TREATMENT OF OPIOID ADDICTION

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Purpose of Study: Opioid addiction is a major problem in Washington State, however office-based treatment is in short supply. The Rural Opioid Addiction Management Program (Project ROAM) trains office-based physicians to prescribe buprenorphine, a medication-assisted opioid addiction treatment that requires a physician to obtain a Drug Enforcement Administration waiver. Project ROAM has trained 120 physicians in the last two years, yet not all have incorporated buprenorphine treatment into their practices. This study aimed to determine what proportion of trained physicians has implemented this treatment modality and to identify barriers that prevent physicians from adopting this clinical approach.

Methods Used: We completed interviews with 92 Project ROAM-trained physicians (response rate = 77%) to determine demographic information, clinic characteristics, attitudes, and barriers to prescribing buprenorphine. Respondents were classified into three groups: non-prescribing physicians, non-prescribing waivered physicians, and prescribing waivered physicians.

Summary of Results: Most respondents reported positive attitudes toward buprenorphine, yet only 29 (31.5%) have prescribed the medication to treat opioid addiction. The majority were family physicians practicing in small safety net or private practice clinics. Prescribing was significantly associated with institutional support (p=0.021) and physician confidence in the management of opioid addiction (p=0.038). Time constraints, lack of patient need, resistance from practice partners, lack of specialty backup for complex problems, and lack of psychosocial support services were other major barriers cited by non-prescribing physicians.

Conclusions: Less than half of Project ROAM-trained physicians have prescribed buprenorphine to treat opioid addiction. The low rate of treatment adoption is not associated with physician attitudes about the medication but may be related to barriers such as a lack of support from clinic management or a physician’s lack of confidence in his/her ability to manage opioid addiction. Future efforts to increase the availability of buprenorphine treatment should continue to include physician education but also emphasize advocacy and education at the level of clinic management.

PANDA: EVALUATION OF A SMARTPHONE-BASED PERIOPERATIVE PAIN ASSESSMENT TOOL

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Purpose of Study: The first step in good pain management is appropriate assessment. Self-report pain assessment tools include the Faces Pain Scale Revised (FPS-R) for ages 4-12 and the Color Analog Scale (CAS) for ages 5-18 (Stinson, 2006). Both are scored on the 0-10 metric. Panda is a smartphone application, which uses digitized versions of FPS-R and CAS. The first or second. Each assessment included a pain score at rest and upon appropriate activity, performed within 10 mins of waking and 30 mins later. Children were asked which version of the tool they preferred. Agreement
was calculated using Bland-Altman’s (1999) interval method with maximum limit of agreement set at 2/10.

Summary of Results: 40 children, median (range) age 7.5 years (4-11), participated in the FPS-R trial. For all pairs of assessments, Panda scores correlated strongly (Pearson’s r = 0.9) with paper scores. Mean differences were within ±2.24 and 95% limits of agreement within ±1.57 to ±1.97. 15 children scored zero in all assessments. 60 children, median (range) age 13.5 years (5-18), participated in the CAS trial. Panda scores correlated strongly (p > 0.9) with the plastic scorer, but mean CAS scores were higher (overall mean difference = 0.31) with Panda than plastic scorer for all pairs of assessments (p < 0.03). 95% limits of agreement were ±1.52 to +2.17. More children preferred the Panda versions of both tools to the originals (p < 0.01).

Conclusions: The Panda was preferred by users and demonstrated substantial agreement with the paper PFR scorer and plastic CAS scorer. The bias toward higher CAS scores on Panda is statistically but not clinically significant. The number of zero pain scores obtained suggests the need to complement self-report with observation in young children.

18

IMPROVING CARE QUALITY FOR CHILDREN ADMITTED FOR ACUTE ASTHMA: A MULTI-HOSPITAL IMPLEMENTATION OF AN ASTHMA CARE PROCESS MODEL

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Purpose of Study: Children admitted for acute asthma commonly receive suboptimal attention to interventions that prevent exacerbations and readmissions. The acute hospital setting is an ideal opportunity to establish effective approaches to chronic symptom management. Objectives are to examine changes in provider compliance with chronic asthma care measures following implementation of an inpatient asthma care process model (CPM).

Methods Used: Prospective, quality improvement study of all children age 2-18 years admitted for asthma at 6 Intermountain Healthcare operated community hospitals. The CPM was implemented through a standardized discharge process in a multistep stepwise fashion between 1/1/2011 and 8/30/2012 and included following components: standardized asthma severity assessment and preventive medication step algorithm; standardized asthma teaching procedure and competency checklist, and provision of a home management plan of care. Impact of the CPM was examined on chronic asthma care measures known to be associated with better ambulatory asthma control, including: completion of asthma education, provision of a home management plan of care, and discharge with appropriate controller medications. Analysis included monthly reporting of physician compliance with these measures. We report changes of compliance at baseline and the end of implementation and used a Fisher’s exact test to determine significance.

Summary of Results: A total of 372 patients were admitted for acute asthma. Compliance with all chronic asthma care measures improved significantly from baseline (p < 0.05): Completion of asthma education: 3% (0-20%); Provision of home management plan management: 2% (0-10%); to 86% (76-100%); prescription of appropriate controller medication: 35% (20-60%) to 93% (86-100%); prescription of appropriate controller medication: 35% (20-60%) to 93% (86-100%).

Conclusions: Implementation of the asthma CPM was associated with improved compliance with evidence-based chronic care measures known to be associated with better ambulatory care for children with asthma. Future studies are needed to document effects on long-term patient outcomes, particularly readmissions.

19

TRENDS IN ON AND OFF-LABEL MODAFINIL USAGE IN A NATIONALLY-REPRESENTATIVE SAMPLE

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Purpose of Study: Modafinil is a non-amphetamine stimulant approved for narcolepsy, obstructive sleep apnea, and shift work sleep disorder. However, off-label usage is often recommended. There is little data about trends in modafinil usage, factors related to usage, or indications for prescription, whether on- or off-label.

Methods Used: Utilizing the National Ambulatory Medical Care Survey, a nationally-representative survey of outpatient visits, we examined trends in modafinil usage (2002-2009), diagnoses associated with modafinil usage, physician specialties most likely to treat patients on modafinil, and concurrent medications.

Summary of Results: The number of patients receiving modafinil increased from 57,768 in 2002 to 555,691 in 2009. Overall 89% of patients receiving modafinil lacked an on-label indication. Moreover, the number of patients receiving modafinil with an on-label diagnosis increased 3-fold while the number without and on-label diagnosis increased over 15-fold. In multivariate analyses, controlling for sociodemographics and survey year: [1] patients with all examined off-label indications had higher odds of taking modafinil, compared to those without such a diagnosis, including multiple sclerosis (OR=84.6; p<0.001), chronic fatigue syndrome (OR=23.4; p<0.001), Parkinson’s disease (OR=19.4; p<0.001) and depression (OR=10.8; p<0.001); [2] patients treated by psychiatrists (OR=21.1; p<0.001) and neurologists (OR=19.7; p<0.001) had higher odds of receiving modafinil, compared to primary care practitioners and other specialists; and [3] patients taking antidepressants, benzodiazepines and amphetamines were each associated with higher odds of concurrent modafinil treatment (OR=8.4, 6.0 and 8.3, respectively; p<0.001 for all). 45% of patients prescribed modafinil were also receiving an antidepressant.

Conclusions: Modafinil usage is increasing rapidly, which appears due in large part to off-label indications. Given that modafinil is often being used in practice for comorbid diagnoses and concurrent medications that do not reflect the populations in which the drug was studied for regulatory approval, further study of modafinil for currently unapproved indications is needed.

20

EVALUATION OF TELEHEALTH TO SUPPORT PEDIATRIC SEXUAL ABUSE EXAMINATIONS IN RURAL COMMUNITIES

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Purpose of Study: To evaluate the impact of telehealth consultation on the ability of a rural examiner to conduct a complete and thorough sexual abuse examination.

Methods Used: Telehealth consultation capability was established in six rural sites in Northern California. Real-time and store-and-forward consultations were provided by child sexual abuse experts from UC Davis Children’s Hospital (UCDCH) to examiners conducting forensic child sexual abuse examinations in the rural communities. Exams were evaluated by the UCDCH experts to identify 1) suggested changes in exam technique; 2) suggested changes in evidence collection; 3) remote examiner ability to accurately identify physical findings; and 4) whether the exam was comprehensive enough to arrive at a diagnosis. An independent, expert reviewer rated exam quality when conducting ‘usual care’ examinations compared to exams aided by telehealth consultations.

Summary of Results: Between 2000 and 2008, 138 evidentiary telehealth examinations were conducted. Of those, 88 were ‘live’ exams and 50 were ‘store and forward’. Consultants recommended collection of additional forensic evidence in 35.5% of live examinations. Rural examiners were able to accurately describe exam findings 46% of the time during live exams; however, when rural examiners conducted exams without telehealth consultation, they were able to accurately describe exam findings only 11.6% of the time (p=0.01). Live telehealth examinations resulted in ‘complete examinations’ in 47% of cases compared to 14.5% of the cases without live telehealth (p=0.01). Independent review of telehealth exam consultations versus control exams demonstrated significantly greater overall exam quality when a telehealth consultation was used (p<0.01).

Conclusions: Telehealth quality assurance consultations result in significant changes to evidence collection, completeness of examination, and accuracy of diagnosis. Further, telehealth results in significantly improved overall exam quality compared to rural communities without this service. In rural communities, expert telehealth consultation provides the gold standard of peer review and supports examiners in an emotionally burdensome area of pediatrics.

21

BASELINE CENTRAL VENOUS ACCESS PERFORMANCES OF GRADUATING SENIOR MEDICINE RESIDENTS

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Purpose of Study: Central venous catheter (CVC) placement is one of the most common invasive procedures performed in hospitals and significantly contributes to both iatrogenic complications and health care cost. No previous study has examined the performance of senior residents placing CVC utilizing high-fidelity simulation.

Methods Used: This observational cohort study was IRB approved. Of 40 total internal medicine senior residents from the classes of 2010 and 2011, 28 participated. Performances were all video-recorded and reviewed by a blinded faculty outside of the department. Three predictors of performance were selected for regression modeling. Multiple linear regression models were created. Regression analysis was used to measure model assumption.

Summary of Results: Of 28 participants, 8 forfeited during the procedure due to various difficulties. None of those who forfeited were able to thread the needle guide wire on the first attempt and required an average of 7 needle sticks before forfeiting. Only 3 out of 8 identified correct anatomical landmarks and demonstrated correct ultrasound machine operation. For those who could finish the procedure, time to successful cannulation averaged 6 minutes with an average of 2 needle sticks; we also noted correlation with the ability to pass guide wire on the first attempt (63%), correct landmark identification (90%) and ultrasound machine usage (95%). With incorrect ultrasound usage, we expect 6.8 more needle sticks and 1.7 more arterial punctures compared to someone who knows how to use it correctly. We also expect residents to be 186 seconds faster to cannulate with proper ultrasound usage. Correct landmark identification predicts 148 seconds faster to cannulate, and successful first attempt on guide wire threading predicts 99 seconds faster to cannulate.

Conclusions: Unexpected high numbers of senior residents forfeited the procedure due to difficulties and considerable variability of chosen predictors of performance was seen among those who were successful. Regression models of predictors quantified the importance of anatomical landmark identification, ultrasound utilization and first attempt guide wire passage to the successful CVC placement. Our study should prompt further investigation on the procedural performance of senior residents.

Findings: The American Federation for Medical Research have developed explicit procedures, the vast majority do not have policies for LGBT cultural competence including health issues. While some institutions are doing more to address these issues. One example we identified of an existing program to identify LGBT-friendly primary care providers and to identify if LGBT-competency training exists for providers at these institutions.

Methods Used: We conducted a systematic survey of academic medical centers to identify LGBT-friendly primary care providers and to identify if LGBT-competency training exists for providers at these institutions.

Summary of Results: Forty-one percent of 109 selected academic medical centers that we contacted responded and completed the interview. Of the participating institutions, 93% do not have a procedure in place to identify LGBT-friendly providers. Only 18% have comprehensive LGBT-sensitivity or competency training available for providers while 33% report to have some diversity training including LGBT topics, and 49% do not have any LGBT-related training available for providers. Nevertheless, 80% of the participating institutions indicate that they believe their institution could be doing more to address these issues. One example we identified of an existing LGBT training utilizes an online webinar to cultivate culturally sensitive care.

Conclusions: This is the first study to systematically categorize the processes, policies and programs that medical institutions have in place to identify LGBT-friendly providers and to determine LGBT cultural competence including health issues. While some institutions have developed explicit procedures, the vast majority do not have policies or programs in place. Further work will include follow up with institutions to assess whether they have revised their processes and programs based on the findings from this study.
Methods Used: Umbilical cord blood was collected from term deliveries. MMCs were isolated and stimulated with GBS (1×10^7) or GBS + IL-17 (100 ng/mL). Cytokine production was measured using in-house developed multianalyte assay employing Lumexin Technology.

Summary of Results: In response to GBS + IL-17, neonatal MMCs produced significantly more proinflammatory IL-1β, IL-6, IL-8, TNFα, and IFNy than with GBS alone (n=12; mean: pg/mL): IL-1β [GBS: (133); GBS + IL-17: (2475); p<0.007]; IL-6 [GBS: (1194); GBS + IL-17: (8192); p<0.001]; IL-8 [GBS: (6555); GBS + IL-17: (9895); p<0.001]; TNFα [GBS: (721); GBS + IL-17: (2409); p<0.01]; IFNy [GBS: (6.3); GBS + IL-17: (15); p<0.02]. In contrast, there was no enhancement of IL-2, IL-4, IL-10, IL-13.

Conclusions: Neonatal MMCs have deficiencies in the Th-1 cytokine production of both IL-17 and IFNy. The addition of GBS + IL-17 to neonatal MMCs significantly enhances the proinflammatory cytokine production of IL-1β, IL-6, IL-8, TNFα, and IFNy. This combined Th-1 type cytokine physiological deficiency likely contributes to the enhanced susceptibility of neonates to GBS and other microbial infections.

25 ANALYSIS OF WOUND HEALING USING HIGH-THROUGHPUT RNA-SEQUENCING

Zhang DX, Lam M, Glass C. University of California, San Diego, La Jolla, CA.

Purpose of Study: Proper control of wound healing is an essential homeostatic process through transcriptome analysis.

Methods Used: A skin punch biopsy wound healing model was used to study the wound healing response in mice. RNA-Seq was conducted on skin samples.

Summary of Results: Compared to unwounded tissue, 7273 genes were differentially expressed during wound healing process through transcriptome analysis.

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Summary of Results: Compared to unwounded tissue, 7273 genes were differentially expressed during wound healing process through transcriptome analysis.

Conclusions: Together, these studies describe a dynamic transcriptional network dedicated to the intricate process of wound healing. Further understanding of this network may provide novel therapeutic targets to enhance the wound healing process in patients.

26 EXPLOITING PROTEASE ACTIVITY TO IMAGE AND UNDERSTAND ASTHMA

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Purpose of Study: Asthma is an inflammatory airway disease with by intermittent, reversible airway obstruction that affects more than 300 million people worldwide. The presence of extracellular proteases, such as elastase and matrix metalloproteinases 2 and 9 (MMP2/9), correlates with lung pathologies in asthma, but their roles in asthma are not well understood. We used activatable cell penetrating peptides (ACPPs) to image and evaluate protease activity in asthmatic murine lungs. ACPPs—synthetic, injectable probes whose cellular uptake depends on cleavage and activation by specific proteases—highlight in vivo proteolytic activity.

Methods Used: With ovalbumin (OVA) as the antigen, asthmatic mice were generated by sensitization (OVA + alumn in saline [PBS]) followed by challenge (OVA in PBS), while control mice were sensitized but not challenged. ACPPs (cleavable and control uncleavable peptides, n = 3-4 mice each) with Cy5 fluorescence (FL) were administered intravenously (6 hr in vivo incubation) or intranasally (2 hr in vivo incubation) 24 hr after the final challenge. Whole lungs were imaged for Cy5 FL (Maestro, CRi) at ex620/em645LP tuned to 670 nm; lung sections (10 μm, 8 images/mouse) were imaged for Cy5 FL and Hoechst nuclear stain on a confocal microscope (SLive, Zeiss) and then re-imaged after hematoxylin and eosin staining.

Summary of Results: First-generation MMP2/9- and elastase-cleavable ACPPs had higher FL in asthmatic lungs than in control lungs (2-fold higher in whole lungs; p < 0.05), but did not have higher FL than control uncleavable ACPPs. Cy5 imaging of lung sections revealed that MMP2/9 ACPPs highlighted inflamed airways while elastase ACPPs had diffuse lung signal; both had higher signal than the uncleavable ACPPs. Second-generation, larger ACPPs had cleavage-dependent FL in asthmatic lungs (2-fold higher uptake for cleavable v uncleavable; p < 0.05). Using a fluorescence resonance energy transfer (FRET)-based ACPP, there was also significant cleavage-dependent uptake into asthmatic lungs (2.7-fold higher in cleavable; 2.9-fold higher in asthma; p < 0.05).

Conclusions: There is cleavage- and asthma-dependent uptake of ACPPs in OVA-induced asthmatic mice; thus, ACPPs can be used to improve our understanding and evaluation of the relevant proteases in asthma. Applying ACPPs to asthma will elucidate therapy targets for ACPP-based therapy delivery and protease inhibitors.
**DISCOVERY OF TGF-BETA MIMETICS THROUGH THE OPTIMIZATION OF A CELL-BASED, HIGH-THROUGHPUT ASSAY**

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**Purpose of Study:** Macrophages (MF) are highly diverse innate immune cells that contribute both to host defense and to the pathogenesis of disease. We hypothesize that the polarization state of the vascular endothelium directs monocytes toward divergent MF subsets. Our high-throughput, cell-based assay uses MF heterogeneity as an indicator of the inflammatory state of the micro-environment. Endothelial cells (EC) pre-treated with TGF-beta were found to give rise to anti-inflammatory MF to a low expression of CD209, CD40, and CD163. However, these three MF markers alone could not adequately distinguish anti-inflammatory MF from homeostatic MF. In this study, we sought (1) to improve our assay through the addition of a fourth MF cell surface marker and (2) to use the improved assay to discover novel anti-inflammatory compounds.

**Methods Used:** Primary human endothelial cells (EC) were stimulated with controls and small molecules, and primary human mononuclear cells were added to the EC. Monocytes were allowed to differentiate along distinct pathways. Co-cultures were labeled with antibodies for MF cell surface markers, and plates were placed in a high-throughput flow cytometer.

**Summary of Results:** Endothelial cells pre-treated with TGF-beta gave rise to MF with low expression of macrophage mannose receptor 1 (MR1), or CD206 (69.7% decrease vs. control MF). Of eighteen physiologically significant cell surface markers, CD206 best discriminated TGF-beta-treated cultures from controls (CD206-low gate included 64.6% of the TGF-beta-treated population vs. 20.7% of the control population). CD206 was included as the fourth marker of MF inflammatory state. Thus far, 1600 compounds have been screened with the improved assay. Each compound has been ranked according to MF expression levels of CD209, CD40, CD163, and CD206. Four compounds appear to be TGF-beta-like (hit rate = 0.25%) based on summed rank. Three of the four belong to a structurally similar family.

**Conclusions:** The ability of our assay to use induced MF marker expression to discern structurally similar, TGF-beta-like compounds is promising. Additional functional assays and in vivo studies are needed to confirm and to elucidate the anti-inflammatory properties of these compounds. Ultimately, this approach may allow us to use the micro-environment to sculpt innate immune responses therapeutically.

**ONCOGENIC ACTIVATION OF MAPK IN RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS**

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**Purpose of Study:** Rheumatoid arthritis (RA) is a destructive polyarthritis in which synovial-like fibroblasts (SFs) invade and erode cartilage by expressing membrane-anchored type I matrix metalloproteinase (MT1-MMP). MAPK is activated in RA SFs, but it is not known if activation is the result of immune mediators of inflammation or oncogenic transformation. Our study was designed to evaluate the role of oncogenic transformation of RA SFs.

**Methods Used:** Aberrant BRAF splice variants were identified in RA SF by RT/PCR. The function of aberrant BRAF splice variants was evaluated in transfected NIH-3T3 fibroblasts transfected with an expression vector containing cDNA of BRAF splice variants. Mitogen-activated protein kinase (MAPK) activation in transfected NIH-3T3 cells was determined by phosphorylation of MEK and ERK. The role of BRAF and CRAF in SF transformation was determined by RNAi, and Membrane-Type 1 Matrix Metalloproteinase (MT1-MMP) was identified in cells with MT1-MMP-specific antibodies. Collagen invasion by transfected NIH-3T3 cells was evaluated in vitro collagen invasion assay.

**Summary of Results:** Aberrant BRAF splice variants with deletions in both the kinase domain (kinase-dead) and RAS-binding domain (RBD) were identified in SFs from the majority of RA patients. Moreover, these BRAF splice variants constitutively activate MAPK, increase expression of MT1-MMP, and enhance fibroblast invasion of collagen.

**Conclusions:** Our studies provide evidence that MAPK activation in RA SFs is the result of oncogenic transformation by aberrant BRAF splice variants.
Methods Used: Infants admitted to LAC+USC Medical Center NICU with birth weight (BW) <3000 grams were included. We recorded SpHb using Masimo Radical-7 (Masimo Corp., Irvine, CA) and compared with tHb. A total of 3 data sets (tHb and SpHb) at 3 time points were obtained for each patient. Regression analysis and Bland-Altman analysis were performed.

Summary of Results: Twenty three patients (BW 1262 ± 631 g, gestational age 28.9 ± 3.9 weeks, median postnatal age 3 days [25th - 75th percentile 1-5 days]) were enrolled and 65 paired samples were obtained. The mean ± SD tHb value was 14.5 ± 1.9 g/dL (range 10.7 - 18.9 g/dL) and the mean SpHb was 14.4 ± 2.4 g/dL (range 9.7 - 18.9 g/dL). There was good correlation between SpHb and tHb (r=0.75, p=0.001) and a good agreement between paired hemoglobin values. The bias and precision for the tHb and SpHb values were 0.14 ± 1.59 g/dL.

Conclusions: Our preliminary results suggest that noninvasive SpHb may be used successfully as an alternative to invasive tHb measurements in newborn infants <3000 grams. Additional studies are needed to more definitively determine if the agreement persists between these two measurements.

THE EFFECT OF PROBIOTICS ON METABOLIC BONE DISEASE IN PREMATURE INFANTS

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Purpose of Study: Premature infants are at increased risk for metabolic bone disease given inadequate mineral stores, stress of prematurity and maternal or neonatal disease. There is evidence in adults that probiotics improve mineral absorption and overall bone structure. Whether this is the case in premature neonates is unclear. Elevated alkaline phosphatase in association with low phosphorus has predictive value for metabolic bone disease of prematurity. Using these markers and signs of osteopenia in x-rays obtained during NICU hospitalization, we analyzed a small sample of premature infants to determine whether a clinical trial of probiotics to prevent bone disease could be justified and the required sample size for such a trial.

Methods Used: We performed a retrospective, single-center, medical record review. Data were collected on 119 total infants involved in prior probiotic trials. One trial compared Culturelle® (n=30), Probioplus® (n=30) and placebo (n=30), and a second trial compared Bifidobacteria infants (n=6), Bifidobacteria lactis (n=6), and the combination of the two (n=9) or placebo (n=8), for a total of 81 infants receiving probiotics and 38 receiving a placebo. Endpoints are serum phosphorus and alkaline phosphatase and evidence of bone demineralization on X-ray examination.

Summary of Results: Of the 119 infants, 39 had X-ray evidence of osteopenia. In the probiotic group (36%) and 10 in the placebo group (26%), RR 1.36 (0.74-2.50). Of the 109 infants in the probiotic trials that had both serum values obtained, 14 had both an alkaline phosphatase > 600 IU/L and a serum phosphorous < 4 mg/dL: 9 in the probiotic group (12%) and 5 in the placebo group (14%).

Conclusions: The x-ray data suggest a possible detrimental effect of probiotics; a sample size of 335 infants per group would be needed to test this hypothesis. The serum data suggest a beneficial effect; a sample size of >4000 infants per group would need to be tested to hypothesis this.

UTILITY OF TORCH INFECTION SCREENING IN SMALL FOR GESTATIONAL AGE INFANTS

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Purpose of Study: The purpose of this study was to determine the utility of TORCH titers screening, urine CMV screening, and cranial ultrasounds in the diagnosis of congenital TORCH infections in small for gestational age infants.

Methods Used: A retrospective review was conducted on all infants admitted to LAC+USC Medical Center from January 2009 to December 2011 with a diagnosis of SGA or IUGR. Birth characteristics such as birth weight, length, head circumference, and gestational age were recorded. TORCH titers results, urine CMV results, and cranial ultrasound (CUS) findings were collected. Additional data on maternal and infant conditions that could predispose to SGA status was also collected.

Summary of Results: During the study period, 60 infants with a diagnosis of SGA or IUGR were admitted to the NICU at LAC+USC Medical Center. Of these, 24 (40%) infants had TORCH tier testing. No positive immunoglobulin M results were found. Thirty infants (50%) had repeated urine CMV testing performed for a total of 88 urine CMV samples. Of these, only one sample was found to be positive and this infant wasn’t treated for congenital CMV infection. Fifty-two (87%) of the infants had a CUS done with none that were positive for calcifications.

Conclusions: TORCH tier testing and urine CMV screening is of low yield in SGA and IUGR infants. In addition, cranial ultrasounds are of low yield in screening SGA and IUGR infants for TORCH infections. We recommend screening clinically symptomatic SGA/IUGR infants.
DISTRIBUTION OF PLASMA LIPOPROTEIN SIZE IN PRETERM INFANTS IN THE FIRST MONTH OF LIFE
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Purpose of Study: The phenotype of increased plasma small LDL particles, small HDL particles and large VLDL particles is associated with coronary artery disease and metabolic syndrome in adults and insulin resistance and Type II diabetes in children. Preterm infants are particularly sensitive to the effects of inflammation, however, little is known about the concentration or predictive value of lipoprotein particles in preterm infants. Diet likely influences this composition, but this has not been explored. Our aim was to determine the concentration and size (small, medium, large) of lipoproteins HDL, LDL and VLDL in preterm infants in the first month of life and to correlate this with enteral and parenteral fat intake.

Methods Used: We collected plasma for lipoprotein analysis and breast milk, if available, for free fatty acid analysis from 15 infants, 5 each in the following gestational age groups: 27 weeks or less, 28-32 weeks and 33-36 weeks. Samples were collected at enrollment, two weeks and four weeks of age. Detailed medical, diet and exposure histories were obtained at the same time points.

Summary of Results: Total plasma HDL levels increased over time in all groups (p = .01). Total LDL levels decreased over time (< 0.05) in the 28-32 week gestational age group with similar trends in the other groups. Lipoprotein subclass analysis by particle size showed trends toward increased small LDL and large VLDL particles but no difference in small HDL particles in the <27 week infants compared to the other two groups at baseline and 2 weeks of age. Milk analysis is ongoing and should be completed by Nov 2012.

Conclusions: In this pilot study of premature infants, HDL particles increased over the first month of life as LDL decreased. We hypothesize that these changes are related to decreasing intravenous intralipid and increasing human milk consumption. Markers associated with insulin resistance appear to be increased in the most premature infants. Upon completion of the milk fatty acid analysis, we will look at possible correlations between dietary fat profile and plasma lipoprotein composition.
Summary of Results: Our results show that Keratocan expression localizes to nephric tubules and collecting ducts, Lumican expression is associated with nephric tubules, and Decorin expression surrounds Bowman’s capsules and nephric tubules. Correspondingly Lmx1b is expressed in Bowman’s capsule and in nephric tubules. Thus the expression of Lmx1b most closely aligns with the expression of Decorin.

Conclusions: Our data suggests that Lmx1b may regulate Decorin during nephrogenesis. The KLD genes are tightly clustered on the genome and have been shown to cross regulate each other during development. Thus, further research is needed to determine if temporal and/or sequential regulation of the KLD proteoglycans is responsible for their unique nephric distribution. Determining the mechanism by which Lmx1b regulates nephrogenesis may provide clues to and therapies for abnormalities of glomerular filtration.

Neonatal Pulmonary I Concurrent Session
12:30 PM Thursday, January 24, 2013
39

ROSIGLITAZONE INDUCES THE DEVELOPMENT OF MACROPHAGE M2 PHENOTYPE AND THE SUBSEQUENT EXPRESSION OF ANTIINFLAMMATORY SIGNALS
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Purpose of Study: Inflammation plays a key role in the pathogenesis of BPD. Inflammation is facilitated by the presence of PMN leukocytes and macrophages in the airway of preterm newborns. Recent studies have shown that macrophages have dual properties; M1 “classical pathway” and M2 “alternative pathway”. M1 initiates inflammation and M2 is involved in anti-inflammatory and repair after initial M1 activation. Preliminary evidence indicates M2 macrophages may be the predominant macrophage phenotype in preterm newborns and prevent or attenuate the development of BPD. In preterm newborns, macrophages exhibit a phenotype similar to M2 macrophages. The immunomodulatory properties of macrophages are under investigation. M2 macrophages have been shown to inhibit the pro-inflammatory effects of macrophages due to their role in the M2 phenotype and the production of anti-inflammatory mediators.

Methods Used: Using RAW 264.7 (a murine immortalized cell line) macrophages as a model for alveolar macrophages, we examined the effect of rosiglitazone (RGZ), a potent PPARγ agonist on their inflammatory profile under basal and lipopolysaccharide-stimulated conditions. At 60-80% confluence, cultured cells were treated with different doses of lipopolysaccharides (0, 1, 10, 100 ng/ml) with or without RGZ (0, 10 and 25 uM) for 24h. Subsequently, IL-6, IL-10 and TNF-α expression were assessed using ELISA.

Summary of Results: RGZ induces a dose-dependent inhibition of LPS-stimulated expression of the inflammatory mediators TNF-α and IL-6 in the RAW 264.7 cell line in vitro. RGZ did not cause stimulation of IL-10 expression.

Conclusions: RGZ inhibition of inflammatory mediators (TNF-α, IL-6) may involve pathways independent of IL-10. RGZ does not stimulate IL-10 under basal conditions but may do so under stress conditions. We speculate that PPARγ agonist-mediated protection against BPD is at least partially mediated via its effects on alveolar macrophage polarization.
Purpose of Study: Intrauterine growth restriction (IUGR) increases neonatal lung disease and alters the structure of the developing fetal lung. Appropriate lung structure depends upon the precise and coordinated expression of genes regulating lung development. The expression of genes is regulated by epigenetic mechanisms, such as histone modifications. Histone 4, lysine 20 (H4K20me) is a histone modification important in regulating genes that contribute to lung development. H4K20Me is placed by the histone methyltransferase, Setd8. We previously showed that IUGR decreases Setd8 expression in male and female rat lung and that this can be reversed with the addition of a diet high in unsaturated fats. However, the typical Western diet is high in saturated fats and a maternal diet high in saturated fat (HFD) is independently associated with alterations in lung development.

We hypothesize that a maternal HFD in combination with IUGR will decrease Setd8 mRNA levels beyond that of IUGR alone, in newborn rat lung.

Methods Used: IUGR was induced by bilateral uterine artery ligation at E19 of gestation. Maternal rats were fed either Standard Rat Chow or HFD chow prior to mating and during gestation. Real-time RT-PCR was used to measure mRNA levels of Setd8 in the lung of rat pups at birth.

Summary of Results: Results are IUGR as % of sex-matched regular diet controls - SD. IUGR alone decreased Setd8 mRNA in both male (82 ± 7%*) and female lung (77 ± 12%*). In female lung, HFD alone did not alter Setd8 mRNA levels. HFD combined with IUGR decreased Setd8 mRNA (79 ± 11%*) in female lung, but not more than IUGR alone. In male rat lung, HFD alone increased Setd8 mRNA (132 ± 27%*). Setd8 expression in male and female rat lung and that this can be reversed with the addition of a diet high in unsaturated fats. However, the typical Western diet is high in saturated fats and a maternal diet high in saturated fat (HFD) is independently associated with alterations in lung development.

We speculate that changes in Setd8 mRNA expression will be reflected by changes in protein levels of Setd8. These data suggest that it may be important to consider fetal sex in the approach to maternal diet in IUGR.

INTRAUTERINE GROWTH RESTRICTION ALTERS mRNA TRANSCRIPT LEVELS OF AROMATASE AND SURFACTANT PROTEIN IN NEONATAL RAT LUNG


Purpose of Study: Intrauterine growth restriction (IUGR) alters lung development and increases the risk of bronchopulmonary dysplasia (BPD), with male infants more affected. Androgens are significantly elevated at birth and delay surfactant production in the lung while estrogens expedite this process. The cytochrome P450 enzyme aromatase maintains tissue balance of androgens to estrogens and delay surfactant production in the lung while estrogens expedite this process. The cytochrome P450 enzyme aromatase maintains tissue balance of androgens to estrogens. It is unknown whether IUGR impacts mRNA transcript levels of aromatase and surfactant proteins in the neonatal rat lung. We hypothesize IUGR alters aromatase mRNA levels in a sex-specific manner in association with decreased surfactant protein mRNA production in males.

Methods Used: IUGR was induced by bilateral uterine artery ligation at day 19.5 of gestation in Sprague-Dawley rats. Lungs of IUGR male and female pups were compared to sex-matched controls at day 0 (prior to alveolar formation) and day 7 (mid-alveolar formation). Aromatase and Surfactant Protein A-D (Sfanp-A-D) mRNA transcript levels were quantified in whole lung by real time RT-PCR.

Summary of Results: At day 0, IUGR decreases aromatase mRNA transcripts in fetal rat lungs relative to female controls (64%, p<0.05), with no significant change in male rat lungs. Additionally, both IUGR females and IUGR males have decreased Sfph (p=0.1), as well as Sfph, SfphC, and SfphD mRNA levels at birth relative to sex-matched controls. By day 7, IUGR males have significantly increased aromatase mRNA levels and increased surfactant protein mRNA levels (p<0.05) compared to all other groups.

Conclusions: We conclude that IUGR influences aromatase mRNA levels in a sex-specific manner. IUGR also decreases surfactant protein mRNA expression prior to alveolarization. We speculate that IUGR increases local androgen to estrogen levels in the lung, decreasing surfactant production at birth.
INVESTIGATION OF MATERNAL, FETAL, AND UTEROPLACENTAL HEMODYNAMICS IN HIGH RISK PREGNANCIES


Purpose of Study: Our objective was to examine the correlation between noninvasive measures of maternal, fetal, and uteroplacental hemodynamic function at mid-pregnancy in a cohort of pregnancies at high risk for adverse outcomes.

Methods Used: A cohort of subjects with risk factors for uteroplacental dysfunction was recruited between June 2011 and August 2012 from the UCSD Placenta Clinic. Maternal cardiac output (CO) and systemic vascular resistance (SVR) were measured non-invasively by electrical impedance cardiography (Aesecum, Cardiozoom, Inc.) in the supine position. Uteroplacental vascular resistance was estimated by uterine artery Doppler ultrasound (pulsatility index, PI). Fetoplacental vascular resistance was estimated by umbilical artery Doppler (systolic/diastolic ratio, S/D). Fetal and placental growth were analyzed as the % estimated fetal weight (EFW%) and the ratio of placental width to length (W/L). Spearman’s R correlations are reported with significance set at alpha = 0.05.

Summary of Results: 38 of the recruited patients completed all studies. The median gestational age was 24.6 weeks, and 44% of subjects were nulliparous. Maternal hemodynamics (CO and SVR) correlated significantly with umbilical S/D (R = 0.44 and 0.46, respectively, p < 0.05), but not with uterine PI, EFW%, or placental W/L (p > 0.05). Uterine PI correlated very significantly with placental W/L (R = 0.53, p < 0.001), but not with S/D or EFW%. EFW% demonstrated a nearly significant correlation to placental W/L (R = 0.31, p = 0.06) and maternal blood pressure (R = 0.31, p = 0.06).

Conclusions: There is a significant correlation between maternal hemodynamics (CO, SVR) and fetoplacental vascular function (umbilical artery S/D) which is independent of the uterine circulation. The uteroplacental circulation does, however, correlate with placental size, but at mid-pregnancy, there is not yet a strong correlation to fetal growth (EFW%). Based on these findings, we speculate that maternal hemodynamics are influenced by factors that mediate placental vascular growth (e.g., angiogenic factors), and that the uterine circulation is refractory to these signals at mid-pregnancy.

CHRONIC ANEMIA AFTER HEART TRANSPLANTATION: IS IT A MARKER FOR POOR OUTCOME?


Purpose of Study: Chronic anemia (CA) has been found to be a marker for poor outcome in many disease states. In heart failure patients (pts) it has been associated with increased morbidity and mortality. A similar association has not been demonstrated in heart transplant pts. After transplant, chronic renal insufficiency may result in CA as well as immunosuppressive agents affecting red blood cell counts. These factors must be taken into account when analyzing the effects of CA in this pt population. The purpose of this study is to assess the effects of CA on long term outcome after heart transplantation while compensating for risk factors such as chronic renal failure and over immunosuppression.

Methods Used: Between 1994 and 2010, we evaluated 484 heart transplant pts who developed CA in the 1st year following heart transplantation. All study pts had conditional survival of up to 1 year. Pts with serum creatinine greater than 2.0mg/dl were excluded from the study. Anemia was defined as the average of 10 blood draws obtained at the time of routine follow-up. Pts were divided into three groups: Hemoglobin greater than 13, between 11-13, and less than 11. The 3 groups were then compared for 5-year subsequent outcome of survival and freedom from transplant coronary disease and non-fatal major adverse cardiac events (NF-MACE, defined as myocardial infarction, heart failure, need for percutaneous cardiac intervention, stroke).

Summary of Results: Pts with CA had a trend for lower survival in the subsequent 5 years, but had similar incidence of transplant coronary disease and NF-MACE (see table). Freedom from rejection was significantly lower in the anemia group. This may represent more immunosuppression thus resulting in more CA.

Conclusions: CA in the first year after heart transplantation appears to be associated with poor outcome. Mechanisms may be related to chronic renal

Methods Used: Between 2000 and 2010, we evaluated 134 heart transplant pts and divided them into those that developed LVH less than 1 year after transplant and those that developed LVH more than 1 year after transplant.

All patients had normal cardiac function (LVEF > 50%) and had no active rejection at the time. A contemporaneous control group matched 1:1 for age, sex and time from transplant to the diagnosis of LVH for each study group was established. All pts were followed for 5 year subsequent survival, freedom from cardiac allograft vasculopathy (CAV) and non-fatal major adverse cardiac events (NF-MACE, defined as myocardial infarction, heart failure, need for percutaneous cardiac intervention, stroke).

Summary of Results: The pts with LVH less than 1 year compared to their matched control group had a trend for less freedom from subsequent 1-year any-treated rejection although 5-year survival and freedom from CAV and NF-MACE were similar. The pts with LVH greater than 1 year compared to their matched control group had a trend for less subsequent 5-year survival although 5-year freedom from CAV and NF-MACE and 1-year any-treated rejection were similar. (see table)

Conclusions: Left ventricular hypertrophy less than 1 year after transplant may be related to the development of rejection although it does not appear to alter long-term outcome. For left ventricular hypertrophy greater than 1 year after transplant, there may be mortality risk possibly due to other factors such as chronic hypertension.

New Onset Left Ventricular Hypertrophy After Heart Transplantation: What Is The Meaning?

Osborne A, Rajefi M, Razi R, Hamilton M, Kobashigawa J. Cedars-Sinai Heart Institute, Los Angeles, CA.

Purpose of Study: Left ventricular hypertrophy (LVH) in donor hearts at the time of heart transplantation has been reported to have poor outcome possibly due to decreased penetration of preservation solutions and subsequent immunosuppression medications. Some heart transplant patients (pts) develop LVH after transplantation which may be scattered in the first year or thereafter. These pts are not having rejection by heart biopsy and have normal systolic cardiac function. It has not been established as to outcomes of these pts who develop subsequent LVH after heart transplantation.
insufficiency and more immunosuppression due to rejection, however, other factors may be involved. It is unclear as to whether treatment of the anemia results in better outcome. A larger cohort of pts need to be studied.

<table>
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<th>OUTCOMES</th>
<th>Hgb &lt; 11 (n = 106)</th>
<th>Hgb 11 - 13 (n = 356)</th>
<th>Hgb &gt; 13 (n = 22)</th>
<th>Log-Rank p-value</th>
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<td>Subsequent 5-Year Actuarial Survival</td>
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<td>83%</td>
<td>90%</td>
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<td>Subsequent 5-Year Freedom from CAV</td>
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<td>70%</td>
<td>75%</td>
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<td>Subsequent 5-Year Freedom from NPMACG</td>
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<td>90%</td>
<td>86%</td>
<td>0.828</td>
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<tr>
<td>Subsequent 1-Year Freedom from Any-Treated Rejection</td>
<td>95%</td>
<td>99%</td>
<td>100%</td>
<td>0.002</td>
</tr>
</tbody>
</table>

49

RIGHT VENTRICULAR LEAD PRECLUSION BY MECHANICAL TRICUSPID VALVE

Rafael A, West MB. University of New Mexico, Albuquerque, NM.

Case Report: A 69 year-old female with a history of tricuspid valve replacement (TVR) was referred for a new dual chamber pacemaker (PM). During TVR surgery a single epicardial lead with an abdominal pulse generator were implanted. Interrogation revealed non-capture and increasing output produced diaphragmatic contractions. The presence of a mechanical TVR precluded placement of a right ventricular (RV) endocardial pacing electrode.

After positioning the atrial lead, great care was taken not to cross the TVR as the coronary sinus (CS) was accessed for left ventricular (LV) lead placement. The lead was advanced through the sheath over a wire into an optimal LV pacing site (Figure). With excellent threshold data and no phrenic stimulation the leads were secured. The new PM was inserted into a percutaneous pocket and the generator in the abdomen was removed.

LV lead placement in dual chamber PM implantation is uncommon. Only one other case has been reported in the U.S. and in 1970 Anagnostopoulos described LV lead placement in a coronary vein in single lead PM implantation. In each of these cases the patient presented with a prosthetic TVR.

As our population ages, challenging situations present more frequently warranting creative techniques and alternative methods. Our case emphasizes the value of improvisation and encourages innovation.

Figure: Left ventricular lead advanced over wire to anterolateral position (black chevron); arrow - mechanical tricuspid valve; white chevron - epicardial lead from abdominal pacemaker.

50

EDUCATING THE ELDERLY OF BAKER, MONTANA ABOUT HEAT-RELATED ILLNESS

Carson LW. University of Washington, Seattle, WA.

Purpose of Study: Hot weather events claim more lives in the United States than any other natural disaster or weather event and disproportionately affect the elderly population, which is the highest-risk group for heat-related illness. Montana experienced record population heat during the summer of 2012. The purpose of this project was to educate the elderly and their caregivers in the community of Baker, Montana about how to prevent and treat heat-related illness such as heat stroke and heat exhaustion.

Methods Used: Five staff members from various fields at the Fallon County Medical Complex were interviewed about the city of Baker’s community health needs. Education of the elderly about heat-related illness was deemed by local staff to be the topic most relevant to the community of Baker. A literature review revealed that public education is an effective intervention for preventing heat-related illness in the elderly. The Activities Coordinator for the retirement community and long-term care facility reserved the dining room of the facility, and advertised the event on bulletin boards, in the local newspaper, and on local television. An educational PowerPoint presentation about heat illness with an emphasis on the elderly and their caregivers was developed and presented.

Summary of Results: The event was attended by twelve people and included seniors from the community and from the long-term care facility and medical staff. It appeared that the event was well received; the audience actively participated and informal feedback after the event was positive.

While the event was well attended by medical staff, the attendance by seniors was less robust than anticipated. In the future, increased attention paid to the venue and the timing of the educational event might help to increase attendance of the elderly.

Conclusions: Heat-related illness is a serious life-threatening condition that disproportionately affects the elderly population. As the climate continues to change and regions of the United States continue to experience hotter than usual weather, heat-related illness is likely to increase in our elderly populations in Montana and across the nation. Educating the elderly and their caregivers about heat-related illness will be a crucial part of mitigating heat’s dangerous effects on the elderly.

51

ADDRESSING HYPERTENSION THROUGH LOCAL DIETARY OPTIONS IN REXBURG, IDAHO

Stecker L. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Implement a simple dietary guideline to increase consumption of heart healthy food and help lower blood pressures. Rexburg, ID like most rural towns has a high prevalence of hypertension and other diet related morbidities. Studies show that successful implementation of Dietary Approaches to Stopping Hypertension (DASH) can have a significant impact on lowering blood pressure, but getting populations to adhere to a DASH diet is a constant struggle. This intervention identifies healthy local foods and addresses questions related to hypertension and diet.

Methods Used: Research indicates that tailored at home interventions can increase dietary knowledge but do not increase adherence to DASH diets. This project targets food purchased on site at the grocery store instead of home education. Small colored 1”x2” colored cards marked “heart healthy” were placed next to the price tag of specific food items. Flyers with a grocery list targeting foods rich in potassium, magnesium, calcium, vitamin D, and Omega 3’s were displayed and distributed. The flyer included information on the DASH diet with links to recipes available through the Mayo clinic. A table was set up with flyers in Broulim’s for 4 hours to measure blood pressures and answer questions about hypertension and diet.

Summary of Results: More than 50 food items were tagged, 20-30 local residents had blood pressure measured and 50 flyers we taken on site. Residents who had their blood pressure measured were more receptive to talking about the effects of hypertension, but many shoppers noted the grocery list with interest. Food tags will be updated twice a semester for the next year with flyers available at the Broulim’s service desk and in the lobbies of local health clinics.
Conclusions: Hypertension was not clearly understood by many residents though most knew that improving diet could positively affect the heart. Many felt dieting was confusing and difficult in general. The aim of encouraging change through small increments and simplification of healthy food was positively received. DASH diets do not introduce new concepts residents have not heard before, but continual visual reminders placed on food may encourage them to try options that differ from their routine, and over time may affect change in a positive direction.

Poster Session I Community Health

2:30 PM Thursday, January 24, 2013

52

SHOULD CADAVER LAB BE INTRODUCED TO PREMEDICAL STUDENTS IN AN EFFORT TO PROMOTE THEIR INTEREST TOWARDS HEALTH CAREERS?


Purpose of Study: Innovative programs to increase the interest of under-represented minority (URM) youth in health careers are needed. The goal of this study was to determine whether introducing high school and undergraduate students to the cadaver lab will increase their interest in health careers.

Methods Used: As a part of a two week summer program at the UC Irvine School of Medicine, high school and college students spent half a day in the cadaver lab and learned about different organ systems in the human body. The students were divided into groups of 7-8 and rotated through different stations that represented different organ systems. Each station was run by a medical student who had an interest in teaching. In addition to a group reflection session, feedback surveys were distributed to the participants. The students were asked to evaluate the effectiveness of the cadaver lab on a scale of 1 to 5, one being least effective in inspiring the students to pursue a career in health care and five being the most effective.

Summary of Results: A total of 250 high school students and 30 college students participated in the program during the summers of 2010, 2011 and 2012. Of 280 students, 84 (30%) were URM. The average rating for the cadaver lab in promoting interest in health careers was 4.44. The average rating was not different among URM vs. non-URM students. Some of the qualitative reflection comments included: “The cadaver lab was an amazing experience…For me to hold a real human brain up close and to be told about the harmful effects of drugs was more compelling than merely being told not to use drugs in a classroom...It was very hands-on and inspiring...I opened my eyes to what medical profession held for me, very different than any previous dissection experience…” Although a couple of the students got lightheaded at the beginning because of the formaldehyde smell, none of the students suffered any serious harmful effects. Some of the student reflections included: “It was very hands-on and inspiring...I opened my eyes to what medical profession held for me, very different than any previous dissection experience…” Although a couple of the students got lightheaded at the beginning because of the formaldehyde smell, none of the students suffered any serious harmful effects. Some of the student reflections included: “It was very hands-on and inspiring...I opened my eyes to what medical profession held for me, very different than any previous dissection experience…” Although a couple of the students got lightheaded at the beginning because of the formaldehyde smell, none of the students suffered any serious harmful effects. 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Conclusions: The cadaver lab was an effective way of promoting their interest in health careers.

54

EFFECT OF PROVIDING COURSE CREDIT ON DROP-OUT RATES IN A MENTORSHIP PROGRAM


Purpose of Study: Diversity in healthcare is becoming more and more important. Therefore effective mentorship programs that promote the interest of underrepresented minority (URM) in healthcare are needed. In this study, we evaluate the effect of providing undergraduate course credit to mentors on the drop-out rate of the mentor/mentee pair from a mentorship program.

Methods Used: In 2009, we implemented a program where undergraduate students were matched with URM high school students through an application process and provided one-on-one mentorship throughout the academic year. In addition to providing guidance and counseling for college entrance, the mentor guided the mentee towards the completion of a project related to a health challenge in their underserved community. Both mentors and mentees stated their interests and their future goals on the applications. The one to one match was made mainly based on shared interests and goals.

Summary of Results: Between 2009 and 2012, we matched a total of 63 mentors and mentees. There were 12, 23, and 28 matches made in 2009-2010 and 2011 respectively. Course credit was offered during 2011-12 academic year only. Of 12 pairs whose mentors took credit for this activity, all mentees stayed in the program until the end of the academic year. While 51 pairs whose mentors did not get credit for the activity, only 26 (51%) completed the program (p<0.05).

Conclusions: Our data suggests that giving course credit for outreach mentorship programs increases retention rates. Further studies are needed to study other variables that may affect retention rates in health-related mentorship programs.

55

THE EFFECTIVENESS OF DELIVERING HEALTH EDUCATION MODULES TO STUDENTS IN REMOTE NORTHERN INDIA


Purpose of Study: Since 2007, UBC students have traveled to Spiti Valley, a remote region in the Indian Himalayas, to work with the community to improve the health of students at Munsel-ling School. Previous community needs assessments identified a lack of education regarding personal health and hygiene. In collaboration with local teachers and health workers, health education modules covering oral health, personal hygiene, water and sanitation, and diarrheal disease were delivered to 517 students. In 2012, the health education curriculum and teaching responsibilities were transferred over to senior students on the Students’ Health Council (SHC). The purpose of this study was to evaluate knowledge retention and the effectiveness of knowledge transition and teaching of health education modules.

Methods Used: Before engaging in health education in 2012, baseline knowledge quizzes were distributed to classes 5, 7 and 10. The same quizzes...
were distributed at the conclusion of the 2011 research period, and the results from both were compared to analyze knowledge retention over one year. Following the distribution of baseline quizzes, transition of all teaching material to the SHC was carried out. The modules were delivered by the SHC to classes 5 and 7, and the quiz was distributed afterwards to evaluate the effectiveness of the teaching. The modules included: (1) Oral health and personal hygiene, and (2) water safety, GI, diarrhea & worms.

**Summary of Results:** Data from the baseline quizzes indicate no significant decline in health knowledge over one year. Furthermore, the results from the post-module quizzes indicate improvement in health knowledge for both class 5 and 7 students after attending modules taught by senior students, with significant improvement demonstrated amongst the Class 7 students (p=0.0013).

**Conclusions:** The findings of these evaluations provide encouraging information about the effectiveness of the health education modules with respect to knowledge retention and sustainability of the health education program. Future directions include continued support and evaluation of health education teaching by the SHC to achieve sustainability of the program and improve the modules to better meet the health needs of the local students.

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**56**

A COMMUNITY-PARTNERED APPROACH TO DEVELOPING A MATERNAL AND NEWBORN CHILD HEALTH PROGRAM FOR RURAL VILLAGES IN NORTHERN INDIA

Walsh C, Wei JJ, Walsh C, Ory J. University of British Columbia, Vancouver, BC, Canada.

**Purpose of Study:** Since 2010, the University of British Columbia's Global Health Initiative (GHI) has established a partnership with a non-governmental organization (NGO) in the northern Indian Uttarakhand province. This NGO’s work focuses on health, education, and advocacy for women and girls. GHI undertook a needs assessment in this community to better understand the challenges present and to develop a collaborative framework to address the Millennium Development Goals of improving maternal health and reducing child mortality.

**Methods Used:** Our team conducted several focus groups with 29 women in rural Uttarakhand. Our goal is to better understand the resources currently available to women, the barriers to accessing these resources, and the cultural elements that limit health. The focus groups identified several areas for the NGOs and for our UBC team to address through education and other interventions.

**Summary of Results:** Adolescent girls cited dietary limitations at home due to food shortages and priority that allows boys to eat first. Many girls admitted to feeling that they are a burden to their families. The girls receive less education than boys and have less understanding of health; no health or sexual education is provided to them. Women are financially dependent on men and have limited autonomy. As such, women often cannot access medical services and are left vulnerable to domestic violence. During pregnancy, they are expected to contribute fully to farming. Access to health care providers is limited due to distance to health care centres and inconsistencies in government-delivered programs that leads to a lack of trust.

**Conclusions:** Currently, the UBC team provides an annual three-day workshop to NGO field workers. Collaborative maternal and adolescent girls workshops are ongoing in the communities. The goal is to gain local support and to ensure sustainability through engagement of local midwives, community leaders, and training of community health workers.

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**Poster Session 1
Health Care Research**

2:30 PM
Thursday, January 24, 2013

**57**

ROOM TO IMPROVE: INFREQUENT USE OF BEHAVIOR CHANGE COUNSELING AND PATIENT-CENTERED COMMUNICATION WITH DIABETIC PATIENTS IN A SAFETY NET CLINIC

Chen KL,1,2. Ratanawongsa N2, 1UCLA, Los Angeles, CA and 2UCSF, San Francisco, CA.

**Purpose of Study:** Behavior change counseling (BCC) related to exercise, diet, smoking cessation, and medication adherence may empower diabetic patients to practice more effective self-management, contributing to improved knowledge, glucose self-monitoring, lifestyle choices, and cardiovascular control. Another correlate of better diabetes self-management is patient-centered communication (PCC), in which clinicians respect patients’ needs and priorities to facilitate individualized care and shared decision making. This study tested the hypothesis that healthcare providers would demonstrate variable skill in behavior change counseling, and particular behavior change strategies would be associated with more patient-centered communication.

**Methods Used:** We videotaped English- or Spanish-speaking adults ≥18 years old with diabetes mellitus during visits with their primary care providers and/or subspecialist providers at a public safety net hospital, coding patient-centered and BCC behaviors; we then calculated clinicians’ PCC scores (range 0-3) across specific BCC strategies. Patients also completed telephone surveys about ratings of quality of care and sociodemographic characteristics (n=10; 70% women; average age 53±158; 80% minority; 50% Spanish language preference).

**Summary of Results:** In general, encounters (n=13) were dominated by medication management discussions, and BCC (62% of visits) focused on adherence to diabetes medications (38%) more often than other BCC topics (diet 31%, exercise 23%, smoking 23%). Providers used a variety of BCC strategies, but certain strategies, such as collaborative agenda-setting and asking about the patient’s feelings about current behavior, were associated with higher average PCC scores. Clinicians with PCC scores ≥1.5 were more likely to be rated as providing “excellent” care in the last 6 months (100%), compared with those with scores <1.5 (63%; p=0.019).

**Conclusions:** Clinicians may need more training to engage in diverse BCC topics, beyond medication adherence. Training may also help clinicians use a more robust toolbox of behavior change counseling strategies, which could ultimately help them provide more patient-centered care to patients with diabetes and thereby improve patient self-management and disease outcomes.

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**58**

AWARENESS OF SICKLE CELL GENOTYPE AMONG NIGERIANS IN THE UNITED STATES

Shahani S1. Ezaneloue EE1, Obaro S2. 1University of Nevada School of Medicine, Las Vegas, NV and 2University of Nebraska, Omaha, NE.

**Purpose of Study:** Nigeria has the world’s highest incidence and prevalence of sickle cell disease (SCD) with an estimated 20 births per 1000 live births occurring in a child with SCD. We surveyed a group of Nigerians living in America to determine awareness of their sickle cell (SC) genotype, their spouse’s SC genotype and when they became aware of spouse’s genotype. We also sought to determine their perception of when an individual should be made aware of their SC genotype to have the greatest impact on marriage/procreation choices. Access to health care and receiving SC genotype were associated with more patient-centered communication (PCC), in which clinicians respect patients’ needs and priorities to facilitate individualized care and shared decision making.

**Methods Used:** Self-administered survey were made available to all participants attending the annual 2012 convention of the Association of Nigerian Physicians in America held in Las Vegas, NV. Survey questions included: demographics (age, gender, birthplace, occupation, marital status); awareness questions (awareness of own SC status, awareness of spouse’s SC status, when became aware of own and spouse’s status and if had relatives with SCD); perception questions (best time to be tested for the SC gene, best time to become aware of SC genotype to have greatest impact on marriage/procreative choices). Data was analyzed using Survey Monkey software. Study was approved by the Institutional Review Board of the University Medical Center of Southern Nevada.

**Summary of Results:** Response rate was 36.5% (73/200). Majority of respondents were aged 50-59 (38.4%, 28), male (64.4%, 47), Nigerian born (85.5%, 59), physicians (79.5%, 58), and married (84.9%, 62). Majority of respondents were aware of their SC status (94.5%, 69), their spouse’s status (85.5%, 53), became aware of their status during university education (41.2%, 28), their spouse’s status prior to marriage (65.4%, 34), and did not have immediate family members with SCD (89%, 65). Majority of respondents think most important time to get tested for SC gene is at birth (87%, 64), while awareness before wedding would have the greatest impact on marriage/procreative choices (31.9%, 23).

**Conclusions:** Although most participants in this survey were aware of their own SC genotype, 35% did not become aware of their spouse’s SC genotype until after marriage. Awareness of SC genotype before marriage should be
encouraged in communities with high prevalence of sickle cell trait to better inform life decisions.

Methods Used:
Using a 2011-dollar base, we itemized all costs associated with our previous traditional nursing skills fair education and our current multidisciplinary simulation based nursing education program on a per nurse basis. Using a line-by-line comparison, we determined specific areas of cost increase associated with the simulation program. These differences were then compared to existing literature to determine if the higher costs are justified.

Summary of Results: Nursing education time is similar before and after. There is a 3-fold increase in cost per nurse associated with the change to a multidisciplinary simulation approach to education. This increase is explained by the inclusion of multidisciplinary team members (i.e., MD involvement) and the additional time spent on quality improvement efforts stemming from systems errors identified during simulation debriefing sessions. Conclusions: Though the dollar-to-dollar comparison shows a significant increase in cost when comparing multidisciplinary simulation based nursing education to traditional skills fairs, our analysis demonstrates that the benefits outweigh the increased costs. Multidisciplinary teams function better and there are several quality improvements that have resulted from simulation sessions. Future work will include a return on investment analysis based on money saved through risk reduction after initiation of the multidisciplinary simulation program.

Table. Medical ID Use and Reasons for Non-adherence in Percentage (N=185)

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>Ant ID</th>
<th>Jewelry</th>
<th>Wall Cut</th>
<th>UEFA Card</th>
<th>UB Driver</th>
<th>No ID</th>
<th>Nobody Recommended</th>
<th>Cost</th>
<th>Don't Know Where to Buy</th>
<th>Don't Want Everyone to Know Medical Problem</th>
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ICE=Cell Phone In-Case-of-Emergency info. *p<0.05, **p=0.05 within

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Volume 61, Number 1, January 2013
EMPOWERING URBAN LATINOS SEEKING MENTAL HEALTH SERVICES WITH CULTURALLY APPROPRIATE INFORMATIONAL MATERIALS ON DEPRESSION AND ANXIETY

Monico-Cristales NS. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Limited access to culturally appropriate mental health services for low-income or uninsured patients, including access to primary care providers sensitive to depression-like symptoms in Latinos and cultural stigma, are major barriers for Latino patients seeking mental health care services. This project attempted to provide culturally appropriate mental health information and identify low-cost, culturally sensitive services for Latinos seeking mental health care in Seattle, Washington.

Methods Used: Health Care Staff and Latino patients at North Seattle Public Health Center (NSPHC) were consulted for culturally appropriate explanations and terminology regarding mental health, including depression and anxiety. In addition, existing mental health literature, such as pamphlets, patient questionnaires targeting Latinos, were consulted. A literature review gave explanatory models, socio-cultural stigma, perceptions on medication and diagnosis, and common experiences of depression and anxiety. “Key Sites” for flyer distribution were identified from Spanish-speaking residents of Seattle, including staff at NSPHC, medical students. Flyers were discussed and distributed with Spanish-speaking residents of White Center at bus stops, businesses, parks, and NSPHC.

Summary of Results: An informational flyer was developed based on these findings and highlighted general definitions of depression and anxiety, local services geared towards Latino community, and the importance of validating the physical and social impact of these conditions. Nearly fifty flyers were distributed and discussed in “key sites” over two days.

Conclusions: Urban Latinos continue to battle disproportionate disparities in health care, including access to mental health care. Low availability of mental health services for uninsured patients, and low availability of primary and mental health care providers sensitive and fluent in depression-like symptoms in Latinos, and cultural stigma often result in undertreatment in this community. Empowering Latino patients, their families, and communities, with culturally appropriate information can normalize discussion around mental health care and increase access to services.

OUTCOME OF PATIENTS IMMOBILIZED BY ED STAFF, BUT NOT BY EMS PROVIDERS

Tello RR, Braude D, Fullerton L, Froman P. University of New Mexico School of Medicine, Albuquerque, NM.

Purpose of Study: Prehospital selective cervical spine immobilization (SCSI) is a relatively new concept. In our EMS system, protocols for SCSI are widely used, yet some patients who are brought to the hospital without cervical spine immobilization (CSI) undergo secondary immobilization and cervical spine imaging in the Emergency Department (ED). Immobilization in the ED after a decision not to immobilize by EMS suggests, either the prehospital assessment is not trusted, or the patient has developed new symptoms over time. We undertook a Quality Assurance study to evaluate whether trauma patients brought to the ED without CSI, who then underwent secondary CSI and imaging in the ED had injuries that were initially missed by the EMS SCSI protocol.

Methods Used: Albuquerque Ambulance Service (AAS) is the primary transport service for Albuquerque, N.M., and surrounding areas. AAS responds to over 100,000 emergency 911 calls annually. A 36-month retrospective data analysis from March 2009, until February 2012, identified patients transported by AAS from the field to the University of New Mexico Hospital, New Mexico’s only level one trauma center. Inclusion criteria were: category trauma, age 18 years and older, transported by AAS without CSI, and cervical spinal imaging done in the ED. Patients were excluded if they were: pediatric, inter-facility transports, prisoners, or refused CSI. A positive finding was defined as any abnormality found on the cervical spinal imaging studies.

Summary of Results: 112 patients met inclusion criteria and were included in the study. Of these, only 1 patient was found to have a cervical spinal fracture: a non-united C2 fracture, which was likely an old fracture and did not require any treatment in the ED. However, this was a 91 year old patient who had a fall from standing and should have been immobilized per our SCSI protocol.

Conclusions: In this retrospective Quality Assurance study only one patient who underwent secondary CSI and imaging in the ED had a cervical injury, and no patients had any adverse effects, or required treatment. A larger study with a sample size of at least 800 patients would be required to confirm our findings with statistical certainty. In the interim, it appears hospital personnel should have confidence in prehospital decisions regarding CSI.

A PILOT STUDY TO IMPROVE IMMUNOSUPPRESSANT MEDICATION ADHERENCE IN ADULT KIDNEY TRANSPLANT RECIPIENTS

Hendren E, Gill J. University of British Columbia, Vancouver, BC, Canada.

Purpose of Study: Kidney Transplant recipients must take immunosuppressant medications regularly (usually twice daily) to avoid rejection of the transplanted kidney. Non-adherence with immunosuppressant medications (NA) is a common problem (estimated prevalence 22.6 cases /100 patient years), causing 50% of late rejection episodes after the first post transplant year, and is estimated to be the cause of approximately 15% of all transplant failures. Importantly minor deviations in immunosuppressant drug dosing may lead to rejection (i.e. taking < 95% of medications as prescribed). Recent advances in immunosuppressant medications have allowed for once daily immunosuppressant dosing. Once daily dosing along with novel behavioral modification strategies may help improve adherence but have not been systematically tested in the kidney transplant setting.

Methods Used: A literature search was performed to identify medication adherence programs that currently exist and analyze their effectiveness. Then several mobile app developers were contacted to determine the cost and logistics of implementing their program.

Summary of Results: Based on our research, we propose a pilot study of n = 50 kidney transplant recipients at least 3 years post transplantation to determine the impact of switching patients to a once daily immunosuppressant medication regimen and a mobile phone medication tracking application on adherence. Adherence will be measured by novel strategies including a patient survey instrument as well as a novel surrogate biochemical test (i.e. variability in drug levels).

Conclusions: We will review the protocol for the proposed pilot study that includes both novel strategies and novel methods of adherence measurement that will be applied for the first time in a controlled study in kidney transplantation. The pilot results will inform the design of a definitive Canadian multi-center study.

HOW MANY WORK HOURS ARE REQUISITE TO PUBLISH A MANUSCRIPT?

Song D1, Abedi N2, Arneja J1. 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: Advances in medicine are driven by propagation of research and dissemination of meaningful results. In clinical research, the most prevalent study design is a retrospective case series. Quantifying the time spent on a retrospective study from idea genesis to manuscript publication is an important metric for clinicians, students/trainees, as well as administrators in academic medical centers. It will allow appropriate allocation of funding for research-based activities including human capital, research infrastructure, academic surgeon compensation and for promotion/tenure purposes. The present study aims to quantify work hours associated with publishing a manuscript with a retrospective study design.

Methods Used: Following research ethics board approval, 16 surgeons with 5 or more published retrospective studies were selected to participate in this study; a survey was designed as the data collection tool. The subjects were asked to estimate the time spent in all previous publications with a retrospective study design as identified on PubMed. Specifically, subjects were asked to estimate time spent per member of the study team towards pre-study planning, literature review, ethics application, data collection and analysis, manuscript preparation and submission.

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SUMMARY OF RESULTS: The results of 171 returned surveys revealed that a median of 177 hours were spent per publication (range, 29 - 1287 hours). Papers with 3 authors made up the largest category (35% of all studies returned) and consist of the principle investigator, the co-investigator and a resident. On average, these individuals spent 38 hours, 18 hours and 51 hours per publication respectively.

CONCLUSIONS: Currently, there is the absence of a good metric in the literature quantifying the hours that go into publishing a retrospective study. Results of this study suggest that it takes a median of 117 hours to take a study from idea genesis to completion. These hours reflect a significant amount of dedication by the clinicians and residents that goes into publishing a retrospective study. We hope to provide the basis for future prospective research in this area to better assist resource allocation and stakeholder appreciation of this academic undertaking.

ADDRESSING UNDER-UTILIZATION OF FAMILY PLANNING SERVICES IN RURAL UGANDA THROUGH SIDE-EFFECT BASED EDUCATION OF HEALTH WORKERS

Wackerbarth J. 1 University of Washington, Seattle, WA and 2Makerere University, Kampala, Uganda.

Purpose of Study: The Kiboga district in rural Uganda has a total fertility rate of 7.2 children per woman. High births are associated with increased maternal and infant mortality and morbidity as well as lower economic indicators. Uganda has a high unmet need for family planning services, as well as low uptake when contraception is available, with fear of side effects being the most common reason for non-use. The purpose of the study was to increase usage of free district hospital family planning methods through directed post-partum counseling and community based education.

Methods Used: Educational materials were developed in English and Luganda that discussed the family planning methods available in the Kiboga district hospital. Locally relevant graphics and messages were used, and common misconceptions about family planning were addressed. The materials were distributed throughout the hospital after conducting a interactive presentation. In addition, a post-partum discharge checklist was created for the maternity ward that emphasizes the need to counsel post-partum women about the options of family planning.

Summary of Results: Sixty-five hospital staff members, including twenty-five nurses, participated in the presentation, and expressed interest and enthusiasm for the topic. Staff reported being motivated to include more directed family planning messages in post-partum education and in other clinical situations and improving family planning messages has become an administrative priority at the hospital. Eight nurses were individually trained with developed materials and there are plans to train ten village health team members and six lower level health centers. One outreach coordinator for a local community based organization received materials and training with emphasis on counseling men. Materials were universally well received and reported to be helpful for educational purposes. Impact on community uptake of family planning methods remains to be seen.

Conclusions: Increased awareness about the true benefits vs. risks of family planning offers a way to improve uptake of services and decrease birth rates. Additional community based strategies with an emphasis on social marketing of contraception and outreach to male heads of households are needed.

DELAIS ASSOCIATED WITH INPATIENT ADMISSIONS FROM THE EMERGENCY DEPARTMENT

Larsen C1,2, Colling D2,1, Maloney C1,2. 1University of Utah, Salt Lake City, UT and 2Primary Children’s Medical Center, Salt Lake City, UT.

Purpose of Study: Emergency department (ED) overcrowding is widespread. Prolonged stay of admitted patients in the ED is one factor. We hoped to identify consistent themes associated with prolonged ED stay.

Methods Used: Using electronic systems for tracking patient flow at Primary Children’s Medical Center, non-surgical patients admitted from January through July 2012 who had more than a 3-hour delay from bed request to arrival at the inpatient unit were identified and reviewed. Each patient was assigned a “delay” category based on the information available in the medical record.

Summary of Results: 142 patients (of 1536 non-surgical admissions) were identified and records reviewed. 42% were delayed due to continued medical treatment in the ED including: labs, imaging, procedures or medication administration. 12% were due to a prolonged time for an inpatient to become available. 10% did not have an identifiable factor contributing to the delay. 8% were not late arriving to the floor, but the electronic time stamp was not completed upon arrival to the inpatient room. Another 8% were late due to a delay in the accepting advertising hearing about or accepting the patient. Only 7% had a documented change in clinical status requiring further evaluation. Less frequently occurring categories included change in room assignment, systems errors, being asked by the floor to wait on transitions of the patient and going to the ICU prior to arrival to the floor.

Conclusions: Continued treatment was the most common theme noted for prolonged ED stay. Change in patient condition was an uncommon cause. Factors not related to ED processes appear to account for over 42% of delays. Retrospective review of the medical record has inherent limitations for developing delay themes. These results will direct a quality improvement project to improve the ED admissions process.
ABIRATERONE-ASSOCIATED DELIRIUM: RECURRENCE WITH RE-TREATMENT

Raymond LW1,2, Carr JP1, Only C1, Yoonmans J1, Salman JS1, 2Carolina HealthCare System, Charlotte, NC and 2University of North Carolina at Chapel Hill, Chapel Hill, NC.

Case Report: A 61 year old African Caribbean male mechanic treated for metastatic prostate cancer, progressive after orchectomy and 8 cycles of IV docetaxel (D), declined further D despite a drop in PSA (763-342). He agreed to oral abiraterone (AB) but 3 days after starting AB (1,000 mg daily plus prednisone, 5 mg twice daily), he disappeared for a day and was unreach-able by his daughter. He was disheveled with bizarre behavior on his return, with belongings and medications strewn about, and potted plants overturned on the rug. His daughter found kitchen concoctions unlit to eat, but no evidence of alcohol or drug abuse. Oncology advised no further AB. Confusion, disorientation and violent outbursts led his daughter to bring him to family medicine clinic, where he sat on the doctor’s lap, described hearing voices and was otherwise inappropriate. Routine and toxicological analyses and brain imaging were non-diagnostic. He was intermittently disoriented and confused and unraveled on the floor on hospital day 3 (HD 1-3) but returned to baseline and went home in his daughter’s care after HD 1-4. AB was restarted at 500 mg daily plus prednisone. His behavior became re-peatedly agitated and confused for the next 5 days until he was found by police wandering and disoriented in a vacant parking lot. He said AB “makes me crazy, confused, I hear voices and feel paranoid.” Readmitted to family medicine’s inpatient service, he was found by psychiatry to be manic, psy-chotic and in need of their inpatient care. Quetiapine (Q) was prescribed, but he became agitated on HD II-3, speaking in multiple languages and require-ing security to restrain him. He responded to increased Q dosage and ben-zodiazepine. Psychiatric re-evaluation on HD II-5 found him reconstituted but still hyperkinetic with an expansive affect. He was again discharged in the care of his daughter, to be followed by oncology, psychiatry and fam-ily medicine. His behavior was at his normal baseline for ensuing weeks with continued Q therapy but no further AB.

Conclusion: We suspect that an underlying bipolar affective disorder may have been unmasked by AB, versus a primary AI-induced delirium. No such adverse effects of AB have previously been described.

SKIN CANCER PREVENTION IN THE HISPANIC AGRICULTURAL COMMUNITY OF OTHELLO, WA

Aalami S. University of Washington, Seattle, WA.

Purpose of Study: Hispanic communities in the United States face a dis-proportionate skin cancer burden. Despite relatively low skin cancer rates, Hispanic populations are more likely to be diagnosed with skin cancer later, have more advanced lesions, and die from the disease. Hispanic communi-ties that perform agricultural work are at increased risk due to high UV radiation exposure. The purpose of this project was to increase skin cancer awareness and prevention behaviors amongst the Hispanic agricultural community of Othello, WA.

Methods Used: Community members were interviewed to assess current knowledge and behaviors. A literature review was performed to develop effective and evidence based educational materials. In collaboration with the Columbia Basin Health Association (CBHA), Adams County Health Department, Othello Police, New Hope, and several other community organi-zations, an educational event was held at the annual Othello Community Health Fair. Participants were educated on sun protection behaviors, self-skin examinations and the early signs of skin cancer, with an emphasis on cancer presentation in pigmented skin.

Summary of Results: There were 111 participants, 107 of which were members of the local Hispanic community. While the results of this project have not been formally assessed, the enthusiastic participation of the community was promising. Participants were given pamphlets in English and/or Spanish. The educational material was given to the Othello Community Health Fair coordinators for future health education, as well as the Othello Cancer Support Group.

Conclusions: Sun protective behaviors and self-skin examinations are es-sential to skin cancer prevention. These require regular attention in Hispanic agricultural communities like Othello, WA. Community-based education events like this one can help reduce the burden of skin cancer in these communities. Given community enthusiasm, this project may serve as a start-ing point for future skin cancer prevention education.

COMPARING THE EFFICACY OF GAS6/MER PATHWAY INHIBITORS Imer and UNC MER TKI WITH AND WITHOUT AN ADP INHIBITOR (P2Y1 AND P2Y12) IN VITRO AND IN VIVO

Law L, Branchford B, Brodsky G, Sumner M, Graham D, Di Paola J. CU Medical School, Aurora, CO.

Purpose of Study: Growth Arrest Specific gene 6 (Gas6) is a ligand that signals through the platelet surface Mer receptors, resulting in platelet acti-vation and thrombus formation through the intermediate molecules P13k and AKT, culminating in J3 integrin phosphorylation. ADP activates this same pathway through P13k, and it is our hypothesis that inhibiting the receptors for ADP should lead to greater inhibition of platelet activation, and further thrombus destabilization. This study investigates the novel anti-platelet agents Imer and UNC MER TKI in the presence of ADP inhibitors in order to further elucidate this pathway involved in platelet activation, and to assess if a combination of these agents lead to superior results.

Methods Used: We used in vitro and in vivo assays of human and mu-rine platelets to measure the effect of platelet inhibition of Imer and UNC Mer TKI with ADP inhibitors. In vitro studies included standard aggrego-metry and aggregate formation on collagen surfaces in a microfluidic flow chamber and flow cytometry. In vivo studies included a FeCl3-induced model of carotid artery injury and a collagen/epinephrine-induced pulmonary em-bolism (PE) model to compare thrombosis protection between lettermate C57BL/6 mice treated with inhibitors or vehicle control. A paired t-test was used to compare samples in aggregation, microfluidic flow surface area coverage, as well as elapsed time to initial and stable occlusions in the FeCl3model and survival time in the PE model.

Summary of Results: Results are pending

Conclusions: None to make yet

FAMILY HEALTH HISTORY & CANCER PREVENTION IN LATINOS OF SOUTHWEST SEATTLE

Delgado F. University of Washington, Seattle, WA.

Purpose of Study: Cancer is the 2nd highest cause of mortality in Latinos after heart disease. Both of these illnesses have genetic as well as envi-ronmental components. Although overall rates of incidence and mortality are lower in Latinos than Whites, Latinos are diagnosed at more advanced stages of common cancers. The goals of this project were threefold a) educate Latinos on the value of knowing one’s family health history b) connect La-tinos with community resources for cancer screening, c) ultimately increase patient-provider communication around family health history and early de-tection in the clinical setting.

Methods Used: A literature review was conducted to determine best practices for delivery of this project; published literature suggested collabo-ra-tion with community organizations, along with bilingual presentations for Latinos of all educational backgrounds. Clinical staff and providers were consulted. Educational posters were made; collaboration with community resources yielded helpful brochures. Using a supported family health history, community members were informed of sponsored cancer screening services and a sliding scale clinic at a community center health fair for almost 200 community members in Southwest Seattle. Motivational interviewing in Spanish and English was employed to empower community members to make lifestyle changes and to seek resources early to reduce cancer risk factors.

Summary of Results: This presentation served as a pilot for bridging the gap between environmental and genetic disease risk. All community mem-bers remarked that they had not seen a focus on family health history and wanted to learn more about how to communicate disease risk with their provider. Staff & community members stressed the importance of continuing to have providers address family health history in a culturally sensitive but helpful way.

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Conclusions: Awareness of familial health history has a role in preventive health, particularly in early detection for at risk families. Family health history may be more reliably acquired if patients feel that their family history is important in their own health. Community stakeholders, in partnership with providers, can mediate awareness of family health and promote healthy lifestyles, including regular cancer screening and access to primary care.

DIAGNOSTIC DISAGREEMENTS & ERRORS UNCOVERED DURING RESEARCH ACTIVITIES

Feng S1, Weaver D2, Reisch L1, Rendi M1, Goodwin A2, Geller IF2, Omga F3, Allison K1, Elmore J3, 1UW, Seattle, WA; 2UVM, Burlington, VT and 3Dartmouth, Hanover, NH.

Purpose of Study: Errors in medical diagnosis have been studied extensively, but less is known about discrepancies uncovered during research. We describe a framework for evaluating diagnostic disagreements discovered during a study of breast pathology interpretations and present our findings.

Methods Used: 407 breast biopsy samples, representing major diagnostic categories from non-proliferative to invasive cancer, were collected from Vermont and New Hampshire pathology registries and interpreted by an expert pathologist. Two additional study pathologists independently abstracted the original diagnosis from the original pathology report; reaching consensus using a modified Delphi method. Potentially significant disagreements, defined as those that might lead to a change in treatment, were identified between the expert, registry, and abstracted original report diagnoses.

Summary of Results: Of the 407 cases, overall agreement between the expert and registry diagnosis was 88%. Of 50 potentially significant disagreements, 3 were missing slides during the expert review, and therefore excluded from further review. Of 47 comparable disagreements, 10 were attributed to data errors (8 study-generated, 2 registry-generated); 38 to diagnostic disagreement, with 1 case being counted as a data error and a diagnostic disagreement. Study data errors resulted from multiple biopsies on the index date or multiple diagnoses per biopsy. Registry data errors were for invasive cases, with one being micro-invasion. Among the 38 diagnostic disagreements, the original pathologist noted that a case was borderline in 6 cases and the expert noted that 15 cases were borderline; with only 1 case considered borderline by both expert and original pathologist.

Conclusions: There is a high level of disagreement between pathologists not just diagnostically, but in recognizing what is a borderline case. Because borderline cases are frequently between two diagnoses with different treatments, further research investigating borderline cases is needed to improve our understanding of which cases these are, why they are occurring, and decrease inter-observer variability. Additional research is also needed to study, standardize, and simplify the way pathologists describe cases so clinicians and patients can accurately understand histologic diagnoses.

OUTCOME OF PATIENTS WITH FOLLICULAR MYCOSIS FUNGOIDES

Krishnasamy S1, Pinter-Brown L2,3, Sergio A3, Chiu M1,4, 1UCLA, Los Angeles, CA; 2UCLA, Los Angeles, CA; 3UCLA, Los Angeles, CA and 4Dartmouth School of Medicine at UCLA, Los Angeles, CA.

Purpose of Study: To evaluate the outcome of patients with FMF at our institution.

Methods Used: FMF cases were selected from the institutional registry of the department of pathology, the institutional database of patients that received a billing code of MF (ICD-9 202.x) from 1/1/2000 to 12/31/2010 and from the personal registry of Dr. Pinter-Brown.

Summary of Results: 21 patients (10 male, 11 female) with a mean age of 51 years were included. At initial presentation, 18 patients were stage I, 1 was stage II, 0 were stage III and 1 was stage IV. Median follow-up time was 18 months. The most common sites of involvement were the head and neck (90%). Oral Bexarotene was the treatment of choice in the majority (67%) of patients. All of the subjects are currently alive with disease.

Conclusions: Patients with FMF at our institution have a good prognosis in the short term. Further observation will be needed in order to determine if our FMF patients have a better outcome than previously reported cohorts, and if treatment with oral bexarotene significantly influences the outcome of these patients.
A FULL VIEW OF THE ONCOLOGY CONTINUUM: LEARNING ONCOLOGY THROUGH A NOVEL INTERDISCIPLINARY CLERKSHIP ELECTIVE

Thau EL1,2, Hamilton S2, Lai L2, Lee A1,2, Ingleweld P1,2, 1UBC, Vancouver, BC, Canada and 2BC Cancer Agency, Surrey, BC, Canada.

Purpose of Study: There is an internationally recognized deficit in undergraduate oncology education. Exposure to oncology occurs sporadically in a discipline-specific manner, limiting students from experiencing the unique interdisciplinary nature of oncology. To address gaps in oncology undergraduate education the goals of this project were two fold: 1) To develop and implement an integrated interdisciplinary oncology clerkship elective; 2) To develop online learning modules and virtual patients (VP) to supplement learning during the elective and throughout undergraduate medical training.

Methods Used: To develop an integrated interdisciplinary elective, the Kern approach to curriculum development was employed. A needs assessment of third-year medical students was conducted. Following analysis of the survey, development of the elective started in 2008. To supplement clinical experiences, online modules complimented by branching-logic VP cases have been scripted, reviewed, and published. Kirkpatrick’s hierarchy of evaluation has been used as an evaluation framework.

Summary of Results: 82 third year medical students at a single medical school completed the needs assessment. 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 an integrated oncology elective and 80% felt that online modules would enhance learning.

The integrated elective was implemented in late 2011 with a core group of students. Initial evaluations have demonstrated a high level of satisfaction and that elective improves student’s knowledge of the interdisciplinary nature of oncology. Online modules supported by VP cases for lung, prostate, breast, skin and colorectal cancer are complete and hosted publicly on the internet. An evaluation of the impact of the modules on learning continues.

Conclusions: The gaps in oncology education may be addressed by the needs-based development of a new integrated oncology clerkship supplemented with an online learning. Additional research will be done to determine the educational benefits of the integrated elective.

METHFORMIN USE AND RECURRENCE IN PATIENTS WITH ORAL CAVITY/OROPHARYNX SQUMOUS CELL CARCINOMA

Sanaiha Y1, Thompson C2, Elashoff D, Kim B1, Wang M2, St. John M2, 1David Geffen School of Medicine, UCLA, Los Angeles, CA; 2University of California, Los Angeles, Los Angeles, CA and 3University of California, Los Angeles, Los Angeles, CA.

Purpose of Study: The protective qualities of Metformin in cancer-related mortality have been investigated in several epidemiological and clinical studies. Positive anti-cancer results justify the investigation of whether metformin provides a protective effect in patients with head and neck squamous cell carcinoma (HNSCC), which accounts for approximately 3% of all cancers in the United States.

Methods Used: To determine if metformin has a protective effect on recurrence in patients with HNSCC we conducted a retrospective analysis of patients with oral cavity/oropharyngeal squamous cell carcinoma (OC/OP SCCA) treated at Ronald Reagan UCLA Medical center from 2001-2012. We identified 77 patients with OC/OP SCCA with type II diabetes. Patient demographics, cancer, TNM stage, treatment, and outcomes were analyzed. Kaplan-Meier(KM) and Cox proportional hazard uni-variate analysis were performed to determine if metformin has an effect on disease persistence or recurrence after primary cancer treatment.

Summary of Results: Within the group of early stage patients, metformin seemed to be protective as indicated by a longer time to recurrence on KM analysis and a hazard ratio of 0.75(p=0.61) from the cox model. Metformin analysis and a hazard ratio of 0.75(p=0.61) from the cox model.

Conclusions: Based on our current study size it seems that metformin does not have a significant effect on time to recurrence despite the promising results in the analysis of early stage patients. An expansion of the current retrospective study will provide an improved understanding of whether Metformin confers protection against recurrences of head and neck cancers.

Poster Session I
Pulmonary and Critical Care
2:30 PM
Thursday, January 24, 2013
79

EGFR MUTATION ANALYSIS IN PRIMARY LUNG ADENOCARCINOMA DIAGNOSED BY RADIAL EBUS-GUIDED BRONCHOSCOPY

Shah H, Chrisian A, Loma Linda University Medical Center, Loma Linda, CA.

Purpose of Study: Primary lung adenocarcinoma is the most common subtype of lung cancer, representing at least 50% in some populations. Mutations in the gene encoding the tyrosine kinase (TK) domain of the epidermal growth factor receptor (EGFR) are implicated in the pathogenesis of some adenocarcinomas. Their presence correlate with good response to therapy with oral TK inhibitors. Because most lung cancers are diagnosed at an advanced stage that preclude surgical intervention, adequate small biopsy sampling has become important in diagnosis and treatment.

Over the last decade, bronchoscopic endobronchial ultrasound (EBUS) has been increasingly used for diagnosis and mediastinal staging of lung cancer. The radial EBUS probe, unlike the built-in curvilinear probe, is independent of the bronchoscope. It helps to locate and guide sampling of a peripheral lung lesion.

Malignant tissue thus acquired is an attractive target in which to evaluate EGFR activating mutations. Recently, the effectiveness of EGFR mutation analysis in metastatic adenocarcinoma within lymph node tissue obtained by curvilinear EBUS bronchoscopy has been shown. However, similar data does not exist for tissue recovered from primary tumor using radial EBUS bronchoscopy.

The purpose of this study is to report the feasibility and effectiveness of obtaining malignant tissue using radial EBUS-guided bronchoscopy to assess for EGFR activating mutations in patients with lung adenocarcinoma.

Methods Used: We conducted an observational retrospective review of patients in whom EGFR mutation analysis was performed on samples of primary lung adenocarcinoma diagnosed by radial EBUS guided bronchoscopy.

Summary of Results: Fourteen patients diagnosed with peripheral lung adenocarcinoma solely by radial EBUS guided bronchoscopy had their tissue samples analyzed for common EGFR activating mutations. Of these, EGFR mutation analysis was feasible in 12 patients (86%).

Conclusions: Malignant tissue obtained from primary tumor by radial EBUS guided bronchoscopy is adequate for EGFR mutation analysis in patients with lung adenocarcinoma. To our knowledge, this is the first report of the practicality of EGFR analysis on samples obtained this way. Most patients had advanced disease at diagnosis, and ascertaining EGFR mutation status aided in guiding therapy.

Behavior and Development
Concurrent Session
3:30 PM
Thursday, January 24, 2013
80

EXECUTIVE FUNCTION MEDIATES EFFECTS OF GESTATIONAL AGE ON BEHAVIOR PROBLEMS IN PRESCHOOL CHILDREN

Aluduncin N, Loe IM, Stanford, Stanford, CA.

Purpose of Study: Preterm birth is associated with behavior and executive function (EF) problems. EF refers to interrelated cognitive skills used to plan goal-oriented behavior. How cognitive skills (measured by either IQ or EF) relate to behavior problems in preterm (PT) and full term (FT) preschoolers has not been well characterized. We hypothesized that EF mediates the effect of gestational age (GA) on behavior.

Methods Used: PT (n=70) and FT (n=80) children, age 3-5 years, were matched for age, gender, and race/ethnicity. Behavior problems were assessed on the Child Behavior Checklist (CBCL); EF on the Behavior Rating Inventory of EF (BRIEF) using the global executive composite (GEC); and
Conclusions: EF mediated the effect of GA on behavior problems, whereas IQ on the Abbreviated Stanford-Binet. Group differences were assessed using t-test or $\chi^2$. Mediation analyses using the method of Preacher and Hayes examined 2 models of cognitive skills assessing the impact of prenatal MA exposure, mediated by postnatal environmental adversity, on neurobehavioral disinhibition (ND) in the multicenter, longitudinal Infant Development, Environment, and Lifestyle Study (IDEAL) study.

Methods Used: IDEAL enrolled 412 mother-infant pairs; MA exposed subjects (n=204) were identified by self-report and/or GC/MS confirmation of amphetamine and metabolites in infant meconium. Matched comparison subjects (n=208) denied MA use and had a negative meconium screen. Children's Memory Scale (age 6.5 years), Conners' Parent Rating Scale (age 7.5 years), and Child Behavior Checklist (age 7.5 years) were administered to 280 enrollees (143 exposed, 137 comparison) to assess for ND. Structural equation modeling was used to establish an association between prenatal MA exposure and ND; covariates used included birth factors, child IQ, and study site. Indicators of postnatal environmental adversity factors included caregiver psychological problems and depression; family socioeconomic status; postnatal caregiver use of MA, tobacco, and marijuana; community violence; domestic violence; number of primary caregiver changes; poor quality of home; and poverty. These indicators were summed to create a single adversity index that was subsequently analyzed using the same covariates.

Summary of Results: Prenatal MA exposure is directly associated with higher neurobehavioral disinhibition in school-age children. This association is mediated by postnatal environmental factors, whereas IQ did not. We propose standard assessment of EF skills in young PT children. EF can serve as markers of behavior problems as well as possible targets for intervention.

Can Readmission For Neonatal Hyperbilirubinemia Be Prevented? Vora F$^1$, Schanler R$^{2,3}$, 1Loma Linda University Medical Center, Loma Linda, CA; 2Cohen Children’s Medical Center of New York, New Hyde Park, NY and 3Hofstra University School of Medicine, Hempstead, NY.

Purpose of Study: Hyperbilirubinemia, one of the most common problems of newborns, often is magnified by feeding issues in the first few days after birth. Despite monitoring, a significant proportion of newborns are readmitted for hyperbilirubinemia. We hypothesized that pre-discharge bilirubin measurements do not reflect the probability of readmission because feeding issues intervene and that readmissions can be decreased by attention to feeding issues in addition to discharge bilirubin values.

Methods Used: This was a retrospective medical record review of consecutive readmissions with a diagnosis of hyperbilirubinemia to two hospitals, from January 2010 to September 2011. Data were collected on birth demographics, weight changes, intervening medical visits, feedings, elimination patterns, and American Academy of Pediatrics (AAP) bilirubin nomogram designations.

Summary of Results: In 21 months 176 infants were readmitted to two NICUs for management of hyperbilirubinemia. The readmission bilirubin was $19.0 \pm 2.9$ (mean ± SD) at 118 hours ± 54 hours. The readmission bilirubin was not correlated with birth weight, gestational age (term or late preterm infant), stool pattern, weight loss from birth $5.6 \pm 3.9$, or percentage of human milk feeding in hospital (76% ± 29% of feedings). Although the discharge bilirubin was not correlated with the readmission bilirubin value ($r=0.11$, $p=0.19$), the relationship between the AAP threshold and actual bilirubin at discharge and readmission was significant ($r=0.48$, $P < 0.001$). The AAP threshold exceeded actual bilirubin values by 2 mg/dL in 23% of readmitted infants. This group had shorter median duration phototherapy 19 vs 29 h and length of hospital stay 2 vs 3 days, $p < 0.001$.

Conclusions: These preliminary data suggest that a large number of infants are readmitted for hyperbilirubinemia and that nearly 1/3 of them may benefit from home management. We found that discharge bilirubin values when compared to the AAP threshold were a better predictor of bilirubin upon readmission than the isolated values or even the bilirubin risk zone.

Teaching Children Healthy Food Choices Through Activities and Visual Displays Jenkins DK. University of Washington School of Medicine, Seattle, WA.

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Purpose of Study: The goal of this project is to teach children in Emmett, Idaho how to make healthy food choices. Gem County, home to the rural community of Emmett, ranks poorly in measures of obesity and physical inactivity compared to other counties in Idaho. In addition, the childhood obesity rate in America has increased by 500% since the 1970s.

Methods Used: One solution to this challenge is to teach principles of health and nutrition, specifically through interactive games and visual displays, a method that has proven to be effective with children. An exhibit booth at the Gem County Fair was used for three days to host activities and displays. Children who are showcasing animals often spend long hours on the fairgrounds between events and seek out activities to stay busy. The activities included a dinner-plate-like game board for practicing the MyPlate guidelines, a matching game with popular snacks and their sugar content as represented by sugar cubes, and a display of animal fat representing theoretical weight gain from daily soda consumption.

Summary of Results: Approximately 40 children and parents participated in the activities. Most children were not familiar with the MyPlate program, but learned the concept very quickly. Both parents and children were surprised by the sugar content of snacks popularly viewed as healthy. Participants returned to the booth multiple times with friends, eager to teach them and play together.

Conclusions: This project was effective at raising awareness in children in demonstrating that health and nutrition can be fun and enjoyable. However, any lasting behavior changes will require ongoing influence from parents and other caregivers who are closely involved in daily food choices.

Summary of Results: Seven students came to the introductory session, representing high school and middle school age groups. Several shared personal stories explaining why they felt this was an important club to start. All agreed to pursue the club further, and scheduled a follow-up meeting for two weeks later.

Conclusions: Public health literature supports the notion that this intervention can impact drunk driving. Specifically, SADD's peer-to-peer nature and emphasis on prosocial community involvement are effective intervention strategies, particularly in rural adolescents. The project is also highly sustainable. The students currently involved span 4 grade levels, increasing the likelihood that the club will survive after the oldest members have left for college. Also, the advising librarian, who is passionate about the cause, has strong community ties and access to a large youth network through existing library programs.

86 DEVELOPMENTAL OUTCOMES OF INFANTS WITH HYPOTHALAMIC ISCHEMIC ENCEPHALOPATHY AFTER WHOLE BODY COOLING

Govindappa K,*, Angkustikir K,*, Scoble J,*, Hansen K,*, U C Davis medical center, Sacramento, CA and *University of California Davis, Sacramento, CA.

Purpose of Study: To assess developmental outcomes of infants with hypoxic ischemic encephalopathy (HIE) who underwent whole body cooling based on HIE severity.

Methods Used: Infants with mild, moderate and severe HIE based on Sarnat scoring, aEEG, brain imaging and neurologic exam evaluated in the high risk infant follow up clinic at UC Davis Medical Center from 2009 to 2012 were identified from record review. All were initially evaluated at a mean age of 9 months with developmental testing (Mullen Scales of Early Learning, AGS edition or Bayley Scales of Infant Development - 3rd edition). Motor, cognitive and language abilities were classified into 3 categories: average / above average, 1-2 standard deviations (SD) below the mean and greater than 2 SD below the mean. Developmental outcomes between the various severities of HIE were compared using chi square analyses.

Summary of Results: 26 infants were included; 11 had mild, 10 had moderate and 5 had severe HIE. Most were term and 13 (50%) were male. Developmental scores were compared between boys and girls and were not significantly different (p = 0.68).

On developmental assessment, 9 (35%) had average developmental scores in all three areas (language, cognitive and motor) 17 (65%) had developmental delays in at least one area.

Language delays (>1 SD) were present in 57.7% (15/26) and motor delays were present in 30.7% (8/26). Cognitive delays were seen in the 3 children (11.5%) who also had both motor and language delays >2SD. Frequencies of language (p=0.08), cognitive (p=0.2) and motor (p=0.49) delays were not significantly different between severities of HIE.

Conclusions: Language delays were found in two thirds of the infants at 9 months after NICU cooling for HIE and was usually mild (1-2 SD below the mean) when present. Global delays were present in only 3 children. There were no significant differences in scores based on gender or HIE severity.
of the population. Homophobia, social and economic marginalization, discrimination, and HIV-related stigma in Lima add layers of complexity for qualitative data acquisition.

**Methods Used:** We have implemented video-based role-playing for additional insight into a very complex issue, which is a new and innovative approach that has not yet been utilized. The raw data will comprise the foundation for a future Telenovela (Spanish soap opera) about sexual risk-management. Weekly workshops were conducted by the investigation team in which participants were asked to perform various scenarios related to a specific theme for each workshop, which were recorded on video. After each improvisational exercise, the group then discussed the performance in a focus group setting.

**Summary of Results:** 9 potential Telenovela characters emerged naturally from the workshops, and video data is currently in the process of being analyzed for patterns of both verbal and non-verbally communicated.

**Conclusions:** Video workshops and focus groups provide an excellent method of acquiring qualitative data regarding high-risk and stigmatized behavior, and encouraged our study participants to share their experiences more freely, thus increasing the quality of our data.

88

HEALTH BEHAVIORS & PERCEPTIONS OF SPANISH SPEAKING EMPLOYEES IN WASHINGTON

Casimiro I1,2, Kahn M1,2, Hannon P1,3, Harris J3,1. University of Washington, Seattle, WA; 1University of Washington, Seattle, WA and 2University of Washington, Seattle, WA.

**Purpose of Study:** Preventable chronic diseases disproportionately affect individuals of lower socioeconomic status including ethnic minorities. Studies have documented that the workplace is an ideal setting to reach the adult population in order to promote healthy lifestyle behaviors through workplace health promotion. However, few of these programs have targeted non-English speaking workers. The purpose of this study was to develop a Spanish version of the American Cancer Society HealthLinks (HL) Survey in order to investigate the health behaviors and perceptions of Spanish-speaking employees (SSE) compared to English speaking employees (ESE).

**Methods Used:** HL survey questions were directly translated and back-translated to Spanish by native speakers. Survey questions ascertain respondent’s health behavior in the areas of nutrition, physical activity, smoking practices, breast cancer, and colorectal cancer screenings. A cross-sectional study was performed in which 92% of SSE surveyed were employed at the one worksite, thus the English sample used for comparison were employees from that site (mean age SSE=42, mean age ESE=46). A frequency scale, SSE perceived their worksite “rarely” or “never” provided physical activity recommendations, while ESE perceived that the workplace “sometimes,” “often,” or “always” did. On average, ESE respondents agreed that their worksite supported them in living a healthier life, while SSE had a “neutral” stance or disagreed with that statement (p=0.0172, SSE n=25, ESE n=20). On a frequency scale, SSE perceived their worksite “rarely” or “never” provided physical activity recommendations, while ESE perceived that the workplace “sometimes,” “often,” or “always” did. On average, ESE respondents agreed that their worksite supported them in living a healthier life, while SSE had a “neutral” stance or disagreed with that statement (p=0.0374, SSE n=24, ESE n=20).

**Conclusions:** We found that Spanish-speaking employees do not perceive that their workplace supports them in maintaining a healthy lifestyle when compared to their English-speaking counterparts in the same worksite. This study highlights the need for worksites to better target Spanish-speaking employees when promoting healthy behaviors. Preventive workplace initiatives can address risks for developing chronic diseases and are useful in reaching a large population of the nation’s workforce including those with limited English proficiency.

89

CHILDBIRTH OBESITY: SOURCES OF MOTIVATION TO BE HEALTHY

Sihotang C, Gutierrez W, Tung A, Westerberg M, Deuba M, Baum M. Loma Linda University School of Medicine, Loma Linda, CA.

**Purpose of Study:** According to “A Patchwork of Progress”, childhood obesity among 5th, 7th, and 9th graders in the San Bernardino County increased from 38.44% in 2005 to 39.25% in 2012. The lifestyle changes necessary to reverse these rates are difficult tasks for children. This study’s goal is to identify whom do these children see as a source of motivation to be healthy and is this motivational source influenced by the child being overweight or by their parent’s birth country of Mexico.

**Methods Used:** Operation Fit 2012 is a week-long fitness and nutrition summer day camp held for San Bernardino County children/teens, 7-17 years of age. Campers are referred from schools and clinics, based on being overweight. Also included in the camp, are non-overweight siblings or relatives of the referred participant. A survey of all campers asked, “Who most motivates you to be healthy?” Each camper was to select all individuals that applied. Their responses were then compared based on their BMI-for-age percentile and on the parents’ country of birth. Fisher exact tests were performed to compare all proportions.

**Summary of Results:** Among the “overweight/obese” campers (BMI ≥ 85%, n=85), the main sources of motivation to be healthy were Parent/Guardian (74%; 95% C.I: 64.8%, 83.4%), Doctors (35%; 95% C.I.: 25.1%, 45.5%), Brother/Sister (20%), Friends (13%), Teachers (11%), and Movie Stars/Singers (5%). These results were compared to the “underweight/normal” campers (BMI<85%; n=30), and no statistically significant difference was found.

Campers with US-born parents (n=50) and those with at least one parent who was born in Mexico (n=51) were compared. The top responses for both groups were Parent/Guardian (74%, 78% respectively) and Doctors (32%, 37%). Again, no statistically significant difference was found.

**Conclusions:** This study showed obese and overweight children, 7-17 years of age, identified their parent/guardian (74%) and their doctors (35%) as the main sources of motivation to be healthy. Similar responses were reported from the underweight or normal siblings/relatives and from all campers despite the birth country of their parents. These findings suggest that the efforts in education, prevention, and treatment to reduce the prevalence of childhood obesity should be focused on parents and physicians.
A SUCCESSFUL PARTNERSHIP BETWEEN GLOBAL HEALTH INITIATIVE MEDICAL STUDENTS AND A NONGOVERNMENTAL ORGANIZATION IN KENYA


Purpose of Study: To investigate the effectiveness and sustainability of global health projects conducted by University of British Columbia (UBC) medical students in conjunction with a nongovernmental organization (NGO) in rural Kenya.

Methods Used: A qualitative and quantitative analysis of the global health projects over the last four years was done by the 2012 Global Health Initiative (GHI) team. The analysis retrospectively examined feedback from the NGO, community members, and previous GHI teams, as well as qualitative data from surveys.

Summary of Results: In 2009, the first UBC GHI team conducted a community needs assessment in conjunction with a local NGO called PCT in Kenya. We have outlined a few implemented projects to show that annual summer visits by medical students working with an NGO can result in success.

The goal project provides back stations where community members bring local goats to be serviced to create milk-producing offspring; this has resulted in numerous successful breedings. The GHI team provided initial funding and workshops. PCT has now partnered with a local agency for technical workshops, and has received government funding to upscale the project.

Secondly, the sack garden project aims to improve nutrition and provide an opportunity for income generation. Sack gardens allow the grower to control the environment of the garden; vegetable seedlings are planted in sacks, allowing for growth of the vegetables in a contained area. This project’s success is evident from the growing interest and participation from the community.

Finally, health education workshops aimed at the school-aged population were initially focused on HIV transmission prevention. Due to overwhelming support, we expanded workshop content and the number of locations. Working in close partnership with PCT, the GHI team is now providing material for quarterly workshops to run smoothly in our absence.

Conclusions: The goal of the GHI-PCT alliance is to establish sustainable data from surveys.

The rate of skilled-attended births in health facilities increased when TBAs were recruited and compensated for bringing their clients to local health facilities to deliver.

A STRATEGY TO INCREASE SKILLED ATTENDANT BIRTHS IN KENYA

Tucker K1, Tomedi A3,1, Mwanthi M2. 1University of British Columbia, Vancouver, BC, Canada.

Purpose of Study: To investigate the effectiveness and sustainability of global health projects conducted by University of British Columbia (UBC) medical students in conjunction with a nongovernmental organization (NGO) in rural Kenya.

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The rate of skilled-attended births in health facilities increased when TBAs were recruited and compensated for bringing their clients to local health facilities to deliver.

EL GRUPO DE APOYO SOCIAL: CREATING A SELF-SUSTAINED SOCIAL SUPPORT GROUP FOR SPANISH SPEAKERS IN ANCHORAGE, ALASKA

Andersen DJ. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Create a social support group for Spanish speakers in Anchorage, Alaska in order to provide opportunities to cultivate cultural strength amongst Latinos, and ultimately improve overall health. Many Hispanic families in Anchorage, Alaska are first generation families to the United States and nearly half report speaking Spanish exclusively. Through acculturation and challenges in English proficiency, the adaptation to a new culture can be taxing on ones health, generally resulting in worse health outcomes (Comrood et al. 2004) (Franzini et al., 2002). This highlights the importance of cultivating cultural attitudes and practices amongst Hispanics through social support, which seem to be protective of health outcomes (Minority Populations and Health, 2005) (Wang HH et al., 2003).

Methods Used: Organized a focus group of Latinos to discuss challenges of adapting to Anchorage. These individuals emphasized a need for additional social support for Hispanics in Anchorage for two reasons: 1) Programs for Hispanics in Anchorage are sparse and 2) Social support is more accessible in their country of origin. Initiated the process of forming a self-sufficient social support group and named it: El Grupo de Apoyo Social, meaning- the social support group. Advertisement for the group was carried out via phone calls and flyers at the AFMR clinic inviting any Spanish speaker in the community to participate.

Summary of Results: Thirteen Spanish speakers attended the first meeting of El Grupo de Apoyo Social. Two Latino members volunteered to be co-presidents of the group. We planned future monthly meetings that include two elements: 1) A potluck and 2) A themed educational pursuit for Hispanics including: September- Computer/internet Training; October- English classes in Anchorage; November- Employment Opportunities in Anchorage. The rate of skilled-attended births in health facilities increased when TBAs were recruited and compensated for bringing their clients to local health facilities to deliver.

Conclusions: The rate of skilled-attended births in health facilities increased when TBAs were recruited and compensated for bringing their clients to local health facilities to deliver.

COMPARISON OF INJURIES IN MARTIAL ARTS AND COMBAT SPORTS: A CROSS-SECTIONAL APPROACH

Lam J1, Kaufman M2. 1University of Washington School of Medicine, Seattle, WA and 2University of Washington Medical Center, Seattle, WA.

Purpose of Study: Each year, millions of Americans participate in martial arts and combat sports. Although the literature describes many benefits of involvement, there is little research examining injuries and risks in the context of regular participation. The goal of this study was to compare injuries across five styles of martial arts and combat sports. We primarily hypothesized that the types and rates of injuries would differ among five styles of martial arts and combat sports: karate, tae kwon do, judo, Brazilian jiu jitsu, and boxing. Secondarily, we hypothesized that risk factors existed for sustaining injury.

Methods Used: Surveys were collected and analyzed from 263 participants as follows: karate (n=68), tae kwon do (n=53), judo (n=41), Brazilian jiu jitsu (n=65), and boxing (n=36). A survey was distributed for self-completion at training facilities and consisted of an injury checklist grouped by body region as well as questions asking about personal characteristics and perceptions about safety. Chi square analysis was used to determine whether there was an association between sustaining injury and style of sport. Logistic regression was used to determine odds ratios (OR) and confidence intervals (CI) for predictors of injury.

Summary of Results: There was strong association between sustaining injury and style of sport (χ² = 27.05, df=4, p<0.0001). The rates of injury varied according to style. The most affected regions were the upper and lower
extremities. Age, training hours per week, and practicing judo style were found to be predictors of overall injury. Risk of injury increases 6% per each additional year (OR 1.06; CI 1.03 to 1.09; p < 0.05) and 21% per each additional hour of training per week (OR 1.21; CI 1.09 to 1.36; p < 0.05). There was at least a fourfold increase in risk of injury from practicing judo compared to karate (OR 4.60; CI 1.65 to 14.50; p < 0.05). For head injury, there was at least an eleven times higher risk in judo compared to karate (OR 11.53; CI 3.44 to 41.76; p < 0.05).

Conclusions: The types and rates of injuries differed among the styles considered in this study. Risk factors that increase likelihood of injury overall include age and hours of training per week. There is increased risk of head injury and overall injury in judo compared to karate.

DEALING WITH “EL CAMBIO DE VIDA”: PROMOTING MENOPAUSE AWARENESS IN THE LATINA COMMUNITY OF LYNDEN, WA

Cholhas-Wood R, University of Washington School of Medicine, Seattle, WA.

Purpose of Study: According to the literature and to community health leaders in Lynden, WA, Latina women have less access to knowledge about menopause and alleviation of its symptoms than other ethnic groups. This limited access is partly due to stigma around discussing personal issues and difficulties navigating the U.S. healthcare system. Studies show that women with little to no menopause education also have the worst severity of physical and psychosocial experience of menopausal symptoms. The purpose of this project was to promote awareness of menopause in the Latina community to improve experiences with this life change.

Methods Used: Community health leaders from Sea Mar clinics and a local Latino organization were interviewed to determine what health issues were important to their clients. Attendees at three health fairs in migrant labor camps were also interviewed and invited to a local health event, at which a discussion and presentation about menopause were held. Studies show this style of educational intervention increases the percentage of women who incorporate healthy menopause-related habits that persist long-term. Culturally appropriate, easy-to-understand educational materials on menopause were developed for the target group.

Summary of Results: Ten Latina women ages 27-67 attended the event. Group discussion on menopause, its symptoms, and coping strategies was lively. Attendees were encouraged to visit health providers and address their health concerns frankly and openly, in contrast to the visit style they were accustomed to before immigrating. Extra copies of menopause education materials were given to community members to encourage further discussion beyond the intervention setting.

Conclusions: Educational interventions based in the community increase healthy perimenopausal behaviors. The group targeted by this educational intervention was excited to discuss menopause among themselves and to carry this information to their family and friends, thus affecting a larger group than present at the time. However, overcoming community-wide barriers to access to health information and care was a major concern for this project. Encouraging this community to initiate frank discussions of health concerns with their providers may improve health outcomes.

FOOD INSECURITY AS A CHRONIC ILLNESS: SEASONAL AND MIGRANT FARMWORKERS IN CHELAN, WASHINGTON

Black LE,1 Parks L2, Mendez M. 1University of Washington School of Medicine, Seattle, WA and 2Columbia Valley Community Health, Wenatchee, WA.

Purpose of Study: Chelan county houses 17,000 seasonal and migrant farmworkers annually, most of whom are Hispanic. Despite the region’s extensive agricultural production, 18% of residents report food insecurity. The toxic relationship between acculturation, food insecurity, and poor nutrition creates and exacerbates health disparities affecting Hispanic seasonal and migrant farmworkers in Chelan.

Methods Used: This intervention identified two target groups: more acculturated seasonal farmworkers with established care at Columbia Valley Community Health Center (CVCH), and less acculturated migrant farmworkers living at the Beebe camp in Manson. A separate tailored outreach event was held for each group, with a cooking demonstration in Spanish and information on community resources.

To clarify topics and methods, community members and leaders were interviewed and a literature review was performed. Cooking demonstrations used ingredients available at the food bank and gleaned organic produce. To publicize the Beebe event, we enlisted a camp resident who is a food bank volunteer and unofficial “promotora.”

Summary of Results: With volunteers from the Chelan Food Bank and Community Farm Connection, we harvested over 150 lbs of donated spinach from Sunshine Organic Farms, which was used for cooking demonstrations, raffles, and donated to food banks throughout the Wenatchee Valley. Community Farm Connection and the Chelan Food Bank plan to continue this partnership.

An educational event was held onsite at CVCH that reached seven participants, mostly middle-aged Mexican women; each received a meal and educational recipe handout. A second event, held at the Beebee migrant camp, reached forty-five single Mexican men and Guatemalan families. Activities included a meal, toothbrush giveaway, hand-washing demonstration, and raffle. Three participants received referrals to the clinic or care coordination team.

Conclusions: Health disparities faced by seasonal and migrant farmworkers present a daunting challenge. Nutrition in these populations encompasses much broader themes such as food insecurity, acculturation, structural violence, and self-efficacy. Such complex issues benefit from a tailored approach that not only anticipates demographic factors, but also approaches the community as an essential partner.

Hematology and Oncology I

Concurrent Session

3:30 PM Thursday, January 24, 2013

OUTFLANKING BCR-ABL DRUG RESISTANCE

Baweja A, Ting P, Colicelli J. David Geffen School of Medicine at UCLA, Los Angeles, CA.

Purpose of Study: Despite the success of tyrosine kinase inhibitors in targeting translocation-derived BCR-ABL fusion oncogenes in leukemias, drug resistance remains a serious issue. Many patients treated with these inhibitors develop drug resistance due to mutations in the ABL1 kinase domain of BCR-ABL1, which directly or indirectly prevent drug binding. A stable long-term remission or cure will require new approaches that target this oncoprotein. Previous work has demonstrated that full BCR-ABL1 catalytic and transforming activity require direct interaction of ABL1 with its regulator protein RIN1. This RIN1 dependence was observed even with the most refractory BCR-ABL1 mutant. In this study we aim to identify a new class of inhibitors that target the interaction between RIN1 and BCR-ABL1 using high-throughput screening and structural biology.

Methods Used: We are using TR-FRET (time-resolved fluorescence resonance energy transfer) to perform a high-throughput screen for compounds that block the interaction of RIN1 with ABL1. We are also attempting to determine the structure of the interface between RIN1 and ABL1, which will assist with drug design and structure-activity relationship (SAR) analysis. The modified forms of RIN1 and ABL1 used for screening and structural analysis are expressed from a baculovirus vector in SF9 insect cells.

Summary of Results: We have screened over 450,000 molecules and selected 60 hits to follow up on. To test selected compounds for inhibition of RIN1-ABL1 binding we are performing co-immunoprecipitation experiments. We are also testing the compounds for their ability to inhibit ABL1-phosphorylation of target substrates. The same approach will be carried out with kinase inhibitor-resistant BCR-ABL1 mutants in order to validate the efficacy of potential drugs.

Conclusions: Our work establishes a new strategy by combining allosteric and catalytic site interference to inhibit an oncogenic tyrosine kinase. Targeting BCR-ABL1 in multiple sites is likely to reduce the propensity for relapse by requiring the acquisition of multiple drug resistance mutations. Further, this strategy could be especially helpful as a new frontline therapy for patients resistant to kinase inhibitors. Hence, this work may lead to new treatments for leukemia patients, including those resistant to currently available drugs.
HUMORAL IMMUNE RESPONSE IN MERKEL CELL CARCINOMA: PRESENCE OF MERKEL CELL POLYOMAVIRUS SPECIFIC IGA AND IGM

Lisberg A1, Paulson K1, Lewis C2, Yelistratova L2, Nghiem P2. 1University of Washington, Seattle, WA and 2University of Washington, Seattle, WA.

Purpose of Study: In 2008, Merkel Cell Polyomavirus (MCPyV) was shown to be integral to the development of Merkel Cell Carcinoma (MCC). Two gene families are produced by MCPyV, the tumor associated antigens (Tag), oncoproteins that inhibit tumor suppressors, and the viral proteins (VP), encoding the viral capsid. Interestingly, IgG titers to Tag reflect tumor burden. The purpose of this study was to evaluate if MCC patients produce Tag and VP specific IgM and IgA.

Methods Used: A multiplex antibody binding assay was used to detect MCPyV antibodies in serum from MCC patients and healthy controls. These antibodies were identified by commercially available secondary antibodies. A net mean fluorescent index greater than 500 was deemed positive and the results were compared to known IgG status.

Summary of Results: In the majority of samples, IgM status correlated with IgG status. 10/12 of the patients studied with positive IgG Tag titers had positive IgM Tag titers. Similarly, 23/24 patients with positive IgG VP titers had positive IgM VP titers. All 7 controls had negative IgM Tag titers and their IgM capsid titers correlated with IgG status.

Conclusions: Differential expression of IgA was seen in patients with positive IgG titers. Specifically, 7/12 patients with positive IgG Tag titers had positive IgA IgG titers, while 14/24 patients with positive IgG VP titers had positive IgA VP titers. None of the 25 patients with negative IgG Tag titers produced IgA to this antigen. Interestingly, 3/18 patients without IgG to VP, produced IgA to the capsid, as did 1/3 controls.

EFFECTS OF FIBROBLAST AND MACROPHAGE CO-CULTURE ON FIBROBLAST ACTIVATION AND COLLAGEN DEPOSITION

Rosen S, Guo Q, Durand-Rougely C, Schedin P. University of Colorado School of Medicine, Aurora, CO.

Purpose of Study: Women have an increased risk of breast cancer after a complete pregnancy and, if diagnosed within five years postpartum, have a worse prognosis than nulliparous or pregnant women. The increased risk and poor diagnosis of breast cancer are thought to be associated with post-partum breast involution, which is a coordinated program of epithelial cell death and stromal remodeling resulting in gland architecture resembling the pre-pregnant state. In rodents, the involuting mammary gland microenvironment has wound healing-like characteristics, such as influx of M2-like macrophages and abundance of fibrillar collagen, which are potential driving forces to determine whether we can use drugs to target this interaction and block subsequent collagen production as a possible prophylactic treatment during postpartum involution.

CONCLUSIONS: These data support a model in which M1 macrophages, an immune cell population in the involuting mammary gland, contribute to collagen deposition. M1 macrophages are known to be the primary responders to wound environments and may contribute to a microenvironment favorable for tumorigenesis. Further research will investigate the interactions between endogenous mammary macrophages and fibroblasts to determine whether we can use drugs to target this interaction and block subsequent collagen production as a possible prophylactic treatment during postpartum involution.

AN EVALUATION OF [F-18]-FLUORODEOXY-D-GLUCOSE POSITRON EMISSION TOMOGRAPHY, BONE SCAN, AND BONE MARROW ASPIRATION/BIOPSY AS STAGING INVESTIGATIONS IN EWING SARCOMA

Newman EN1, Jones RL1,2, Hawkins DS1,2,3. 1University of Washington School of Medicine, Seattle, WA, 2Fred Hutchinson Cancer Research Center, Seattle, WA and 3Seattle Children’s Hospital, Seattle, WA.

Purpose of Study: Staging investigations following the diagnosis of Ewing sarcoma may include chest computerized tomography (CT), technetium bone scintigraphy (bone scan), [F-18]-fluorodeoxy-D-glucose positron emission tomography (FDG-PET) scan, and bone marrow biopsy and aspiration (BMA/Bx). Each of these staging investigations provides complementary prognostic information, however the optimal combination of staging investigations is not clear.

Methods Used: We conducted a retrospective study of 91 patients diagnosed with Ewing sarcoma and consecutively treated at our medical facilities between January 1, 2001 and December 31, 2011. We compared the radiologist’s interpretations of staging FDG-PET and bone scans. We additionally compared the results of imaging evaluations to bilateral and unilateral BMA/Bx.

Summary of Results: We found FDG-PET and bone scan to have an examination-based concordance rate of 98% (one discordant case with a positive FDG-PET and negative bone scan). The region-based concordance rate for the imaging modalities was 97% for all cases and 63% for only metastatic cases. The ipsilateral concordance rate for BMA/Bx was 98% with BM/Bx detecting metastases in 7 cases and BMA detecting metastases in 4 cases. The left versus right concordance rates for BM/Bx and BMA were 98% and 97%, respectively. In all cases where bone marrow metastases were detected by BMA or BM/Bx, FDG-PET and bone scan detected osseous metastases.

Conclusions: Our study indicates FDG-PET is sufficient for initial screening for osseous metastases and identified all patients who also had bone marrow metastases. If osseous metastases are detected, a bone scan can detect additional osseous lesions and BM/Bx may indicate prognostic bone marrow metastases.
analyzer and the resonant frequency was monitored by LabView. The interaction of PSA with anti-PSA antibody was measured as a change in the resonant frequency (kHz) of the device.

**Summary of Results:** The FBAR was used to estimate that the Kd of anti-PSA for Protein G is 76 nM. Furthermore, we were able to detect PSA at levels less than 25 ng/mL, and by obtaining measurements for non-specific proteins, we have proved that our device detects PSA by specific antibody-antigen interactions.

**Conclusions:** While further studies hope to illustrate our capability to detect biomarkers at lower levels and in more complicated biological samples, the FBAR device can provide significant advantages over existing label-free detection methods including flexibility, sensitivity, and decreased cost, and has the potential to be integrated into a surgical device to provide molecular information about tissue at the point of dissection.

**SMALL INTERFERING RNA TO TREAT PANCREATIC CANCER**

 Julien DC1, Giri A2, Hill RA2, 1University of Washington School of Medicine, Seattle, WA and 2University of Idaho, Moscow, ID.

**Purpose of Study:** Most pancreatic cancers possess point mutations in the K-Ras oncogene. The majority of K-Ras point mutations result in K-Ras being constitutively activated leading to increased cell proliferation, growth, and inhibition of apoptotic pathways. Studies have suggested that small interfering RNA (siRNA) designed against mutated K-Ras (mK-Ras) may be a treatment option for pancreatic cancers. The aim of this study was to characterize the effects of mK-Ras siRNA on cell viability, proliferation, and metabolic activity in pancreatic cancer cell lines.

**Methods Used:** mK-Ras siRNA and scrambled siRNA was designed as ready-annealed, purified duplexes. Panc1, Panc 8.13, Panc 10.05, cell lines with mK-Ras, and BxPC3 cells, with wild type K-Ras (wtK-Ras), were seeded in quadruplicate in 96 well plates at 1.2 × 104 cells per well and incubated for 24 hours. Cells were then treated with either cycloheximide (positive control), scrambled siRNA, or mK-Ras siRNA designed against a point mutation at the 12th codon of the K-Ras oncogene. Cells in proliferation studies were treated with trypan blue and enumerated. Cells in the metabolic assays were treated with CellTiter Blue and quantified with a fluorometer. Measurements were taken at 24, 48, and 72 hours.

**Summary of Results:** Studies showed significant down-regulation of mK-Ras compared to cells treated with scrambled siRNA at all time-points, while BxPC3 cells showed no significant change in wtK-Ras expression. Viable cell numbers were significantly reduced in cells treated with mK-Ras siRNA compared to scrambled siRNA in cell lines with mK-Ras. BxPC3 viable cell number was not significantly affected by mK-Ras siRNA. Cell lines with mK-Ras that were treated with mK-Ras siRNA had significantly lower metabolic activity compared to scrambled siRNA at all time-points. The effect that mK-Ras siRNA had on BxPC3 cell metabolic activity was only significant at 37°C. Cells were then treated with either cycloheximide (positive control), scrambled siRNA, or mK-Ras siRNA designed against a point mutation at the 12th codon of the K-Ras oncogene. Cells in proliferation studies were treated with trypan blue and enumerated. Cells in the metabolic assays were treated with CellTiter Blue and quantified with a fluorometer. Measurements were taken at 24, 48, and 72 hours.

**Conclusions:** The mK-Ras siRNA utilized in this study appears to specifically downregulate mK-Ras mRNA and not wtK-Ras mRNA. Treatment of cells possessing mK-Ras point mutations with mK-Ras siRNA inhibits cancer cell proliferation, while cells with wtK-Ras are unaffected. Metabolic activity of cells with mK-Ras is inhibited by treatment with mK-Ras siRNA.
PMNs form neutrophil extracellular traps (NET) to kill microbes extracellularly. NETs are complex lattices of extracellular, decondensed chromatin decorated with anti-microbial proteins and degradative enzymes. Whether PMNs isolated from patients who have recently undergone bone marrow transplant form NETs is unknown. We hypothesized that BMT patients are at increased risk of severe infection due in part to failed NET formation.

Methods Used: We studied 13 BMT study subjects, 4 adult and 9 pediatric. The indications for BMT included: leukocyte severe combined immune deficiency, neuroblastoma, myelodysplastic syndrome, and leukemia. They received stem cells for BMT from different sources including: autologous transplant (2), cord blood (2), matched related donor (3), and matched unrelated donor (6). Ten study subjects completed transplant and engraftment (ANC >500 cells/microliter for three consecutive days) prior to enrollment. We enrolled 3 participants prior to BMT and tested their PMNs before and after transplant. PMNs were isolated via positive immunoselection. We induced NET formation in healthy control and participant PMNs with LPS (100 ng/mL; 1 h). We assessed NET formation in vitro using live cell imaging via confocal microscopy and histone H3 release assay.

Summary of Results: We found that all LPS-stimulated PMNs isolated from subjects post-engraftment formed NETs (18 - 199 days post-transplant). We followed three human subjects from their pre-transplant conditioning regimen through to engraftment. PMNs isolated post-BMT formed NETs in vitro. However, PMNs isolated post-BMT but before engraftment failed to form NETs. In vitro NET competency was achieved by PMNs from all three subjects at or just after the day of engraftment.

Conclusions: PMNs isolated from post-engraftment patients following BMT form NETs following LPS-stimulation in vitro. PMNs isolated from pre-engraftment BMT participants fail to form NETs, but gain NET competency at the time of engraftment. These results suggest that the increased susceptibility to bacterial and fungal infections characteristic of BMT patients in the first year post-transplant does not result from failed NET formation.

Inflammation and Infection
Concurrent Session
3:30 PM, Thursday, January 24, 2013
107
CHRONIC STRESS & SALIVARY BIOMARKERS
Mallick A,1,2, Bergen A2, Nishida D2, Wei X2, Michel M2, David SP2,2, Swan GE2, Reid MW2, Simons AD3,1, Andrews J1, 1Stanford School of Medicine, Palo Alto, CA; 2SRI International, Menlo Park, CA; 3ORI International, Eugene, OR; 1University of Oregon, Eugene, OR and 2Notre Dame, South Bend, IN.

Purpose of Study: To understand correlates of chronic stress & their influence on substance use in a population-based cohort (OYSUP).

Methods Used: We evaluated clinical & salivary RNA metrics and gene expression in saliva samples (n=48, 31% female, 55% ever-smoking) from two groups (high vs. low stress) based on Life Events and Difficulties Schedule. We used multiple analytical platforms, multiple reference genes and 18 replicates of all gene expression assays. We chose 38 candidate genes previously identified as differentially expressed in the RNA of 11 caregivers of cancer patients and 10 matched control subjects.

Summary of Results: We observed significant differences in ever smoking (OR=3.7, 95%CI 1.03, 13.64, P=0.045) and RNA integrity score (t=2.12, P=0.039) between stress strata. We observed significant under expression of 9 assays in the high stress stratum, all of which interrogate glucocorticoid receptor regulated genes. Post-hoc analyses identified significant over expression of 3 UTR adenylate uridiylate (AU)-rich elements among differentially expressed genes. IL8 expression remained significantly associated with chronic stress after multivariate adjustment for biospecimen, clinical, demographic & genetic variables.

Conclusions: A gene expression signature of chronic stress previously observed in hematopoietic samples is observed in the unfractionated saliva of young adults.

Salivary RNA and Clinical Covariates of Significantly Differentially Expressed Test Assays

<table>
<thead>
<tr>
<th>Gene</th>
<th>CBC</th>
<th>RBC</th>
<th>Gender</th>
<th>Stress</th>
<th>Smoking</th>
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<td>IL8</td>
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<tr>
<td>IFN-γ</td>
<td>2.59</td>
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<td>TNF-α</td>
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108
HIGHER INCIDENCE OF IGG ANTI-IGA ANTIBODIES IN IGA DEFICIENT FEMALES WITH SUSPECTED CELIAC DISEASE
Martins TB1, Iaskowski T1, Brickell L1, Augustine N2,2, Kumanovics A1,2, Tebo AE1,2, Hill HR1,2,1, ARUP Institute, Salt Lake City, UT and 1University of Utah School of Medicine, Salt Lake City, UT

Purpose of Study: IgA deficiency is the most common human immunodeficiency occurring in 1:500 to 1:700 Caucasians. IgA deficient individuals have a higher incidence of respiratory tract and gastrointestinal infections, but are often asymptomatic. Additionally, IgA anti-IgA antibodies are found in about 10% of patients with IgA deficiency which may lead to anaphylactic reactions in individuals receiving blood transfusions or intravenous immunoglobulin (IVIG). Up to 3% of celiac disease patients are IgA deficient, but the incidence of anti-IgA antibodies in these patients has not been thoroughly investigated. The purpose of this study was to determine the incidence of anti-IgA antibodies in IgA deficient celiac patients compared to IgA deficient non-celiac as well as normal individuals.
Methods Used: We developed a quantitative multiplexed immunoassay for detecting IgG anti-IgA antibodies to IgA subclasses 1 and 2, as well as total IgA.

Summary of Results: Female IgA deficient celiac patients had over two times greater incidence of anti-IgA antibodies (23.1% 12/52) vs IgA deficient non-celiac patients (9.6% 20/208). Male IgA deficient celiac patients had a similar incidence of anti-IgA antibodies (11.5% 3/26) as IgA deficient non-celiac patients (9.6%). None of the 126 normal controls (63 female, 63 male) tested positive for anti-IgA antibodies. The IgG against IgA antibodies did not appear to be class specific; as they recognized both IgA1 and IgA2 equally in positive patients.

Conclusions: The higher incidence of anti-IgA antibodies in suspected female celiac patients is an intriguing novel finding. This multiplexed assay should be useful in the further investigation of anti-IgA antibodies in these patients, as well as identifying patients at risk to adverse reactions to transfused blood products containing IgA.

109 CONGENITAL CYTOMEGALOVIRUS KNOWLEDGE AND AWARENESS AMONG WOMEN IN RURAL IDAHO COMMUNITIES

Moreno BL1, Fortunato EA2,3 1University of Washington, Seattle, WA; 2University of Idaho, Moscow, ID; and 3University of Washington, Seattle, WA.

Purpose of Study: Among congenitally acquired infections, cytomegalovirus (CMV) is the most common infection of viral origin that can result in birth defects and permanent disability. In the United States it is expected that 1% of all births will result in a congenitally infected newborn. Of those born with a CMV infection, 10% will show sequelae at birth, while another 10% will develop disabling sequelae over time. During pregnancy a mother can contract the infection from contact with bodily fluids such as urine, feces, or saliva. There is irrefutable evidence that limiting a pregnant mother's exposure can help prevent CMV infection and potential spread to the fetus.

In our study, we have explored the novel idea of assessing the knowledge and awareness of congenital CMV in rural versus urban regions.

Methods Used: Surveys were used to assess the knowledge of lay-women aged 18 to 44 years old. The rural regions assessed included Lewiston, ID and its satellite communities. The urban site assessed was Spokane, WA. To estimate the percentage of CMV+ individuals in the regions being studied, Inland Northwest Blood Center (INBIC) blood bank data was collected on CMV serostatus of randomly sampled blood donors in the given regions.

Summary of Results: 2359 Donors in Spokane, WA and 1282 Donors in Lewiston and its satellite communities were assessed between January 2005 and January 2012. We found that 42.5% of all women in Spokane and 48.6% of all women in Lewiston and surrounding communities tested positive for CMV. We used surveys to assess the knowledge of CMV that women in these different areas had. What was clear from these surveys was a need for preventative education on congenital CMV. As a result, several seminars on disease prevention were conducted at local childcare facilities and community meetings. Community members and childcare providers proved receptive to the seminars and were eager to learn more about CMV.

Conclusion: Our preliminary findings lead us to believe that women need to be educated about CMV and are eager to learn about the virus and its potential effects on newborns. This has strengthened our resolve to be the providers of that needed information to our local rural and urban inland Northwest communities.

110 IDENTIFICATION OF PLASMODIUM GENOMIC VARIANTS THROUGH A STREAMLINED PIPELINE, WITH DRUG DEVELOPMENT APPLICATIONS

Manary MJ, UCSD, La Jolla, CA.

Purpose of Study: While recent advances in high-throughput sequencing are rapidly being integrated into the methodology of human genomics, the application to other species, especially non-diploid, is slow. We introduce a streamlined pipeline for the analysis of Plasmodium spp. sequencing data, with special emphasis on genetic modifications resulting in drug or vaccine resistance.

Methods Used: Internally, we have already implemented the program to identify the genetic targets of novel pharmaceutical candidates. In this pipeline, which includes sequence alignment and quality control as well as single nucleotide and copy number variant detection, we provide both a tabular output of suspected variants and visualization in a user-friendly graphical interface.

Summary of Results: Filtering options allow for the customization of specificity and sensitivity parameters to fit the needs of the user. The CNV calling algorithm we present is completely novel for a haploid species, and has been rigorously tested on a number of known amplifications and deletions in Plasmodium.

Conclusions: We believe that this feature in particular will increase the consistency with which researchers can report copy number mutations because it reduces spurious results. The program is immediately and freely available to all researchers.

111 A RARE CASE: MYCOBACTERIUM AVIUM COMPLEX SYNOVITIS IN AN IMMUNOCOMPETENT PATIENT

Tan T, Baksh K, Colburn K, LLUMC, Loma Linda, CA.

Case Report: Introduction: Mycobacterium Avium complex (MAC) infection has been associated with immunocompromised patients such as those with HIV/AIDS. This case presents MAC synovitis of the right knee in an immunocompetent patient.

Case Presentation: A 31-year-old male presented to with right knee swelling for two weeks that occurred after playing a game of basketball. Patient had experienced an episode of bilateral knee pain about four months prior to this presentation that resolved on its own. Patient was evaluated by orthopedic surgery prior and underwent an MRI of left knee demonstrating a 1.5 cm full thickness cartilage defect of the trochlear groove with associated large subchondral osteophyte, overall mild chondromalacia in the lateral compartment; however, with a 1.5 cm full-thickness cartilage defect of the posterior weight bearing surface of the lateral femoral condyle and small tricompartmental marginal osteophyte formation with moderate joint effusion.

On physical exam patient had bilateral synovitis and underwent arthrocentesis with cultures from synovial fluid growing MAC as verified by DNA probe. Patient was negative for HIV screening and had no health history that would indicate immunocompromise. Infectious disease was consulted and patient was started on clarithromycin and ethambutol with resolution of symptoms.

Discussion: MAC has been most notably appreciated with pulmonary disease in immunocompromised patients, however, there are case reports that point to MAC infection in the skin and joints of patients that have been immunocompromised as a result of HIV/AIDS infection or prolonged exposure to immunosuppressive medications such as prednisone or biologic medications such as those used in various rheumatoid conditions. This patient was negative for HIV screening and had not been receiving any medications, nor had any underlying chronic disease that would render him immunocompromised. In addition, patient had no history of recent travel or trauma to his knees. One complication of MAC infections is the possibility of necrosis. The patient above did not suffer from any necrosis to his knee, however his illness presents the importance of testing synovial fluid for possible MAC even in immunocompetent patients so as to ensure treatment in a timely manner to prevent such complications.

112 USING NATRIURETIC PEPTIDE LEVELS TO PREDICT AND PREVENT 30-DAY HOSPITAL READMISSIONS FOR HEART FAILURE PATIENTS

Kern T1,2, Kedan F1, Kimchi A2, UCLA DGSOM, Los Angeles, CA and Cedars-Sinai Medical Center, Los Angeles, CA.

Purpose of Study: Secretion of B-type natriuretic peptide (BNP) and amino-terminal pro-B-type natriuretic peptide (NT-proBNP) is increased in patients in heart failure. Peptide levels can be measured and used by physicians to determine the condition and prognosis of a failing heart. High readmission rates for these patients are a problem for hospitals and this issue is specifically addressed by the Affordable Care Act (ACA). The purpose of this study is to determine if data can provide convincing evidence for natriuretic peptides levels to be used to predict and prevent 30-day readmissions.

Methods Used: We conducted a thorough literature review of PubMed publications related to BNP and NT-proBNP. Each article was evaluated based on sample size, patient population, study design, follow-up time, and relevant findings.

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Summary of Results: The highest rate for patient readmission and death occurred within the first 30 days after discharge. A strong negative predictor of events during follow-up was observed in patients that experienced a reduction in NT-proBNP levels greater than 42% during the first two weeks of hospitalization. Patients that experienced less than a 50% decrease in NT-proBNP levels during hospitalization had a 57% greater risk for readmission or death. Patients with a BNP level greater than 300pg/mL at discharge and a reduction of BNP levels less than 46% during hospitalization experienced the most cardiac-related readmissions and deaths.

Conclusions: Studies have shown a direct correlation between natriuretic peptide levels and the frequency of hospital readmission for heart failure patients. However, due to the insufficient number of studies with 30-day follow-up, there is a lack of evidence and guidance available to physicians on how to best treat these patients using natriuretic peptide levels as a predictor. More research on this topic is necessary to evaluate natriuretic peptides as a tool for predicting 30-day heart failure readmissions. Our group plans to review how BNP levels are used in a large urban hospital and whether knowledge of these values is helpful in reducing 30-day readmission rates.

BETA BLOCKER EFFECT ON SURVIVAL IN SEPTIC SHOCK

Means R.1, Friese R.1, Ibrahim-Zada I.1, Weller J.1, Jones T.1 (Univ. of Arizona, Tucson, AZ) and 2St. George's Univ, St. George, Grenada.

Purpose of Study: B-blockers (BB) have been shown to modulate inflammatory response and may be a potential adjunctive treatment for sepsis. The study’s purpose was to examine continuous delivery of low doses of BB on the effect on survival after endotoxinosis. We hypothesized that a dose-response relationship exists between BB usage and survival after septic insult in a murine model.

Methods Used: C57BL/6 male mice underwent intraperitoneal injection of lipopolysaccharide (LPS). Four hrs post-injection, animals underwent cannulation of the external jugular vein with placement of an osmotic pump. Pumps delivered a β-1 selective antagonist (100, 50 or 10 ug/ml esmolol) or an equal volume of saline. Outcome was measured by survival at 120hrs post LPS injection.

Summary of Results: There was no statistical difference observed in survival across BB doses or compared to saline. The BB groups were combined and compared to the saline groups. Both saline and a combined BB group had a median survival of 48hrs. BB-treated animals had an increased mean survival (65.5hrs) than saline (56hrs) but this difference was not significant with our small sample size. The survival rate in the BB group increased after 48hrs compared to that in saline group: 13/26 (50%) in BB vs. 3/16 (19%) in control group.

Conclusions: BB may have a delayed effectiveness in improving overall survival after septic insult. Perhaps this is secondary to products from gene expression having an immunomodulatory effect. These findings warrant further studies to explore the mechanism of action of BB in sepsis.
to A549.shRNA.scr cells. Moreover, RhoA inhibition augmented anchorage-independent growth in both cell lines.

**Conclusions:** Syndecan-1 loss by lung cancer cells promotes a more aggressive phenotype. Compared to lung cancer cells replete with syndecan-1, we found that cells lacking syndecan-1 demonstrated augmented anchorage-independent growth and activation of the tumor suppressor PTEN, with concomitant suppression of the AKT cell survival pathway. RhoA appears to be involved in the syndecan-1 pathway in a capacity that counters the development of malignant characteristics, including the ability to grow in the absence of anchorage. The effects of manipulating syndecan-1 expression and RhoA activation on the development of tumor malignancy should be investigated further.

**Summary of Results:**

Presence of culture supernatant of A549.shRNA.scr cells, significantly increased cell growth and an increased percentage of cells reaching 80% confluence. In addition, A549.shRNA.scr cells had increased phosphorylation of MAPKs (Erk 1/2, p42 and p44), as well as reduced apoptosis in comparison to A549.shRNA.scr cells. Moreover, RhoA inhibition augmented anchorage-independent growth and activation of the tumor suppressor PTEN, with concomitant suppression of the AKT cell survival pathway. RhoA appears to be involved in the syndecan-1 pathway in a capacity that counters the development of malignant characteristics, including the ability to grow in the absence of anchorage. The effects of manipulating syndecan-1 expression and RhoA activation on the development of tumor malignancy should be investigated further.

**Methods Used:**

1. To accomplish this goal, the project will focus on the quantification of a number of stress markers that were collected from the serum of patients in a critically ill study (WATTCH Trial, 203 patients with day 1 to day 28 samples available). Specifically, I will be examining the stress markers shown by previous work in patients and elite Tour de France athletes and other extreme professional athletes to relate to the severity of a patient’s catabolic state. Markers to be analyzed will include: total serum cortisol, albumin, total creatinine, LDL, ACH, GH, testosterone, troponin I, C-reactive protein, and EPO.

2. **Summary of Results:**

   Preliminary data analysis of testosterone, LDL, and creatinine kinase does not show a statistically significant association between these serum marker levels over time and death or sepsis. After accounting for age and sex, analysis of cortisol showed for every unit increase in the log(cortisol) level the result was an increase in the odds ratio for death or sepsis by 2.674 and 2.685, respectively. The p-values for this association were 0.03 and 0.026, respectively. In addition, for every μg/dl increase in the log of the mean cortisol level correlated with an increase of the log mean IL-10 value by 1.845 pg/ml.

   **Conclusions:** Cortisol levels correlated well with adverse patient events such as death and sepsis while the analysis of LDL, creatinine kinase, and testosterone were found to be statistically insignificant.

**Neonatal Pulmonary II**

**Concurrent Session**

3:30 PM

**Thursday, January 24, 2013**

**117**

**VITAMIN D SUPPLEMENTATION BLOCKS INCREASED UPPER AIRWAY REACTIVITY IN A RAT MODEL OF PERINATAL VITAMIN D DEFICIENCY**


**Purpose of Study:** There are strong epidemiologic data suggesting a link between perinatal vitamin D (VD) deficiency and childhood asthma; however, there is little evidence of intervention studies to prevent or treat perinatal asthma. There is no effective intervention to prevent or treat Bronchopulmonary Dysplasia (BPD). Curcumin has potent antioxidant and anti-inflammatory properties, and it modulates signaling of PPARγ, an important molecule in the pathobiology of BPD. Curcumin protects against hyperoxic-induced lung injury in the short-term; however, its role in longer-term prevention of BPD is not known. Therefore, we determined if curcumin has a protective effect against hyperoxic neonatal rat lung injury for 5 days at 21 days of age.

**Methods Used:** 1-day old Sprague-Dawley rats were exposed to either 21% O2 or 95% O2 for 5 days with or without curcumin (5 mg/kg) administered i.p. once daily in 100 μl volumes. During this time period, the pups were allowed to breast feed ad libitum. To prevent hyperoxic lung injury to the mother, the dams were interchanged every 24 h between the 21% and 95% O2 groups. At postnatal day (PND)21, pup lung development was studied, including the determination of pulmonary function, gross and cellular structural and functional effects, and molecular mediators of inflammatory injury. To gain mechanistic insights into how curcumin’s protective effect against hyperoxic-induced lung injury, embryonic day 19 rat lung fibroblasts were cultured and examined for markers of apoptosis and MAPK activation following in vitro exposure to hyperoxia for 24 h in the presence or absence of curcumin (5μM).

**Summary of Results:** Systematic analysis for markers of lung injury (apoptosis, Bcl-2/Bax, collagen III, oSM and lung morphology (radial alveolar count, matrix proteins elastin, tropoelastin, FGF3, 4, Fibrillin2, 5 and LDL) demonstrated that curcumin effectively blocks hyperoxic-induced lung injury. Exposing e19 lung fibroblasts to 95% O2 for 24 h inhibited cell division, an effect that was dose-dependently reversed by curcumin; mechanistically, curcumin prevented the hyperoxic-induced increases in cleaved caspase-3 and phosphorylation of MapKinase mediators (Erk 1/2, p42 and p44).

**Conclusions:** Structural and cytoprotective molecular effects of curcumin suggest that its effects against hyperoxic-induced lung injury are mediated via Erk 1/2 activation and that it is a potential intervention against BPD (Grant: NIHHD5187, HD56731, HD71731).
119

NEBULIZED NANO-CURCUMIN: A NOVEL APPROACH AGAINST HYPEROXIA-INDUCED LUNG INJURY

Husain SM, Sakurai R, Siddiqui M, Torday JS, Rehan VK. Los Angeles Biomedical Research Institute, Torrance, CA and Utah, Salt Lake City, UT.

Purpose of Study: Curcumin (diferuloyl methane) has potent anti-oxidant and anti-inflammatory properties, and it is known to modulates PPARγ signaling, a key molecule in the pathobiology of bronchopulmonary Dysplasia (BPD). We have shown that curcumin accelerates lung maturation by stimulating key alveolar epithelial-mesenchymal interactions and it blocks hyperoxia-induced neonatal lung injury, suggesting it as a potential intervention against BPD. However, its usefulness as a therapeutic modality has remained limited due to its low bioavailability. We hypothesized that curcumin delivered directly to lungs via nebulization in nanoparticle form would be an effective alternate strategy to overcome the issue of its low bioavailability.

Methods Used: Curcumin-loaded nanoparticles (nanocurcumin) were prepared by sol-oil chemistry according to previously described methods. To determine the effect of nanocurcumin on lung maturation, embryonic day 19 rat lung fibroblasts or 1-day old neonatal Sprague-Dawley rat pups were exposed to graded doses of nanocurcumin, in vitro (0-10 μM), or in vivo (0-25 mg/kg administered via nebulization in 2 ml saline), respectively, for 24h. Furthermore, nebulized (10 mg/kg once daily) nanocurcumin’s effect on hyperoxia (95% O2 for 72h)-induced lung injury was determined by analyzing for functional biomarkers of lung injury/repair.

Summary of Results: Both in vitro and in vivo, nanocurcumin administration increased functional biomarkers of lung maturation dose- and time-dependently (increased parathyroid hormone-related protein receptor, PPARγ, C/EBPα, C/EBPβ, and XIAP) and increase in fibronectin and vimentin) in markers of lung injury/repair. Similarly, in vivo hyperoxia-induced changes in molecular markers of lung apoptosis (decreased BCL2/Bax ratio) were effectively blocked in the nanocurcumin-treated group.

Conclusions: Nanocurcumin, which has significantly increased bioavailability over curcumin itself, accelerates lung maturation by stimulating key alveolar epithelial-mesenchymal interactions, and blocks hyperoxia-induced neonatal lung injury, suggesting it as a potential intervention against BPD. (Grants: NIH HD51857, HD67319 HL107118, and HD071731).

120

GENDER-SPECIFIC EFFECTS OF PERINATAL NICOTINE-INDUCED ASTHMA ON UPPER VS LOWER AIRWAY OF RAT OFFSPRING

Liu J,1 Naeem E,2 Tian J,1 Lombardi V2, Kwong K,1 Lombardi V,2 Akbari O,2 Torday J1, AIRWAY OF RAT OFFSPRING NICOTINE-INDUCED ASTHMA ON UPPER VS LOWER GENDER-SPECIFIC EFFECTS OF PERINATAL

121

VENTILATION APPROACH IS RELATED TO COLLATERAL BRAIN DAMAGE IN CRONICALLY VENTILATED PRETERM LAMBS

Alvord JM, Houston B, McCoy M, Dong L, Wang Z, Dahl MJ, McIntyre RA, Null DM, Yoder BA, DiGeronimo RJ, Lane RH, Albertine K. University of Utah, Salt Lake City, UT.

Purpose of Study: Respiratory failure and mechanical ventilation (RFMV) predisposes preterm babies towards lung injury (bronchopulmonary dysplasia or BPD). MV is necessary to keep many preterm babies with RF alive. Therefore, MV is life-saving. But MV has collateral consequences. An important collateral mechanism is neurodevelopmental impairment that often is life-long. The mechanisms by which impairment occurs are not known and therapies are not available. We recently showed that MV of preterm lambs is associated with shifts in apoptosis and proliferation in the lung and brain. The molecular mechanisms leading to these multiple-organ effects are not known. We hypothesized that a molecular mechanism is epigenetics for two reasons. First, epigenetic mechanisms influence cell apoptosis and proliferation. Second, lung and brain damage are responses to the environmental shocks of prematurity, RF, and MV.

Methods Used: Preterm (PT) lambs, treated with antenatal steroids and postnatal surfactant, were managed by (1) MV, (2) MV+valproic acid (VA; non-specific histone deacetylase inhibitor, HDACi), (3) MV+trichostatin A (TSA; specific HDACi), or (4) nasal high-frequency ventilation (HFV; positive gold standard for alveolar formation) (4 each). Treatment was 1/d (im) for 3d.

Summary of Results: Histone covalent modifications in the lung and periventricular white matter are differentially affected by ventilation mode or therapy with HDACi during MV. MV alone led to significantly more histone hypoacetylation of histone3/s3ysine14 (H3K14ac) and H3K18ac in the lung and brain compared to MV+HDACi or nasal HFV.

Conclusions: We conclude that epigenetics is a common mechanism that links evolving lung and brain injury in preterm neonates that have RF that requires MV. We speculate that clinical approaches that preserve histone hyperacetylation (e.g., postnatal HDACi or steroids) may reduce the incidence and/or severity of lung and brain injury, and perhaps reduce long-term outcomes (e.g., hypereactive airways and neurodevelopmental impairment) (HL110002, HL062875, HL056401, HD41075, HL07744).

122

EPIRINBI LIGAND AND EPFA2 RECEPTOR PROTEINS ARE UNAFFECTED IN THE BRAIN OF FORMER MECHANICALLY VENTILATED PRETERM LAMBS

Hanack A1, Skaré C2, Wimmer J1, Dahl MJ1, Dong L, West J2, McIntyre RA1, Null DM1, Yoder BA1, DiGeronimo RJ2, Lane RH1, Albertine K1. *University of Utah, Salt Lake City, UT and +Lawrence University, Appleton, WI.

Purpose of Study: Preterm (PT) neonates with evolving neonatal chronic lung disease (CLD) frequently have long-term neurodevelopmental structural and functional impairments. Underlying molecular players are unknown. The family of tyrosine kinase receptors, ephrin ligands and eph receptors, play a role in development, synapse formation, and vascular growth. Multiple modes of epigenetic regulation are evident in ephrin ligand and eph receptor expression. We asked whether their expression is persistently affected in the brain of former PT lambs at the equivalent of 2 years of age in humans.

Methods Used: We modified our PT lamb model of neonatal CLD to deliver fetuses earlier in gestation, wean them from mechanical ventilation...
(MV), and let them recover for ~3 months, which is equivalent to ~2 years postnatal age in humans. PT lambs (delivered at 128d gestation) were managed by MV for 3d, weaned to nasal high-frequency ventilation for 3d, weaned from ventilation support, and lived for 10-11 wk more (PT weaned; n=6). Control lambs were born at term gestation (~3wk after the PT lambs were delivered) and lived for 8wk more (T+8wk control; n=6). Bralndal lobe tissue was analyzed by immunoblot for ephrin B and ligands as well as EphA and B receptors, using commercially available antibodies.

Summary of Results: Protein bands were evident by immunoblot for ephrin B1 ligand and EphA2 receptor in the brain. Protein abundance of ephrin B1 ligand and EphA2 receptor was the same between PT weaned and control lambs. No bands were detected for other ephrin B ligand isoforms, any ephrinA ligand isoforms, EphA1, A3 and A4 receptor isoforms, or EphB receptor isoforms in the brain. These ephrin family members were present in the lung of the same lambs.

Conclusions: These initial results suggest that EphrinB1 ligand and EphA2 receptor proteins are not persistently altered in the brain of PT weaned lambs. We speculate that their regulation of expression is not influenced epigenetically by the stresses related to PT birth and prolonged ventilation support.

HLL10002, HL062875, L1-R1)

123

INCREASED IGF-1 EXPRESSION CAUSES ALVEOLAR SIMPLIFICATION IN CHRONICALLY VENTILATED 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. Whether IGF-1 causes alveolar simplification in this context is not known. We hypothesized that IGF-1 causes alveolar simplification.

Methods Used: Preterm (PT) lambs, treated with antenatal steroids and postnatal surfactant, were managed by (1) mechanical ventilation (MV) alone, (2) nasal HFV alone, (3) nasal HFV plus IGF-1 receptor agonist (n=4 each).

Summary of Results: Results: 16000 genes were found detectable in lung AM from newborn infants. Bioinformatics identified 748 genes whose expression was altered by greater than 10 fold in the lungs of 24 week infants compared to 35 week and 40 week controls. Further analyses showed that the differentially expressed genes constitute a wide array of functional categories. Notably, Notch a morphoregulatory gene with also immune regulation functions was reduced by 44 fold in the 24 wk infant, whereas its inhibitor, Nemo-Like-Kinase (NLK) was over-expressed by nearly 21 fold. The analyses further demonstrate a shift in expression of AM polarization markers within the first week of life in the more mature infants, indicating a functional transition from the pro-inflammatory M1, AM to the more repair-promoting M2, AM populations. Further analyses are underway to elucidate the entire repertoire of AM gene expression in the immediate in-utero-to-extra-uterine transition period.

Conclusions: The results of this study have the unique potential of elucidating fundamental mechanisms in maturational in-utero immunity at birth and its relationship to pathogenesis of chronic lung disease. They may further help to understand the mechanisms of “developmental origins of childhood and adult diseases” such as asthma.

125

PRIMARY NEONATAL RESUSCITATION WITH NASAL CANNULA: A PROSPECTIVE, OBSERVATIONAL STUDY

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Purpose of Study: To evaluate whether a specially designed nasal cannula (NC) may be an effective, alternative interface to face-mask, for ventilation of newborns requiring resuscitation in the delivery room.

Methods Used: All patients who were resuscitated with a Neotech RAM NC in the delivery room were included in the study. Patients who received any form of mask ventilation were excluded. An appropriate size NC was applied to the newborn nares and attached to a T-piece resuscitator. PEEP was set at 5 cm H2O and PIP was set at 20 cm H2O and adjusted based on the response of the patient. NCPAP was delivered initially to patients requiring pressure support. For patients who did not respond to NCPAP alone, sustained inflation for 5-10 seconds was considered for lung recruitment. Patients who required further support were resuscitated with NC-IMV. Once stabilized, patients were transported on either NCPAP or NC-IMV, without intubated. Patients that were intubated in the delivery room, were extubated to NC-IMV or NCPAP when deemed ready by the attending neonatologist.

Summary of Results: A total of 102 infants were resuscitated with NC. Gestational age ranged from 23-41 weeks. Birth weights ranged from 270-4675g. 20 patients (19.6%) were <1000g, 29 (28.4%) were between 1000-2000g, 28 (27.4%) were between 2001-3000g, 25 (24.5%) were >3000g.

Eight (7.8%) patients were intubated in the delivery room. Four of the eight (50%) patients intubated, were extubated within 24hrs to NC-IMV. The other four patients (50%) that remained intubated were all <1000g. Five (4.9%) patients required chest compressions in the delivery room, secondary to bradycardia from unsuccessful intubation attempts, or from inadequate duration of positive pressure ventilation. Five (4.9%) had pneumothorax noted on the first chest x-ray. Patients that developed pneumothoraces were >35 weeks gestational age. All of the pneumothoraces resolved spontaneously without intervention.

Conclusions: NC may be an effective, alternative interface to face-mask for ventilation of newborns requiring resuscitation in the delivery room. Prospective, randomized studies comparing NC versus mask in providing primary resuscitation are needed to confirm our study findings.

Neuroscience 1

Concurrent Session
3:30 PM Thursday, January 24, 2013

126

WIRELESS SENSORS TO CAPTURE HOME AND COMMUNITY WALKING FOR CLINICAL TRIALS AND DAILY CARE

Norberg A1, Dorsch A2, Thomas S2, Dobkin B2. 1UCLA David Geffen School of Medicine, Los Angeles, CA and 2UCLA, Los Angeles, CA.

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Purpose of Study: Until recently, clinicians have had limited methods by which to quantify the physical activity performed by patients outside of a clinical setting. In the case of walking, gait speed measured in a controlled environment is often used as a surrogate for the walking that occurs in patients’ homes and communities. Though frequently used, it has been suggested that this lab-based measure does not accurately reflect how patients walk in real-world settings. Clinicians also have a need for tools to monitor patient compliance with exercise and to characterize the quality of movements used to perform the activities of interest. To create more precise and meaningful measures, the UCLA Wireless Health Institute has developed wireless sensors and machine-learning algorithms that remotely monitor the activity of patients in their daily lives. The purpose of this study was to demonstrate the different types of information that can be obtained using wireless health technology.

Methods Used: Sixteen adult subjects with neurologic diseases resulting in gait impairment (Parkinson’s disease, Huntington’s disease) were equipped with wireless sensors at each ankle consisting of a tri-axial accelerometer. They performed four 50-foot timed training walks in clinic followed by three days of monitoring in the community. Data were processed to identify episodes of walking and gait parameters including the average daily walking speed, number of walking episodes per day, and the duration of each walking episode.

Summary of Results: Subjects wore the wireless sensors for an average of 12 hours each day (range 4-17 hours). There was no significant difference between the casual walking speed used in the clinic and the average speed of walking in the home (Wilcoxon rank sum test, p=0.05). In a given day, an average of 63% of all of a subject’s walking occurred in episodes lasting less than 30 seconds. There was a wide variation in the speed used to walk over short distances.

Conclusions: Wireless sensors can obtain multiple measures of gait and other physical activities in an inexpensive and unintrusive manner. These devices offer investigators, both in neurology and other areas of medicine, the opportunity to design better evidence-based interventions using daily real-world performance as feedback in place of self-reports.

SEX DIFFERENCES IN CENTRALLY MEDIATED EFFECTS OF INSULIN ON ENERGY HOMEOSTASIS

Ku S, Wagner EL. Western University of Health Sciences, Pomona, CA.

Purpose of Study: While extensive literature exists regarding peripheral modulation of insulin and energy metabolism, the molecular mechanisms underlying central modulation of insulin and energy metabolism remain unclear. This study examines the interaction between insulin and the hypothalamus in regulating energy homeostasis.

Methods Used: Male and female Topkea guinea pigs were randomly assigned to one of four experimental groups (brain-damaged vehicle, gene-based diet insulin, high-fat diet vehicle, high-fat diet insulin). Feeding behavior and metabolic data were recorded using a Comprehensive Lab Animal Monitoring System (CLAMS) from Columbus instruments. Changes in five indices of feeding behavior and meal pattern (cumulative food intake, incremental food intake, meal frequency, meal duration, meal size) were observed over 12 hours each day (range 4-17 hours). There was no significant difference between the casual walking speed used in the clinic and the average speed of walking in the home (Wilcoxon rank sum test, p=0.05). In a given day, an average of 63% of all of a subject’s walking occurred in episodes lasting less than 30 seconds. There was a wide variation in the speed used to walk over short distances.

Conclusions: Wireless sensors can obtain multiple measures of gait and other physical activities in an inexpensive and unintrusive manner. These devices offer investigators, both in neurology and other areas of medicine, the opportunity to design better evidence-based interventions using daily real-world performance as feedback in place of self-reports.

128

β2-CHIMAERIN-MEDIATED REGULATION OF STEREOTYPED PRUNING IN CORTICOSPINAL AXONS FROM THE VISUAL CORTEX

Shim JR1,2, Riccomagno M2, Koledkin A1,2. 1University of Washington School of Medicine, Seattle, WA; 2The Johns Hopkins University School of Medicine, Baltimore, MD and 1Howard Hughes Medical Institute, Chevy Chase, MD.

Purpose of Study: During brain development, the infrapyramidal tract (IPT) of the hippocampal dentate gyrus undergoes stereotyped retraction-like pruning, which histologically resembles axonal repulsion. Secreted Sema3F has been shown to mediate both the repulsive steering effects during axonal guidance and IPT axonal pruning. Recently, it was revealed that β2-Chimaerin is required for Sema3F-mediated pruning of the IPT but not for Sema3F-mediated axonal repulsion. This finding demonstrates that the process of synapse elimination with subsequent pruning is regulated by molecular mechanisms that are distinct from the established repellent activities of Sema3F. In light of these data, we investigated whether β2Chn is necessary for Sema3F-dependent pruning of the visual CST.

Methods Used: Performed stereotactic BDA injections into the visual cortex of transgenic β2-Chimaerin-/- and control mice brains (n=8).

Summary of Results: In both WT and β2Chn-/- mice, axon terminals were observed in the pons without extending into the medulla. In contrast, Npn2, PlexinA3, and PlexinA4 mutants showed axonal projections extending past the caudal pons and into the medulla. This suggests that β2Chn is not required for visual CST pruning.

Conclusions: The process of synapse elimination with subsequent pruning is regulated by molecular mechanisms that are distinct from the well-known repellent activities of Sema3F. Although repulsion and IPT pruning histologically appear similar, β2Chn is dispensable for repulsion, suggesting that it may be required only for pruning events and not for guidance events. However, our work demonstrating the expendability of β2Chn in visual CST pruning is not consistent with this hypothesis. Consequently, since these processes are molecularly distinct, it is particularly interesting to consider the key mediators of each process and how an axon ‘knows’ to undergo one process and not the other. Further understanding of how the semaphorin family of signaling molecules mediates axonal pruning is of considerable interest to the study of axonal regeneration and re-growth following injury or neurodegeneration.

HYPOXIA INDUCIBLE FACTOR-1 ALPHA EXPRESSION IS CRITICAL FOR POSTNATAL OLIGODENDROCYTE SURVIVAL IN THE MOUSE

Messier-Giert A1, Li L2, Wang R3, Wright K2, Cunningham L2. 1University of New Mexico, Albuquerque, NM and 2University of New Mexico, Albuquerque, NM.

Purpose of Study: Preterm birth is associated with neurodevelopmental disabilities. While matter injury is an important etiologic factor; and is likely secondary to disrupted postnatal oligodendrocyte development. Hypoxia inducible factor-1α (HIF-1α) is a prominent transcription factor expressed in hypoxic conditions, and has been identified as a regulator of neural stem cell (NSC) development in the adult subventricular zone (SVZ). As oligodendrogenesis occurs in a physiologically hypoxic fetus during the third trimester, HIF-1α could play a role in perinatal oligodendrocyte development from the NSC population. However, its specific role in supporting oligodendrogenesis, and how it may be disrupted by prematurity is unknown.

Methods Used: We utilized a conditional and inducible Cre:LoxP approach to label NSCs during the perinatal period in a mouse model. Yellow fluorescent protein (YFP) reporter expression was induced in NSCs of nestin-CreERT2/YFP transgenic mice by tamoxifen administration at postnatal day 3 (P3). Mice were sacrificed at P16 and P49 and YFP+ NSCs were immunophenotyped using cell-type specific markers for astrocytes, postmitotic neurons, and oligodendrocytes in the SVZ, hippocampus and corpus callosum. In addition, we utilized inducible HIF-1α knockout mice in which tamoxifen resulted in concomitant expression of YFP and bi-allelic HIF-1α exon 2 gene deletion in nestin+ NSCs and their progeny (nestin-CreERT2:YFP:HIF1αfl/fl). Summary of Results: At P16 and P49, the distribution of YFP+ neurons and astrocytes was relatively conserved in both nestin-CreERT2:YFP and

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nestin-CreERT2:YFP;Ifit1cre/Ifit1fl strains. However, the percentage of YFP+ oligodendrocytes was significantly reduced in nestin-CreERT2:YFP;Ifit1cre/Ifit1fl mice at P49 in the corpus callosum (31% vs 42%; p<0.0001) and SVZ (9% vs 22%; p<0.0001).

Conclusions: HIF-1α appears to play a critical role in supporting oligodendrocyte survival during postnatal NSC development. In humans, premature birth exposes the developing brain to increased oxygen concentrations, which may impede HIF-1α expression and thus oligodendrocyte development.

Supported by the Dedicated Health Research Funds from the University of New Mexico School of Medicine.

130
DIFFERENCES IN DISEASE PATTERNS BETWEEN AQUAPORIN-4 ANTIBODY-POSITIVE AND ANTIBODY-NEGATIVE PATIENTS WITH NEUROMYELITIS OPTICA
Kim S1, Traboulsee T2. 1University of British Columbia, Port Moody, BC, Canada and 2University of British Columbia, Vancouver, BC, Canada.

Purpose of Study: Neuromyelitis optica (NMO) is an autoimmune disorder of the central nervous system (CNS) characterized by optic neuritis and longitudinally extensive transverse myelitis. Since the discovery of NMO-specific autoantibody to aquaporin-4 channels (NMO-IgG), seropositivity status has been incorporated into the diagnostic criteria of NMO. However, there is a subset of patients who remain seronegative but display the full spectrum of disease. This study contrasts the clinical features between seropositive and seronegative patients who have been diagnosed with NMO.

Methods Used: With IRB ethics approval, patients meeting the 2006 NMO diagnostic criteria were sorted according to their NMO-IgG status. The following were reviewed: gender, age, ethnicity, history of autoimmune disease and age at symptom onset. Clinical severity was assessed by reviewing disease duration, time from onset to relapse, time to reach NMO diagnosis, expanded disability status scale score (EDSS), wheelchair dependence, death, and time to reach disability outcomes. Data was analyzed with a Mann Whitney-U test.

Summary of Results: Out of 46 patients diagnosed with NMO, 26 were seropositive and 20 were seronegative. The female to male ratio was significantly higher in the seropositive group, with higher proportion of Asians in the seropositive and Caucasians in the seronegative group. Seropositive patients were significantly younger at disease onset (p=0.04) and had longer disease duration (p=0.04). However, there were no differences between the patient age and autoimmune disease burden. The time from onset to first relapse and time to reach diagnosis of NMO was longer in the seropositive group, although not statistically significant. Greater proportion of patients reached EDSS scores ≥6 in seropositive group, but there was no difference in the fraction of patients who became wheelchair bound. There were 2 deaths only from the seronegative group. Time to reach wheelchair dependence was significantly longer for seronegative patients (p=0.03).

Conclusions: There are clinical differences in the disease patterns between NMO-IgG positive and negative patients, with earlier disease onset, longer disease duration, and worse disability outcomes in the seropositive population.

132
FUNCTIONAL CONNECTIVITY OF BASAL GANGLIA NETWORKS IN PARKINSON’S DISEASE PATIENTS COMPARED WITH HEALTHY, OLDER ADULTS
Kennel CE1, Berman B2, Shelton E3. 1University of Colorado School of Medicine, Denver, CO and 2University of Colorado School of Medicine, Aurora, CO.

Purpose of Study: 1) Use functional connectivity magnetic resonance imaging (fMRI) to characterize basal ganglia (BG) circuitry during a finger tapping task in healthy adults and in those with Parkinson’s disease (PD); 2) compare BG networks between healthy controls and PD patients; and 3) identify an imaging biomarker in PD patients that corresponds to symptom severity.

Methods Used: PD subjects aged 50-80 and age-matched, healthy volunteers who passed exclusion criteria received physical, neurological, and cognitive examinations, then were scanned at the University of Colorado School of Medicine’s Brain Imaging Center. fMRI involved five-finger serial tapping sequences paced with audible cues and monitored via observation and electromyography. Scans were realigned to correct for subject motion, coregistered to a mean image, and normalized to the Montreal Neurological Institute’s brain model. Image data was analyzed with SPMB, DPARSF and a MATLAB toolbox for functional connectivity that focused on six BG seeds per hemisphere plus the subject-specific motor cortex region of interest for each side. Automatic anatomic labeling mapped functional connectivity of each seed with 116 brain regions. Future work includes describing the BG functional connectivity patterns observed in healthy and PD patients, analyzing differences between the two groups, and correlating PD disease severity with changes observed in functional connectivity.

Summary of Results: Analysis is ongoing and we expect that: 1) we will be able to detect differences between BG networks of healthy controls and PD patients; 2) the detectable level of motor network disturbance of PD patients will correspond to the motor symptom severity as measured by the Movement Disorders Society’s Uniform Parkinson’s Disease Rating Scale; and 3) in addition to disturbances in the BG’s motor networks, imaging will show disturbances in the BG’s limbic and cognitive circuits in PD patients.

Conclusions: At this stage we have found differences in functional connectivity between PD patients and healthy volunteers for each BG seed, and we are in the process of characterizing these differences.
an imaging technique used to measure regional cortical changes in MRI scans following global brain shape normalization. We hypothesize that cortical thickness in the hippocampus, prefrontal cortex (Brodman area 10), and the temporal-occipital-parietal junction of healthy older men is increased following low-dose supplementation compared to placebo and usual-dose groups.

**Methods Used:** 32 healthy older men (mean: 64.0 yrs, range: 60-82 yrs) with low-normal testosterone levels (200-350 ng/dl) were randomized into one of three intervention groups: 1) no testosterone supplementation, 2) low-dose (25 mg/day), and 3) usual-dose (50 mg/day). T1-weighted brain MRI was acquired prior to and at the end of the one-year supplementation period. VBM was performed using an automated algorithm consisting of: mapping participants to a template MRI scan, extraction of gray matter for analysis of cortical thickness, modulation to account for brain size, and smoothing with a Gaussian kernel. Statistical analyses were performed with a mixed-effects ANOVA.

**Summary of Results:** Preliminary analysis showed no group differences in the change in cortical thickness between the pre- versus post-supplementation scans when using an uncorrected significance threshold of p<0.005. No significant differences in age, baseline testosterone, or education level were found between the groups prior to the study.

**Conclusions:** Further analysis of inter- and intra-group differences as well as confounding factors is needed to fully understand the effects of testosterone on neuroanatomy in older men. Participants also underwent fMRI scanning, and future analysis of these data could provide additional insight into effects of testosterone on the brain.

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**Surgery I**

Concurrent Session

3:30 PM

Thursday, January 24, 2013

134

**A “SENSATE” SURFACE REPLACEMENT SCAFFOLD TO MEASURE LOAD CHANGES IN-VIVO DURING CARTILAGE FORMATION**

Rojas J, Ouelfette J, Diggins N, Ruth J, Szivek J. Univ. of Arizona COM, Tucson, AZ.

**Purpose of Study:** Degenerative joint disease (DJD) affects over 30 million people in the United States. Focal and large cartilage defects can result from trauma to the tissue and predispose it to developing osteoarthritis (OA). Previous studies have employed polymer scaffolds as an engineered cartilage- replacement vehicle and a device capable of measuring real-time in-vivo load measurements. A surface replacement scaffold seeded with adipose derived stem cells (ASCs) has been previously used to grow canine cartilage on scaffolds were calibrated using a loading procedure involving a servo-hydraulic materials testing system. ASCs were extracted from each test animal and placed into chondrogenic media and cultured for 48 hours. The trabecular bone pattern extracted from the μCT files in combination with the peg scans were assembled into the overall shape using Solidworks. Scaffolds were built of polyethylene terephthalate (PBT) with a fused deposition modeler. Gauges on scaffolds were calibrated using a loading procedure involving a servo-hydraulic materials testing system. ASCs were extracted from each test animal and placed into chondrogenic media and cultured for 48 hours.

**Summary of Results:** Telemetry data was first collected 3 weeks post-operatively, the peak strain value was 510 μstrain, and average strain was 420 ±110 μstrain. The peak strain rate was 3950/sec and average strain rate was 2190 ±1290 μstrain. Eight weeks post-operatively, peak μstrain was 1220 μstrain, average μstrain was 560 ±330 μstrain; the peak strain rate was 4213/sec and average12 μstrain rate 2000/sec ±1100/sec.

**Conclusions:** These results could suggest an altered gait pattern with increased peak loads rate with post-op time. This implies tissue growth over the surface replacement scaffold due to ASCs differentiation into cartilage tissue. Ultimately, instrumented scaffolds can provide a monitoring system to elucidate rehabilitation regimens optimized for cartilage tissue growth in patients needing cartilage tissue regeneration.

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**135**

**INTERSPINOS SPACE REPLACEMENT SCAFFOLD TO MEASURE LOAD CHANGES IN-VIVO DURING CARTILAGE FORMATION**

Rojas J, Ouelfette J, Diggins N, Ruth J, Szivek J.

**Purpose of Study:** The goal of this study was to develop femoral surface replacement scaffold due to ASCs differentiation into cartilage tissue. Untimately, instrumented scaffolds can provide a monitoring system to elucidate rehabilitation regimens optimized for cartilage tissue growth in patients needing cartilage tissue regeneration.

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**136**

**PERIOPERATIVE OUTCOMES OF PRIMARY RENAL TUMOR RESECTIONS: COMPARISON OF IN-HOURS TO OUT-OF-HOURS SURGERY**

Forbes CM1, Aljalihlah A2, Butterworth SA3, 1University of British Columbia, Richmond, BC, Canada and 2BC Children’s Hospital, Vancouver, BC, Canada.

**Purpose of Study:** Primary resection is typically performed for children with localized suspected Wilms’ tumors. Surgical access limitations may necessitate performing these operations nights and weekdays. We hypothesize that outcomes will be worse in patients having nephrectomies out of hours (OOH) compared to those in standard hours (IH).

**Table 2.** Operation variables for in hours (IH) versus out of hours (OOH) primary resections of renal tumours

<table>
<thead>
<tr>
<th>Variable</th>
<th>IH</th>
<th>OOH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Operating Room Time (min)</td>
<td>206</td>
<td>211</td>
</tr>
<tr>
<td>Mean Incision-to-Closure Time (min)</td>
<td>148</td>
<td>148</td>
</tr>
<tr>
<td>Mean Intraoperative Blood Loss (cc)</td>
<td>178</td>
<td>244</td>
</tr>
<tr>
<td>Patients Receiving Intraoperative Blood Product</td>
<td>4 (9%)</td>
<td>3 (11.5%)</td>
</tr>
</tbody>
</table>

**Table 3.** Operation outcomes for in hours (IH) versus out of hours (OOH) primary resections of renal tumours

<table>
<thead>
<tr>
<th>Outcome</th>
<th>IH</th>
<th>OOH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsule Rupture</td>
<td>12 (27%)</td>
<td>8 (42%)</td>
</tr>
<tr>
<td>Major Intraoperative Complications</td>
<td>1 (2%)</td>
<td>5 (26%)</td>
</tr>
<tr>
<td>Mortality</td>
<td>0 (0%)</td>
<td>1 (5%)</td>
</tr>
</tbody>
</table>
Methods Used: With IRB ethics approval, primary renal tumor resections performed on oncology patients between 2000-2011 were reviewed retrospectively. IH operations were defined as Monday-Friday 0745-1530. Outcomes included major intraoperative complications, capsule rupture, blood loss and operating time. Data were analyzed using Fischer Exact and Mann-Whitney U tests.

Summary of Results: There were 64 patients with renal tumors who underwent primary resection. Forty five procedures were performed IH, 19 OOH. Groups were similar in age, ASA status, tumor size and grade. IH compared to OOH major intraoperative complications, capsule rupture, mean blood loss and mean operating times were 2% vs 26% (p=0.007), 27% vs 42% (p=0.05), 178 ml vs. 244 ml (p=0.15) and 148 minutes for both groups respectively. There was one perioperative mortality (OOH).

Conclusions: Primary renal tumor resections performed OOH were associated with an increase in major complications compared to those performed in standard hours. Avoidance of OOH operating may reduce morbidity for children undergoing primary renal tumor resections.

137

UPPER POLE ACCESS: DOES IT INCREASE THE COMPLICATION RATE FOLLOWING PERCUTANEOUS NEPHROLITHOTOMY?
Ng C, Culpepper DJ, Crouch JD, Mai AT, Baldwin D, Arnold DC, Wallner CL, Huang GO, Engebretsen S, Olgin G. Loma Linda University School of Medicine, Loma Linda, CA.

Purpose of Study: Percutaneous nephrolithotomy (PCNL) is a common treatment used for the removal of staghorn calculi. Upper pole access often affords the surgeon the most efficient and direct access for treating large branched calculi. However, upper pole access has been reported to result in a higher complication rate. At our institution we routinely employ fluoroscopy and ultrasound guidance to avoid chest complications in upper pole access PCNL. The purpose of this retrospective review is to compare the complications of upper pole access PCNL to access obtained in the middle and lower pole of the kidney.

Methods Used: A retrospective review was performed of 325 patients treated with percutaneous nephrolithotomy (PCNL) at a single academic institution between 2002 and 2012. Demographic characteristics, stone size, operative time, length of hospital stay, transfusion rate, stone-free rate, Clavien-Dindo score, and perioperative complications were compared between patients with upper pole access and those with access at other locations. Comparison between groups was performed using Pearson-Chi squared test and Mann-Whitney U Test with p<0.05 considered significant.

Summary of Results: We found no difference in BMI (P=0.465), operative time (P=0.795), overall stone burden (P=0.976), Estimated blood loss (P=0.592), and post-operative hospital stay (P=0.68). We did find a statistical difference in age (P=0.002). Controlling for access location, we found no significant difference in Clavien-Dindo score (P=0.072), complication rate (P=0.112), stone-free rate (P=0.349), and transfusion rate (P=0.927). Post-operative pain measured in parenteral morphine equivalents was not significantly different for post-operative day one (P=0.247) and day two (P=0.782).

Conclusions: The complication rate for upper pole access and mid/low pole access was similar in our population.

138

COMPARISON OF RENAL FUNCTIONAL OUTCOMES AFTER PERCUTANEOUS CYROABLACTION
Mai AT, Wallner CL, Huang GO, Ng C, Crouch JD, Culpepper DJ, Baldwin D, Engebretsen S, Arnold DC, Olgin G. Loma Linda University School of Medicine, Loma Linda, CA.

Purpose of Study: Partial nephrectomy (PN) and percutaneous cryoablation (PC) are nephron-sparing approaches for the treatment of small renal mass. The purpose of this study was to compare the short term and intermediate changes in glomerular filtration rate (GFR) in patients undergoing PN and PC.

Methods Used: A retrospective chart review was performed on 138 patients who underwent PC or PN between 2001 and 2011 for renal mass 5cm or less. A total of 95 had complete data sets for analysis. Patient data was analyzed for: age, gender, BMI, ASA, renal mass size, mass location, operative time, pre- and postoperative hemoglobin, perioperative complications, and serum creatinine. Furthermore, serum creatinine levels were compared between PC and PN postoperatively, at 1-3, 4-9, 10-20, and 21+ months of follow-up. Renal function was estimated by calculating glomerular filtration rate (GFR) from serum creatinine using Modification of Diet in Renal Disease (MDRD) study guidelines. GFR changes were compared using a Mann-Whitney U Test and chi-square test with p<0.05 considered significant.

Summary of Results: When the 42 PC patients were compared to 53 PN patients there was no significant difference in gender, tumor size, pre-op Hgb, and pre-op GFR. The PC patients were older (median age 71 vs 60 yrs; p=0.01), but had lower mean ASA score (2.1 vs 2.5; p=0.01) and lower mean BMI (28.3 vs 30.7 kg/m^2; p=0.02). The percent change in GFR was significantly different on post-operative day one, but no different between groups at other time points. When performing a multivariate analysis controlling for difference in age, ASA, BMI, operative time, hospital stay, and change in Hgb, the percent change in GFR on postoperative day one was correlated with operative time (p=0.038).

Mean GFR at 1 year follow up was the same in PC group compared to PN group. Mean follow-up was 33 months for PN group and 18 months in PC group.

Conclusions: Patients undergoing PN have a decreased GFR postoperatively compared to PC, which resolved by 1-3 months and remained relatively stable throughout the duration of follow-up. Selection of treatment modality for treatment of a small renal mass should be based on factors other than potential change in GFR.

139

KIDNEY DONOR RADIATION EXPOSURE PRIOR TO TRANSPLANTATION
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Purpose of Study: During the evaluation of kidney donors, patients may receive substantial radiation exposure. Donors represent a high-risk population due to their excellent health and relatively young age. It is important that physicians fully understand all implications of each of the donor imaging studies including the potential radiation exposure. The purpose of this study is to characterize radiation exposure received by living donors during evaluation.

Methods Used: A retrospective, single-center review of 363 donor nephrectomy patients evaluated over a 12-year period was performed. By protocol each donor received a chest x-ray, nuclear GFR, renal scan, and a 3-phase CT of the abdomen. CT effective dose was estimated by multiplying the dose length product by standard conversion factors. Effective dose for renograms, mammograms, and chest x-rays were estimated using published values. Effective dose was compared during study intervals using Microsoft Excel® with p<0.05 considered significant.

Summary of Results: Of 363 donors, complete yearly data including dose length product was available in 166 patients. Mean total effective dose was 29.7 mSv, with 83.6% of exposure resulting from the CT imaging. 20.5% of donors received ≥ 40 mSv, the estimated average radiation exposure of the atomic-bomb survivors in Japan. Furthermore, 6.6% received ≥ 50 mSv, which is the maximal occupational radiation exposure allowed annually. Radiation exposure from CT imaging decreased by 42.9% (p<0.01) during the study period likely reflecting an increased awareness of radiation risks.

Conclusions: Renal donors are exposed to significant ionizing radiation. Knowledge of the radiation exposure received by donors may allow transplant centers to more accurately counsel donors regarding risk and stratify imaging protocols to maximize patient safety.

140

COMPARISON OF ARTHROSCOPIC VERSUS OPEN SUTURE ANCHOR REPAIR OF THE LATERAL LIGAMENT ANKLE COMPLEX: A CADAVER STUDY
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Purpose of Study: Ankle inversion injury is a common injury in the United States. Operative treatment of mechanical ankle instability is indicated for patients with multiple sprains and instability despite bracing and rehabilitation. The objective of this study is to compare the biomechanical strength of open fixation to lateral ligament stabilization using a novel arthroscopic surgical technique.

Methods Used: Power analysis showed the need for seven matched pairs of cadaver ankle specimens. One specimen from the pair underwent open...
fixation and the other underwent arthroscopic stabilization. The calcaneo-
fibular ligament (CFL) and anterior talofibular ligament (ATFL) were ex-
cised from their origin on the fibula. In the first group, a #2 fibrowire suture 
was placed in the CFL and another suture in the ATFL in a running Krackow 
fashion. Suture anchors were used to reattach the ligaments anatomically. 
In the second group, identical suture anchors were used to repair the lateral ligament 
complex via an arthroscopic technique. Surgical repairs were performed by 
board-certified, fellowship-trained Foot and Ankle Orthopaedic Surgeons. The 
ligaments were tested to failure. Torque to failure, degrees to failure, initial stiff-
ness, and stiffness were measured. A matched pair analysis was performed. 

**Summary of Results:** Torque at failure was 18.3 Nm for the open group 
and 15.6 Nm for the arthroscopic group (p=0.47). Degrees to failure in the arthroscopic group 
was 58.4 degrees compared to 46.6 degrees in the open group (p=0.10). 
Initial stiffness in the arthroscopic group was 0.43 Nm/degree compared to 
0.30 Nm/degree in the open group (p=0.11). Stiffness was 0.57 Nm/degree in 
the arthroscopic group and 0.50 Nm/degree in the open repair group (p=0.71).

**Conclusions:** There is no statistical difference in torque at failure and stiffness 
of a traditional open repair as compared to an arthroscopic repair of the lateral 
ligaments of the ankle. An arthroscopic technique can be considered for lateral 
ligament stabilization in patients with mild to moderate mechanical instability. 

141

**HUMAN MESENCHYMAL STEM CELLS CULTURED ON BIPHASIC NANOFIBER SCAFFOLDS FOR ROTATOR CUFF REPAIR**

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**Purpose of Study:** Injuries to the rotator cuff often occur at the tendon-to-
bone insertion which consists of a continuous multi-tissue transition from 
tendon, non-calcified and calcified fibrocartilage, to bone. However, this 
complex matrix heterogeneity is not regenerated with the current surgical 
treatment approaches to repair torn rotator cuff, leading to high surgery failure rate. 
We aim to develop tissue engineering strategies to regenerate the tendon-to-bone 
interface in the rotator cuff. To this end, we designed a biomimetic biphasic 
scaffold consisting of poly lactide-co-glycolide (PLGA) nanofibers and 
composite nanofibers of PLGA and hydroxyapatite (HA) nanoparticles 
(PLGA-HA). We hypothesized that when seeded with mesenchymal stem 
cells (MSCs), this biphasic scaffold would promote regeneration of a fibro-
cartilage-like interface, thus improving biological fixation of the rotator cuff.

**Methods Used:** Electrospun scaffolds were cut into 1.8 cm \( \times \) 1 cm pieces 
and secured in clamps. Human MSCs were seeded onto the scaffolds at 
a density of 6\( \times \)10\(^4\)/phase of scaffold. The cells were cultured for 28 days on 
the biphasic scaffolds (experimental group) with the monophasic PLGA 
(0%/HA) and PLGA-HA (15% HA) scaffold groups serving as the control. 
End point analyses include cell viability and morphology (n=2, days 1, 14, 21, 
and 28), and proliferation (n=5, days 1, 14 and 28).

**Summary of Results:** It was observed that MSCs readily attached to the 
scaffold, and conformed to the aligned organization of the underlying 
nanofiber matrix. Moreover, the cells grew and became confluent on all three 
types of scaffolds at all time points evaluated.

**Conclusions:** Based on these results, we found that the biphasic scaffold did 
not decrease the viability and proliferation rate of the MSCs when compared 
to the single phase scaffolds. It is expected that cells on the biphasic scaffold 
would have the ability to produce collagen rich, fibrocartilage-like ECM. 
Future studies will be performed to test this hypothesis, as well as animal studies 
to test the effectiveness of the biphasic scaffold in rotator cuff repair in vivo.

143

**ABNORMAL SINOATRIAL NODE PACEMAKING ACTIVITY OF ATRIAL-SPECIFIC SODIUM-CALCIUM EXCHANGER KNOCKOUT MICE**

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Angeles, CA and \(^2\)Cedars Sinai Heart Institute, Los Angeles, CA.

**Purpose of Study:** The sodium-calcium exchanger (NCX) is the dominant 
calcium (Ca\(^+\)) efflux mechanism in cardiac cells, and is hypothesized to be 
a critical component of sinoatrial node (SAN) pacemaker activity. It is 
surprising that atrial-specific NCX knockout (KO) mice live into adulthood. 
However, these mice have lower heart rates than wildtype (WT) mice, and no 
P waves on surface electrocardiogram, suggesting abnormal SAN pacemaking 
activity. To test the hypothesis that NCX is required for initiation of 
pacemaking in SAN, we examined the cellular level activity of atrial-specific 
NCX1 KO mice through optical voltage mapping.

**Methods Used:** We isolated the right and left atrium and the SAN and 
placed it on the bottom of an imaging chamber coated with Sylgard 
and stretched by pinning the atria. We loaded the tissue with the voltage-sensitive 
indicator di-4-anepps for 40 minutes and performed optical voltage mapping 
on a 400 diode mapping system (WuTech Instruments, H469-V Photodiode Array). 
Data were recorded using custom software programmed in IDL 6.1 (ITT Exelis, McLean,VA).

**Summary of Results:** In the WT, there was an organized and rapid spread 
of depolarization from the SAN to both atria, with the points of initiation 
clustered within a small area. The leading pacemaker region in KO was 
poorly defined, with multiple initiation points involved in the depolarization. 
The depolarization spread more slowly throughout the preparation and the 
SAN did not reliably depolarize the atria. The beta agonist isoproterenol 
(ISO, 100nM) increased depolarization frequency of initiation points in both 
WT and KO, but didn’t increase the success of atrial depolarization in the KO.

**Conclusions:** The inability of KO mice to depolarize the atria could explain 
the lack of P waves on ECG. However some cells within the NCX KO SA 
node do spontaneously depolarize and respond to ISO, albeit slower and more 
irregular than WT. This suggests that a rudimentary but disorganized spontane-
ous depolarization mechanism can function in SAN cells despite the 
lack of NCX. Thus NCX appears to be required for organized pacemaker activity 
in mouse SAN.
A STRATEGY TO INCREASE SKILLED ATTENDANT BIRTHS IN KENYA

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Purpose of Study: To increase the number of skilled birth attendant (SBA) deliveries in health facilities in Kenya with assistance from traditional birth attendants (TBAs).

Methods Used: In Yatta District of Kenya, less than 20% of births occur in the presence of an SBA. TBAs were recruited to attend community health education interventions, where they were encouraged to educate pregnant women about the importance of delivering at local health facilities and offered a small stipend for future pregnant clients they brought to a facility for an SBA delivery. Primary outcome was the proportion of antenatal care (ANC) patients who delivered at the intervention health facilities compared to control facilities. Outcomes were evaluated after one year.

Summary of Results: During the year that preceded the intervention (baseline), there were 102 births and 524 ANC patients in the intervention facilities, and 413 births and 2068 ANC patients in the control facilities. During the study period, there was a 113% increase in the number of births occurring at the health facilities in the two intervention areas compared to the preceding year. The proportion of ANC patients who delivered in a facility during the study period was 49.3% at the intervention facilities compared to 20.8% at the control facilities (p < .0001).

Conclusions: The rate of skilled-attended births in health facilities in Kenya with assistance from traditional birth attendants to local health facilities to deliver.

THE ESET HISTONE METHYLTRANSFERASE IS CRITICAL TO OSTEObLAST DIFFERENTIATION AND TRABECULAR BONE FORMATION

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Purpose of Study: The ESET protein functions as a histone methyltransferase. Our purpose was to identify an epigenetic regulator of osteoblast differentiation thus gaining new insight into skeletal development and disease processes.

Methods Used: Histological characterization in wild-type and ESET-null mice was carried out with alkaline phosphatase (ALP) and TRAP staining kits. MicroCT scans of the whole body and tibia were performed on 5 week animals. Mesenchymal stem cells (MSC) were isolated from mouse bone marrow and cultured in standard osteogenic medium before staining for ALP.

Summary of Results: The tibia of the knockout mutant is significantly shorter than that of the wild-type animal, and lacks a physis. Another prominent feature of the knockout mice is the lack of trabecular bone. Histological staining demonstrated ALP activity was significantly stronger in the wild-type tibia than in the knockout. MSC from wild-type bone marrow efficiently differentiated in become osteoblasts, whereas very few MSC from the ESET knockout bone marrow were able to become osteoblasts.

Conclusions: In this study, we have demonstrated that the ESET histone methyltransferase is critical to trabecular bone formation. Decreased trabecular bone formation in ESET-null animals appears to be mainly caused by significantly impaired MSC differentiation into osteoblasts.

PHARMACOLOGICAL INHIBITION OF NFkB IN COMBINATION WITH TAXANE-BASED CHEMOTHERAPY FOR TREATING ADVANCED THYROID CANCER

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Purpose of Study: Nuclear factor-κB (NFκB) is activated in many cancers and plays a key role in promoting cell proliferation, survival, and invasion. This pathway has also been shown to play a role in resistance to chemotherapy and radiotherapy in some cancers. Most patients with advanced thyroid cancer are fairly resistant to standard chemotherapy. We hypothesized that inhibition of NFκB signaling (bortezomib) will sensitize thyroid cancer cells to standard chemotherapy (docetaxel).

Methods Used: One anaplastic thyroid cancer cell line (8505C) and one papillary thyroid cancer cell line (BCPAP) were used to study the effects of bortezomib and docetaxel in combination or alone. An SRB-based growth proliferation assay was used to assess cell growth inhibition (3 days; 0-20 nM docetaxel, 0-10 nM bortezomib), while a Matrigel based invasion assay was used to assess invasion (18 hours; 0.31 nM docetaxel, 1.25 nM bortezomib). Apoptosis was studied using the Promega 3/7 Caspase Assay kit (24 hours; 8505C Bliss Index: -0.145, BCPAP Bliss Index: -0.362;). Invasion is inhibited cell proliferation, decreasing cell growth more than either drug alone (8505C: 16% invasion combo, 84% bortezomib, 73% docetaxel, BCPAP: 38% combo, 125% bortezomib, 91% docetaxel). The combined drug treatment activates the apoptosis pathway as indicated by Caspase activity, while only bortezomib activates the Caspase pathway alone (5 nM docetaxel, 30 nM bortezomib, 8505C: 6.48-fold Caspase increase bortezomib, 1.07 docetaxel, 6.89 combo; BCPAP: 7.90 bortezomib, 1.30 docetaxel, 8.63 combo).

Conclusions: These data indicate that the combination of bortezomib and docetaxel is an attractive therapy for advanced thyroid cancer. Global decreases in growth and invasion with bortezomib and docetaxel in combination using clinically achievable IC50 values are encouraging for preclinical in vivo studies.

VIRAL BREAKTHROUGH IN HEPATITIS C

Ferguson JD, Zhou K, Bau S, Saab S. DGSOM at UCLA, Los Angeles, CA.

Purpose of Study: Despite improved virologic response with the addition of direct acting agents (DAA) to peginterferon and ribavirin treatment in chronic hepatitis C virus (HCV) genotype 1 infection, a subset of patients experience viral breakthrough while on therapy. Defining viral breakthrough and patient characteristics is important for ongoing and future HCV treatment.

Methods Used: Fifty-eight patients treated with either boceprevir or telaprevir between June 2011 and July 2012 were retrospectively evaluated for presence of viral breakthrough. Baseline HCV characteristics, time to viral breakthrough, and HCV resistance patterns were determined.

Summary of Results: Viral breakthrough was seen in 15.5% of patients. All patients with viral breakthrough were on telaprevir treatment. 8 out of 9 patients experienced breakthrough in the peginterferon and ribavirin
(PR) only phase of treatment with mean time to breakthrough of 21.6 weeks (±6.5). Viral breakthrough was primarily seen in patients with genotype 1a, prior null response, advanced liver fibrosis and presence of resistant mutations at time of breakthrough.

**Conclusions:** A significant proportion of patients experience viral break-through after completion of treatment with direct acting agents (DAA). More frequent virologic assessments during the PR-only phase may be necessary to reduce cost and adverse effects of treatment.

**Characteristics of Patients with Late Viral Breakthrough**

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<th>Race</th>
<th>Ethnicity</th>
<th>Pretreatment</th>
<th>Viral Load Breakthrough</th>
<th>Viral Load 4 Weeks</th>
<th>Viral Load 12 Weeks</th>
<th>Time to Viral Breakthrough</th>
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**Purpose of Study:** Neonatal diseases, e.g. hemolytic anemias, ischemia/ reperfusion injury, and inflammation, can result in severe hemolysis and lead to the accumulation of pro-oxidative free heme (FH). Heme oxygenase (HO) is primarily responsible for detoxifying FH. Since neonates have an increased RBC turnover rate, a functional HO system is critical for the neonate and could be exhausted in these conditions. Thus, we studied the protective effects of HO in a model of heme overload.

**Methods Used:** For in vitro studies, NIH/3T3 cells, with the full-length HO-1 promoter fused to the reporter gene luciferase (HO-1-luc), were incubated with vehicle or 10, 30, or 60 μM FH or methemalbumin (MHA). HO-1 promoter activity was assessed 3, 6, and 24 h after treatment by in vivo bioluminescence imaging (BLI). Cell survival was indexed by LDH and viability assays. For in vivo studies, 1-wk-old and adult (~5-wk-old) FVB mice were injected IP with 60μmol FH/kg BW. After 24 h, AST levels were determined. Livers were harvested and HO activity and lipid peroxidation (LP) measured.

**Summary of Results:** In HO-1-luc cells, HO-1 promoter activity peaked 6 h after incubation with 30μM FH (1.6-fold) or 60μM MHA (2.1-fold) compared to baseline. 24 h after exposure to 60μM FH, a cytotoxicity of 48% and an 80% decrease in viability were found; whereas, no cytotoxicity or decrease in viability were seen after exposure to 60μM MHA. In 1-wk-old pups given 60μmol FH/kg, we found a significant 3.9-fold increase in HO activity and no changes in LP or AST levels. In adult mice, HO activity similarly increased (3.6-fold), but, the absolute level of this increase was <50% of 1-wk-old levels (107-382 vs. 213-432 pmol CO/lmg fresh weight, respectively), and LP and AST levels significantly increased 11- and 1.5-fold, respectively.

**Conclusions:** FH is highly toxic, but toxicity is abolished when bound to albumin (MHA). In contrast to adults, newborns appear to be protected from the pro-oxidative effects of FH. This protection may be mediated by a higher HO capacity at baseline and after FH induction. We conclude that HO activity and heme binding are critical in early life; and, if either are deficient, can lead to the development of stress-related diseases, and may even explain the observed association between hemolytic jaundice and neurologic injury.
151

COST-BENEFIT ANALYSIS OF INDIRECT ANTIGLOBULIN SCREENING IN RH(D) NEGATIVE WOMEN AT 28 WEEKS GESTATION

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Purpose of Study: Current professional guidelines recommend Rh(D) blood typing and anti-D antibody screening at the first prenatal visit and re-peat screening at 24-28 weeks for Rh(D) negative mothers who are not iso-immunized. However, the rate of isoimmunization of Rh(D) negative women before the 28th week is below 0.18%. Our study updated this seroconversion rate before the 28th week and constructed a decision tree model to analyze the costs and benefits, and under what circumstances, elimination of the second antiglobulin screen for Rh (D)-negative mothers during pregnancy would be cost-beneficial.

Methods Used: A chart review of all Rh(D) negative mothers delivering at the University of WA from 2002-2012 was conducted to determine the rate of gestational seroconversion to anti-D antibodies before 28 weeks. This seroconversion rate was used to construct a decision analysis tree to estimate the economic benefits of eliminating the antiglobulin screen at 28 weeks, and instead immunizing all Rh(D) negative, anti-D antibody negative women with anti-D immune globulin at that time. A theoretical cohort of 100,000 women was modeled. Probabilities and costs were derived from published literature, chart review, and expert opinion. A Monte Carlo analysis was used to test for sensitivity.

Summary of Results: The seroconversion rate of development of anti-D antibodies before 28 weeks in the cohort analyzed was 0.099% (2,029 women). The expected cost savings from implementing the reduced anti-globulin screening strategy ranged from $6 - $7.7 million. The cost savings for implementing this strategy in the U.S. for one year ranged from $34.7 - $35.6 million. This strategy remains cost beneficial when varying cost and parameters to their logical extremes. The Monte Carlo analysis verified the cost savings of our strategy.

Conclusions: The updated seroconversion rate and our model suggest that eliminating the 28 week antibody screen would be cost beneficial from a societal perspective and pose minimal potential harm.

152

SMALL INTERFERING RNA TO TREAT PANCREATIC CANCER

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Purpose of Study: Most pancreatic cancers possess point mutations in the K-Ras oncogene. The majority of K-Ras point mutations result in K-Ras being constitutively activated leading to increased cell proliferation, growth, and inhibition of apoptotic pathways. Studies have suggested that small interfering RNA (siRNA) designed against mutated K-Ras (mK-Ras) may be a treatment option for pancreatic cancers. The aim of this study was to characterize the effects of mK-Ras siRNA on cell viability, proliferation, and confluence in pancreatic cancer cell lines.

Methods Used: mK-Ras siRNA and scrambled siRNA was designed as ready-annealed, purified duplexes. Panc1, Panc 8.13, Panc 10.05, cell lines with mK-Ras, and BxPC3 cells, with wild type K-Ras (wK-Ras), were seeded in quadruplicate in 96 well plates at 1.2 x 10^4 cells per well and incubated for 24 hours at 37°C. Cells were then treated with either cycloheximide (positive control), scrambled siRNA, or mK-Ras siRNA designed against a point mutation at the 12th codon of the K-RAS oncogene. Cells in proliferation studies were treated with trypsin blue and enumerated. Cells in the metabolic assays were treated with CellTiter Blue and quantified with a fluorometer. Measurements were taken at 48, 72, and 96 hours.

Summary of Results: Studies showed significant down-regulation of mK-Ras compared to cells treated with scrambled siRNA at all time-points, while BxPC3 cells showed no significant change in wK-Ras expression. Viable cell numbers were significantly reduced in cells treated with mK-Ras siRNA compared to scrambled siRNA in cell lines with mK-Ras. BxPC3 viable cell number was not significantly affected by mK-Ras siRNA. Cell lines with mK-Ras that were treated with mK-Ras siRNA had significantly lower metabolic activity compared to scrambled siRNA at all time-points. The effect that mK-Ras siRNA had on BxPC3 cell metabolic activity was only significant at the 24 hour time-point.

Conclusions: The mK-Ras siRNA utilized in this study appears to specifically downregulate mK-Ras mRNA and not wK-Ras mRNA. Treatment of cells possessing mK-Ras point mutations with mK-Ras siRNA inhibits cancer cell proliferation, while cells with wK-Ras are unaffected. Metabolic activity of cells with mK-Ras is inhibited by treatment with mK-Ras siRNA.

153

A HIGH-THROUGHPUT, MECHANISM-BASED WHOLE-CELL SCREEN USING ESKERCHIA COLI TO IDENTIFY INHIBITORS OF THE SEC PATHWAY OF BACTERIAL PROTEIN EXPORT

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Purpose of Study: Due to the increasing prevalence of antimicrobial resistance among human pathogens, antibiotics that work by attacking novel microbial targets are needed. Our research targeted the Sec pathway, a bacterial membrane transport system that mediates export of proteins from the cytoplasm to the cell envelope. Recent studies suggest this pathway could be an excellent drug target in both Mycobacterium tuberculosis and gram-negative bacteria. We developed a novel screening assay and conducted a high-throughput screen for small molecules that inhibit this pathway.

Methods Used: We used a genetically engineered strain of Escherichia coli that produces a b-galactosidase (b-gal) protein with a lambda signal sequence, which is exported from the cytoplasm into the periplasm where it is inactive. The screen was conducted in 384 well plates using sodium azide, an inhibitor of the SecA ATPase, as a positive control, and LB growth media as a negative control. Experimental compounds were added to all other wells. Inhibition of the Sec pathway showed an increase in b-gal activity, corresponding to an increase in absorbance at 405nm. Median absolute deviation based Z-score values were assigned to each experimental well, which were then ranked as strong, medium, or weak hit, or not a hit.

Summary of Results: We screened a total of 57,476 compounds in duplicate which included 7,721 known bioactives, 38,843 commercial compounds, and 10,912 natural product extracts. A total of 612 hits were detected in duplicate, which included 269 weak hits (Z-score > 2.5 - < 3), 176 medium hits (Z score > 3 - < 4.5), and 167 strong hits (Z score > 4). Of the 335 non-natural product hits, 109 of those have been identified as medium or strong hits that are devoid of potential liability.

Conclusions: Though data analysis is ongoing, our screen has identified more hits than previous screens of the Sec pathway. Previous screens focused on a single target, such as SecA ATPase, while our cell-based assay focused on the entire Sec pathway. Follow-up studies will involve confirmation of inhibition of Sec-mediated protein translocation in the strong to medium hits and evaluation of their effects on microbial growth.

154

ACUTE KIDNEY INJURY: B-CELLS AND THE ROLE OF IL-10

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Purpose of Study: Ischemia/reperfusion injury (IRI) to the kidneys results in a robust inflammatory response. The role of B-cells in this response is very complex and experimental data suggests that distinct B cell subsets can cause both aggravation and mitigation of injury. Evidence for a protective role of B-cells has been linked to the expression of the anti-inflammatory cytokine IL-10. It is the goal of this research to monitor changes of IL-10 expression following ischemia and identify the role of IL-10 in limiting renal IRI.

Methods Used: Kidney ischemia was induced in mice by bilateral clamping of the renal pedicles for 24 minutes followed by reperfusion for 24 to 96 hours. Serum, kidneys, and spleen were collected at various timepoints after reperfusion. analysis of IL-10 expression was performed and compared with sham-treated mice. IL-10 protein in the serum was measured by ELISA. Tissue expression of IL-10 RNA in kidneys and spleen were examined with quantitative PCR.
Summary of Results: Serum analysis of IL-10 protein showed a 2-fold increase at 24 hours of reperfusion relative to sham-treated mice. Serum levels returned to sham levels at 48 hours and increased again at 72 hours. IL-10 expression in the spleen increased approximately 2-fold compared to that of sham-treated animals after 24 hours of renal reperfusion, and maintained increased levels of expression at 48 and 72 hours. IL-10 expression in the kidney increased 5-fold relative to sham-treated animals at 24 hours of reperfusion. Expression had declined at 48 and 72 hours but remained elevated relative to sham-treated animals.

Conclusions: In response to kidney ischemia, RNA expression of IL-10 in the kidney and spleen increases by 5-fold and 2-fold, respectively, when compared to sham treated animals. Additionally, expression of the IL-10 protein also increases based on increased levels of IL-10 in serum in experimental mice compared to sham-treated mice. This increased expression of IL-10 may be part of a protective response by B-cells against damage to the kidney caused by ischemia and subsequent inflammation. Future experiments will be focused on further characterization of IL-10 expression in B-cell populations, and modulating IL-10 expression in mouse models in order to observe the effects on renal IRI.

157

VENTILATION APPROACH IS RELATED TO COLLATERAL BRAIN DAMAGE IN CHRONICALLY VENTILATED PRETERM LAMBS


Purpose: Respiratory failure and mechanical ventilation (RFMV) predisposes preterm babies towards lung injury (bronchopulmonary dysplasia (BPD)). MV is necessary to keep many preterm babies alive. Therefore, MV is life-saving. But MV has collateral consequences. An important collateral consequence is neurodevelopmental impairment that often is life-long. The mechanisms by which impairment occurs are not known and therapies are not available. We recently showed that MV of preterm lambs is associated with shifts in apoptosis and proliferation, and that expression of key transcription factors and histone acetylation is reduced by MV treatments. The molecular mechanisms leading to these multiple-organ effects are not known. We hypothesized that a molecular mechanism is epigenetic for two reasons. First, epigenetic mechanisms influence cell apoptosis and proliferation. Second, lung and brain damage are responses to the environmental shocks of preterm birth, RF, and MV.

Methods: Preterm (PT) lambs, treated with antenatal steroids and postnatal surfactant, were managed by (1) MV, (2) MV+valproic acid (VA; non-specific histone deacetylase inhibitor, HDACi), (3) MV+trichostatin A (TSA; specific HDACi), or (4) nasal high-frequency ventilation (HFV; positive airway pressure, as a gold standard for alveolar formation) (4 each). Treatment was 1/2 (im) for 3d.

Summary of Results: Histone covalent modifications in the lung and periventricular white matter are differentially affected by ventilation mode or therapy with HDACi during MV. MV alone led to significantly more histone hypoacetylation of histone3/lysine14 (H3K14ac) and H3K18ac in the lung and brain compared to MV+HDACi or nasal HFV.

Conclusions: We conclude that epigenetics is a common mechanism that links evolving lung and brain injury in preterm neonates that have RF that requires MV. We speculate that clinical approaches that preserve histone hypoacetylation (e.g., postnatal HDACi or steroids) may reduce the incidence and/or severity of lung and brain injury, and perhaps reduce long-term outcomes (e.g., hyperreactive airways and neurodevelopmental impairment) (HL110002, HL062875, HL056401, HD41075, HL07744).

156

HANDHESS IN RASOPATHIES

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Purpose of Study: Rasopathies are a group of genetic disorders which often have language, motor, and neurocognitive delays. Other syndromes associated with language and cognitive delays have shown differences in handedness. Our objective was to determine non-right-handedness among patients with Rasopathies.

Methods Used: Individuals and/or parents of individuals with neurofibromatosis type 1 (NF1), cardiofaciocutaneous (CFC) syndrome, Costello syndrome, and Noonan syndrome were asked which hand is dominant in the process of testing them for grip strength. Grip strength using handgrip dynamometers were performed on both hands. Data were compiled and compared to published data from the general population (11.5% non-right-handed).

Summary of Results: A total of 300 individuals with a Rasopathy had data on handedness (mean age 13.6 yrs) [NF1 (N=163), CFC (N=29), Costello (N=53), and Noonan syndromes (N=55)]. Non-right-handedness was significantly increased compared to the general population in individuals with CFC syndrome (28%; p=0.007) and Costello syndrome (23%; p=0.06, but not in NF1 or Noonan syndrome (9%) or NF1 (6%). While the differences in hand grip strength of the dominant vs. non-dominant hand across disease groups were compared, individuals with CFC had lower differences as compared to the other syndromes suggesting disturbances in development of hand dominance.

Conclusions: These data suggest an increased number of left handed and ambidextrous individuals in individuals with Costello and CFC syndrome. These data are consistent with those found in other conditions with language or cognitive delays (e.g. autism spectrum disorders, Down syndrome, Williams syndrome). CFC and Costello syndrome typically have more cognitive delays than NF1 and Noonan syndrome. Animal studies of primates do not show as strong a bias toward right handedness and some primates have shown no bias at all suggesting that lateralization potentially provides an evolutionary advantage. It is possible that the evolution of language ability and cognitive reasoning in humans - mostly in the left brain - gave rise to a right hand preference. This study suggests that delays in cognition, independent of the signal transduction pathway affected, may lead to disturbances in hand preference development.
THE EFFECT OF MEDICARE VS. PRIVATE INSURANCE ON ACCESS TO KIDNEY TRANSPLANTATION

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Purpose of Study: Kidney transplantation is superior to dialysis for patients with kidney failure as it prolongs survival and improves quality of life. To receive a kidney transplant, patients must be waitlisted for a deceased donor (DDK) or receive a living donor transplant (L DK). Many factors affect this access to transplantation (ATT), including type of insurance. Patients without insurance are dialyzed under emergency coverage, but cannot enroll on the waiting list until they dialyze for at least 90 days and qualify for Medicare. We studied kidney waiting list patients to evaluate ATT, and to quantify the effect of insurance on the probability of receiving a transplant.

Methods Used: The United Network of Organ Sharing database was used to identify 128,088 adult kidney candidates and recipients from 1995-2011 who dialyzed prior to registering on the waiting list. Individuals receiving a transplant before beginning dialysis were excluded. The time from dialysis to listing, and the waiting list events of transplantation, death, and delisting were assessed as outcomes based on insurance type and age. Data management, T tests, and the Fine and Gray competing risk method were performed using STATA.

Summary of Results: 62-68-year-old patients with Medicare were delayed an additional 126 days from dialysis to listing compared to 62-68-year-old-patients with private insurance (P < 0.001). Furthermore, the Medicare group received fewer transplants (SHR, 1.183; 95% CI, 1.11-1.27; P < 0.001) than the group with private insurance. While the Medicare group received fewer L DK than the privately insured group (SHR, 1.77; 95% CI, 1.49-2.10; P < 0.001), there was no significant difference in the number of DDK. Within the Medicare group, 62-64-year-old patients were delayed by 67 days vs. 66-68-year-old patients (P < 0.001). There was no difference in transplant rate within the Medicare group.

Conclusions: Privately insured patients have increased access to transplantation. While the rate of DDK transplantations are similar regardless of insurance type, Medicare patients take longer to list and receive fewer LDK than patients with private insurance.

RNA EXPRESSION PATTERNS IN SERUM MICROVESICLES FROM PATIENTS WITH GLOBLASTOMA MULTIFORME AND CONTROLS

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Purpose of Study: To come up with a novel non-invasive molecular marker for the diagnosis of glioblastoma multiforme.

Methods Used: Microvesicle RNA from serum from patients with de novo primary glioblastoma multiforme (N = 9) and normal controls (N = 7) were analyzed by microarray analysis. Samples were collected according to protocols approved by the Institutional Review Board. Differential expressions were validated by qRT-PCR in a separate set of samples (N = 10 in both groups).

Summary of Results: Expression profiles of microvesicle RNA correctly separated individuals in two groups by unsupervised clustering. The most significant differences pertained to down-regulated genes (121 genes > 2-fold down) in the glioblastoma multiforme patient microvesicle RNA, validated by qRT-PCR on several genes. Overall, yields of microvesicle RNA from patients was higher than from normal controls, but the additional RNA was primarily of size < 500 nt. Gene ontology of the down-regulated genes indicated these are coding for ribosomal proteins and genes related to ribosome production.

Conclusions: Serum microvesicle RNA from patients with glioblastoma multiforme has significantly down-regulated levels of RNAs coding for ribosome production, compared to normal healthy controls, but a large over-abundance of RNA of unknown origin with size < 500 nt.

CHRONIC LUNG ALLOGRAFT DYSFUNCTION: DO DISTINCT SPRIOMETRIC PHENOTYPES EXIST?

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Purpose of Study: Chronic lung allograft dysfunction (CLAD) is the major limitation to long-term survival after lung transplantation. The course of CLAD is variable suggesting different phenotypes may exist. The purpose of the study was to distinguish and characterize two phenotypes of CLAD—bronchiolitis obliterans syndrome (BOS) and restrictive allograft syndrome (RAS)—using spirometric parameters, radiographic findings, and inflammatory chemokine biomarkers. We also wanted to evaluate risk factors for BOS and RAS.

Methods Used: Bilateral lung and heart/lung transplant recipients were included in this retrospective, observational cohort study. CLAD was diagnosed using standard spirometric criteria. CLAD subjects were divided into obstructive (BOS phenotype) and nonobstructive. Nonobstructed CLAD patients were further divided into restrictive (RAS phenotype) or indeterminate groups. We examined CT scans for key findings. Bronchoalveolar lavage fluid CXCR3 chemokine concentrations were determined by a bead immunoassay and compared between groups. We determined the impact of CLAD phenotypes on survival with Kaplan-Meier plots and used Cox Proportional Hazard models to assess risk factors.

Summary of Results: BOS, severe POD, Pseudomonas, and Aspergillus all appear to be unique risk factors for BOS, but not RAS. Air trapping (78%) and bronchiectasis were the most common CT findings for BOS, while pleural fibrosis (35%) and parenchymal fibrosis (75%) were more commonly seen for RAS. Both BOS and RAS were associated with a worse post-transplant survival compared to no CLAD. After diagnosis, the RAS phenotype had a more rapid progression to death. The RAS group had higher BALF concentrations for each chemokine measured with CXCL-10/IP-10 being significantly higher.

Conclusions: While BOS is the most common form of CLAD, a separate “restrictive” phenotype can be distinguished by spirometry. RAS appears to be associated with a more inflammatory chemokine milieu and a more rapid progression to death after diagnosis. Limitations of the study include a low sample size in the RAS group, however with an enlarged sample size, we hope to further investigate if inflammatory chemokines can be used to predict survival.

PROGNOSTIC BIOMARKERS IN PATIENTS WITH DOWNSTAGED PANCREATIC CANCER

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Purpose of Study: Pancreatic ductal adenocarcinoma (PDAC) is the 4th leading cause of cancer-related deaths in the United States with an overall five-year survival rate of less than 3 percent. Approximately 40 percent of PDAC patients present with locally advanced tumors, which prevents them from being surgically resected. These patients are treated with chemotherapy and/or radiation therapy with the goal of downstaging their tumors to permit surgical resection. Despite successful resection, many still develop recurrences and die of their disease. To address this issue, we examined three prognostic biomarkers SMAD4, S100A2, and microRNA 21 (miR-21), in patients who underwent surgical resection for early stage disease. We hypothesized that these biomarkers would predict their prognosis after surgical resection.

Methods Used: Detailed clinical and survival data was collected for 11 patients diagnosed with locally advanced PDAC who were downstaged and surgically resected at UCLA. Expression of SMAD4 and S100A2 was performed using immunohistochemistry and miR-21 in situ hybridization on fresh frozen paraffin embedded sections. Biomarker expression was correlated with each patient’s clinical history and outcome. Data analysis was performed using IBM SPSS 18.

Summary of Results: SMAD4, S100A2, and stromal miR-21 were expressed in 6 (54.5%), 1 (9.1%), and 4 (36.4%) patients respectively. Down-staged patients with intact SMAD4 expression had a median survival of 41.7 months (95% CI: 27.3 - 56.2 months), in contrast to 21.3 months (95% CI: 10.6 - 32.0 months) in SMAD4 inactivated patients. The log-rank chi-square analysis for survival was 3.575 with a p-value < 0.05. This survival advantage corresponds to a cumulative 30 months survival after surgery of 71% in patients with SMAD4-intact compared to 36% of patients with SMAD4-negative tumors. Patients lacking stromal miR-21 expression had better survival but did not reach statistical significance in our small cohort.

Conclusions: Of the three biomarkers analyzed, SMAD4 expression strongly correlated with survival in this patient subgroup. Therefore, patients with SMAD4 negative downstaged tumors should be strongly considered for adjuvant therapy following surgical resection.
MATERNAL OBESITY AND RISK OF CEREBRAL PALSY

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Purpose of Study: To determine whether a maternal hospital diagnosis of obesity during pregnancy is associated with risk of cerebral palsy (CP) in the child.

Methods Used: For this population-based historical cohort study, we linked the following three sources: 1) newborn hospital discharge abstracts from 6.2 million California births in 1991-2001; 2) maternal hospitalization discharge abstracts up to twelve months before delivery; and 3) California Department of Developmental Services records of all children who received services for CP before 2006. We identified maternal hospital discharge diagnoses of obesity (ICD-9 646.1, 278.00 or 278.01) and morbid obesity (ICD-9 278.01), and performed logistic regression to explore the relationship between maternal obesity diagnoses and CP.

Summary of Results: 67,200 (1.1%) mothers had a diagnosis of obesity and 7878 (0.1%) were diagnosed with morbid obesity; 8797 (0.14%) children had CP. A maternal diagnosis of obesity (RR 1.30, 95% CI 1.09-1.55) or morbid obesity (RR 2.70, 95% CI 1.89-3.86) was associated with increased risk of CP. In a multivariable model adjusting for maternal race, age, education, prenatal care, insurance status and infant sex, both obesity (RR 1.33, 95% CI 1.25-2.35) or morbid obesity (RR 3.79, 95% CI 2.35-6.10) remained independently associated with CP. Adding maternal and perinatal complications to the model attenuated but did not eliminate the association between CP and obesity. On stratified analyses, the association of a diagnosis of obesity (RR 1.72, 95% CI 1.25-2.35) or morbid obesity (RR 3.79, 95% CI 2.15-6.10) with CP was only significant among the 7.1% of women who were hospitalized prior to the birth admission. This association persisted even after adjusting for intrapartum factors. In contrast, there was no association between obesity and CP among women who did not require prenatal hospitalization.

Conclusions: A diagnosis of maternal obesity was associated with increased risk of CP in this study. Given the unprecedented rate of obesity in the US and the fact that obesity is a potentially modifiable condition, further studies are warranted to confirm and better understand this association.

VITAMIN D ATTENUATES LUNG INJURY AND IMPROVES SURVIVAL IN INFANT RATS AFTER ANTEnatal ENDOTOXIN EXPOSURE

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Purpose of Study: Chorioamnionitis contributes to the pathogenesis of BPD. Although Vitamin D (Vit D) has immunomodulatory and anti-inflammatory properties, but whether Vit D can prevent the adverse effects of antenatal inflammation is unknown. In this study, we sought to determine whether vit D treatment could enhance lung survival and preserve fetal lung vascular alveolar growth.

Methods Used: Fetal rats were exposed to ETX (10μg), ETX + Vit D (1ng/ml), or saline via intra-amniotic (IA) injection at 20 days gestation (term: 22 days) and delivered two days later. Newborn pups were randomized to receive daily intraperitoneal (IP) injections of Vit D or saline for 2 weeks. Radial alveolar counts (RAC) were assessed at 14d. The effects of Vit D on cell growth and tube formation were studied with pulmonary artery endothelial cells (PAEC) from fetal sheep. PAEC were exposed to ETX (1ng/ml), or saline via intra-amniotic (IA) injection at 20 days gestation (term: 22 days). Both saline and ETX were assessed. RAC were assessed at 14d. The effects of Vit D on cell growth and tube formation were studied with pulmonary artery endothelial cells (PAEC) from fetal sheep. PAEC were exposed to ETX (100-400nM) alone or during exposure to ETX (1ng/ml).

Summary of Results: Preliminary Vit D treatment improved survival (100% 10/10 animals) in rat pups that were exposed to IA ETX when compared to ETX exposure alone (65% 15/25 animals) at DOL 14 (p < 0.001). In comparison to rats exposed to IA ETX + Vit D alone, the addition of postnatal treatment with Vit D improved RAC at 14 days by 54% (p < 0.05). In control PAEC, Vit D increased cell growth and tube formation by 64 and 44% (p < 0.001), respectively. ETX decreased PAEC growth and tube formation by 57% and 53% in comparison with controls (p < 0.05), and additionally Vit D treatment preserved PAEC growth and tube formation in a dose-dependent manner (p < 0.001).

Conclusions: Vit D improved survival and enhanced lung structure after antenatal ETX exposure, and prevented ETX-induced PAEC injury in vitro. We speculate that vitamin D therapy may preserve lung growth through enhancement of endothelial survival and growth in experimental chorioamnionitis.

CHECKPOINT KINASE 1 INHIBITION SUPPRESSES CELL GROWTH AND ENHANCES RADIATION SENSITIVITY IN MEDULLOBLASTOMA CELLS

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Purpose of Study: Medulloblastoma is the most common malignant brain tumor in children and remains a therapeutic challenge due to its significant therapy-related morbidity. Checkpoint kinase 1 (CHK1) is highly expressed in many cancers and regulates critical steps in mitotic progression and DNA-damage response. Activation of CHK1 pathway promotes radiation resistance in tumor cells. Recent studies suggest that targeting CHK1 with a small molecule inhibitor, to sensitize tumors to a variety of DNA-damaging agents, is a promising approach to tumor therapy.

Methods Used: The expression of CHK1 mRNA in medulloblastoma tumor samples was examined using microarray analysis. Western blot analysis was conducted on all tumor samples to analyze expression level of CHK1 protein. The impact of CHK1 on cell proliferation was evaluated by inhibiting its function using a small molecular inhibitor AZD7762. Colony formation studies were conducted to examine the long-term impact of AZD7762 on medulloblastoma cell growth. Flow cytometry was used to measure apoptosis.

Summary of Results: Analysis of gene expression and western blot analysis revealed that CHK1 mRNA and protein levels are overexpressed in all medulloblastoma patient samples when compared to normal cerebellum. Inhibition of CHK1 by a low nanomolar concentration of AZD7762, a small molecule inhibitor of CHK1, potently inhibited cell growth, suppressed the colony formation ability, and increased cellular apoptosis of medulloblastoma cells.

Conclusions: Our data suggest that targeting CHK1 with a small molecule inhibitor is an attractive strategy in treatment of medulloblastoma. Future experiments will be focused on treating medulloblastoma cells with CHK1 inhibitor prior to ionizing radiation exposure to examine its effect on radiation sensitivity.
had lower geometric mean (±SEM) CB at study weeks 8 (0.7±0.3 vs. 2.7±1.3 mg/dL, p<0.05) and 9 (0.5±0.2 vs. 2.8±1.5 mg/dL, p<0.05) and non-significantly lower median percent CB change/week (17% (range, -33-60%) vs. 30%-44% (10-172%), p=0.1) compared to CON. LOW weighed less at discharge compared to CON (3.2 vs. 3.5 kg, p=0.02), but weight change was comparable. 15% of CON developed intestinal failure, while none of LOW subjects developed this condition. When LOW was compared to CON, total caloric intake was similar except during study weeks 1 and 2 (90 vs. 106 and 92 vs. 111 kcal/kg/d, p=0.05 each). There was no statistically significant difference in the caloric intake primary outcome (25 vs. 23%, p=1) and other secondary outcomes when LOW was compared to CON.

Conclusions: Considering the sample size and unequal distribution of confounders, it remains unclear if low dose soybean oil is effective and safe for the prevention of cholestasis in this population. Further study is warranted.

Adolescent Medicine, General Pediatrics, and Nephrology I
Concurrent Session
12:30 PM
Friday, January 25, 2013

166
INTRAUTERINE GROWTH RESTRICTION AND MATERNAL HIGH FAT, HIGH CHOLESTEROL DIET INCREASE HEPATIC CHOLESTEROL AND DECREASE HEPATIC SREBP2 IN RAT OFFSPRING AT BIRTH
Purpose of Study: Maternal consumption of a high fat, high cholesterol diet (mHFCD) during pregnancy predisposes the newborn towards non-alcoholic fatty liver disease (NAFLD) at birth. Intrauterine growth restriction (IUGR) similarly predisposes the infant towards NAFLD in adolescence. Little is known about how mHFCD and IUGR combined affect NAFLD. High hepatic cholesterol characterizes NAFLD. Hepatic cholesterol depends on the expression of sterol-responsive element binding protein protein 2 (SREBP2) and its target HMGCoA reductase (HMGRCR). We subsequently hypothesized that IUGR and mHFCD would each increase hepatic cholesterol and decrease SREBP2 and HMGR mRNA compared to either IUGR or mHFCD alone.

Methods Used: Virgin female rats were fed either a regular diet (RD) or a HFC diet for 5 weeks prior to mating. IUGR was induced by bilateral uterine artery ligation at day 19 of a 21 day gestation. Pup liver lipids and mRNA were isolated at birth. Intrauterine growth restriction (IUGR) similarly predisposes the infant towards NAFLD in adolescence. Little is known about how mHFCD and IUGR combined affect NAFLD. High hepatic cholesterol characterizes NAFLD. Hepatic cholesterol depends on the expression of sterol-responsive element binding protein protein 2 (SREBP2) and its target HMGCoA reductase (HMGRCR). We subsequently hypothesized that IUGR and mHFCD would each increase hepatic cholesterol and decrease SREBP2 and HMGR mRNA compared to either IUGR or mHFCD alone.

Summary of Results: Compared to control offspring of RD fed dams (Con-RD), control offspring of maternal HFCD fed dams (Con-mHFCD) and IUGR offspring of RD fed dams (IUGR-RD) did not have increased liver cholesterol levels or decreased SREBP2 or HMGRCR mRNA levels. Compared to Con-mHFCD, female IUGR pups from mHFCD dams (IUGR-mHFCD) increased hepatic cholesterol at birth (131±10%, p=0.05). Compared to Con-mHFCD offspring, IUGR-mHFCD decreased SREBP2 mRNA (77±6%, p=0.05 in female, and 67±7%, p=0.01 in male) and HMGRCR mRNA (66±7%, p=0.05 in female). Conclusions: We conclude that IUGR-mHFCD increased hepatic cholesterol and decreased SREBP2 and HMGRCR mRNA levels more than IUGR or mHFCD consumption alone. Maternal HFCD and IUGR disrupt the nutritional environment of the developing fetal pup. Combined in utero insults of mHFCD and IUGR may alter SREBP2 and HMGRCR expression thereby predisposing to increased hepatic cholesterol levels in UG offspring.

167
ENVIRONMENTAL IMPACTS ON PEDIATRIC RURAL ASTHMA
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Purpose of Study: Pediatric asthma is a leading chronic disease for children. Environmental factors influence asthma outcome in urban studies, yet rural studies remain few. We assessed environmental risk factors and asthma control in a population of Latino children in an agricultural area.

Methods Used: This study involved 52 school-aged children with asthma participating in a longitudinal study of agricultural factors and asthma. They were recruited from a rural farmworker clinician’s asthma education program. Surveys assessing environmental risk behaviors or factors in their households before and at exit from the educational program were obtained and reviewed. The larger study provided data from biweekly Asthma Control Questionnaires (ACQ). Mean annual ACQ scores were calculated and compared to survey data on environmental risk behaviors and factors, both individually and as a bimodal exposure intensity score (greater than or less than 65% of the factors).

Summary of Results: Participants were aged 7-15 years at enrollment and 92% self-identified as Latino. Common outdoor factors on exit survey included agricultural pesticide exposure (44%) and crop farms and unpaved dusty roads within 0.25 miles (both 48%). Bedroom carpet (60%), strong perfumes/sprays (37%), and home pesticide use (30%) were commonly reported indoor factors. The presence of a burn barrel (p-value<0.11) and household smoker (p-value=0.07) were suggestive of poorer asthma control based on higher mean ACQ scores. Contrary to our hypothesis, children with bed dust mite covers had poorer mean ACQ scores (p-value=0.04). Using the composite score, the mean ACQ for children with consistent (same exposure factor intensity before program and on exit survey) low trigger exposure was 0.52, consistent high trigger exposure was 0.60, increasing trigger exposure was 0.38, and decreasing trigger exposure was 0.53.

Conclusions: Rural cohorts may face a high number of potential environmental asthma triggers, including factors unique to the agricultural environment. As observed in urban studies, individual factors do not appear to influence asthma control. Techniques to characterize the impact of these multiple and somewhat distinctive factors on asthma control in rural children with asthma are needed.
Conclusions: Concussions are an underemphasized issue for children in this social problem rather than encourages it. A reason to avoid drinking and driving may help raise a generation that fights to avoid drinking and driving. Our study provides new evidence that suggests that the majority of students who were asked if they had experienced a concussion had not reported it to their doctor. We hope that this study will help parenting more seriously about the effects of concussions and the importance of seeking medical attention for concussions.

Summary of Results: Roughly 100 members in the community attended the event. The attendance, participation, and positive feedback indicate that the information was well received. All students received handouts, as well as the parent that attended, and the younger children also received free helmets if they did not own one already. All project materials were given to Eureka Health Promotion Committee as informative tools for future use.

Conclusions: Concussions are an underemphasized issue for children in Eureka, Montana. After attending the educational events, community members are motivated to take head injuries in children more seriously and advocate for early recognition and conservative care. Research shows that concussions have a cumulative effect and are more detrimental the younger the individual; therefore educating students at an early age is essential. Low cost educational programs partnering with other prominent community leaders to raise awareness and community involvement are key to this project's success. Future research will be needed to determine the long-term effects of this project.

AN INTERESTING CLUSTER OF OSTEOSARCOMAS IN THREE ADOLESCENTS

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Case Report: Conventional high-grade osteosarcoma is a rare, highly malignant primary bone tumor. Only about 400 cases of osteosarcoma are diagnosed each year in the U.S. in patients under age 20 which is 0.5 cases per 100,000 persons. Because of its rare occurrence and seemingly benign initial presentation, it is imperative that pediatricians have a high index of suspicion for osteosarcoma and learn about diagnosis and management early in the disease. We report 3 cases of osteosarcoma, all of which presented in August 2012 to the Children’s Hospital of Nevada.

The first case is a 17 year old African American male presenting with pain and swelling to his left leg. Pain began 5 months prior, after hitting his left shin on a car door. A month later, he noticed swelling over the same location. His diagnosis was delayed because his family did not initially think his complaint was serious. X-ray showed a soft tissue mass with associated lucencies and elevation of the periosteum over the left anterior distal tibia which was verified with MRI. An open biopsy confirmed diagnosis of osteosarcoma.

The second case is a 13 year old Hispanic female presenting with right leg swelling and pain for 6 months that started after she fell in PE. She was initially diagnosed with growing pains. A week prior to admission, she had an injury that exacerbated her pain out of proportion to the injury. Xray and MRI showed an infiltrative malignant-appearing mass arising from the right proximal fibula and a CT scan of the chest suggested possible metastatic disease. Her osteosarcoma was confirmed with open biopsy.

The third case is a 13 year old Filipino female presenting after one month of increasing left tibial swelling and pain without trauma. She had noticed the mass grew quickly. Xray and MRI showed osseous abnormalities suspicious for highly aggressive malignant neoplasm. Her open biopsy showed a high-grade osteosarcoma.

This cluster of cases of a rare bony tumor presenting within a month gave us the opportunity to review the presentation and management of this tumor. The rarity with which osteosarcomas present made this interesting and through this case report we hope to stress the importance for pediatricians to be aware of this highly malignant tumor and to have a high index of suspicion for early diagnosis.

HAVE “SUN” SENSE: SUN SAFETY AWARENESS FOR YOUTH IN MILES CITY, MT

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Purpose of Study: The Miles City community is largely agriculturally based and has many opportunities for outdoor recreation. Both of these factors result in prolonged sun exposure for community participants. Evidence suggests that ultra-violet radiation from sun exposure during early life is associated with increased risk for various adulthood skin cancers. The project’s purpose was to implement a sun safety curriculum that teaches youth how to limit sun exposure and prevent skin damage.

Methods Used: Studies suggest optimum health behavior modification occurs where a learning infrastructure already subsists. I partnered with a youth summer enrichment program (ROCKS) to implement an evidence-based curriculum. It encompassed sun safety knowledge and behaviors from current literature including: the sun’s benefits and harmful effects, healthy skin functions, components of sun protection, and proper sunscreen use. The program was conducted in a multistep fashion that included interactive learning. The first activity was a sun safe relay that reinforced the effectiveness of wearing sun protective articles. In the second activity, children constructed UV sensitive bead bracelets that enhance exposure awareness to damaging UV rays and promote sunscreen use.

Summary of Results: The project conveyed sun safety behaviors to 48 children (grades 1-6). Education material was interactive, succinct, and age appropriate. The attendance level, enthusiastic participation, and positive feedback from the program’s staff suggest that the project was well received. Children were able to acknowledge appropriate sun safety methods and were given to staff for future use.

Conclusions: Agricultural and outdoor recreation based communities like Miles City increase children’s risk to sun exposure. Fortunately, community programs like ROCKS take interest in youth health and education. They provided great support and guidance throughout the development of this project. By introducing an evidence-based curriculum for youth participants, it seems reasonable to expect promising results related to sun protective methods and awareness. Further studies should be conducted to see if the project leads to increased sun safety behavior among Miles City youth participants.

GO WHERE THE WILD THINGS ARE - AN EXPERIENCE IN BECOMING A WILDERNESS FELLOW WHILE A PEDIATRIC RESIDENT

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Purpose of Study: To demonstrate the feasibility of pursuing designation as a Fellow of the Academy of Wilderness Medicine (FAWM) during pediatric residency.

Methods Used: The Wilderness Medical Society (WMS) has a program “for accomplished individual who desire distinction for professional education in wilderness medicine (WMD)” under the designation FAWM. Fellowship status is attained by the acquisition of credits with required and elective WM topics from a core curriculum by involvement in eligible activities which are previewed, accepted and scored by the WMS, as well as credits in WM experience. These credits are earned within 5 years of becoming a fellow candidate.

Summary of Results: Setbacks include misinterpretation of fellowship details, conflicts scheduling eligible activities, and difficulty gaining access to approved wilderness medicine experiences. Paramount in overcoming the obstacles and realization of the designation were initiating FAWM candidacy, regular communication with the WMS, connecting with UCSF...
COST-BENEFIT ANALYSIS OF INDIRECT ANTIGLOBULIN SCREENING IN RH(D) NEGATIVE WOMEN AT 28 WEEKS GESTATION

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Purpose of Study: Current professional guidelines recommend Rh(D) blood typing and anti-D antibody screening at the first prenatal visit and repeat screening at 24-28 weeks for Rh(D) negative mothers who are not immunized. However, the rate of in immunization of Rh(D) negative women before the 28th week is below 0.18%. Our study updated this seroconversion rate before the 28th week and constructed a decision tree model to analyze the costs and benefits, and under what circumstances, elimination of the second antiglobulin screen for Rh(D) negative mothers during pregnancy would be cost-beneficial.

Methods Used: A chart review of all Rh(D) negative mothers delivering at the University of WA from 2002-2012 was conducted to determine the rate of gestational seroconversion to anti-D antibodies before 28 weeks. This seroconversion rate was used to construct a decision analysis tree to estimate the economic benefits of eliminating the antiglobulin screen at 28 weeks, and instead immunizing all Rh(D) negative, anti-D antibody negative women with anti-D immune globulin at that time. A theoretical cohort of 100,000 women was modeled. Probabilities and costs were derived from published literature, chart review, and expert opinion. A Monte Carlo analysis was used to test for sensitivity.

Summary of Results: The seroconversion rate of development of anti-D antibodies before 28 weeks in the cohort analyzed was 0.099% (2,029 women). The expected cost savings from implementing the reduced anti-globulin screening strategy ranged from $6 - $7.7 million. The cost savings for implementing this strategy in the U.S. for one year ranged from $3.47 - $3.56 billion. This strategy remained cost beneficial when varying our parameters to their logical extremes. The Monte Carlo analysis verified the cost savings of our strategy.

Conclusions: The updated seroconversion rate and our model suggest that eliminating the 28 week antibody screen would be cost beneficial from a societal perspective and pose minimal potential harm.

DIAGNOSIS AND MANAGEMENT OF INITIAL URINARY TRACT INFECTION IN INFANTS YOUNGER THAN TWO MONTHS OF AGE

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Purpose of Study: The AAP recently updated guidelines for the diagnosis and management of urinary tract infections (UTI). Diagnosis requires a positive urine culture. Routine renal ultrasound is recommended, but voiding cystourethrogram (VCUG) is not. Test of cure is recommended only if sensitivities are not available. The recommendations specifically exclude premature infants and infants less than 2 months, and management varies. This retrospective study was designed to determine the applicability of the AAP guidelines to infants less than 2 months of age.

Methods Used: The electronic database at LAC+USC Medical Center (LAC+USC) was searched for patients with UTI or VCUG between 2000 and 2009. Data was gathered from available medical records. Patients were excluded if VCUG was for indications other than UTI or if the UTI occurred after 49 weeks postmenstrual age. UTI was defined as a positive culture that was treated. Sensitivity and specificity of UA results were calculated using each subject's previous and following UA as controls. Results were compared with those published in the 2011 AAP Clinical Practice Guideline.

Summary of Results: Total of 94 UTIs and 79 VCUGs were reviewed. Median postmenstrual age in weeks was 39 at diagnosis and 41 at VCUG. Abnormal ultrasounds were more frequent in our population when compared to older children (38 vs. 15%, p<0.001), while the rate of reflux was lower (20 vs. 34%, p=0.009). There was no association between ultrasound results and reflux. Eighty samples included UA. The sensitivity of each UA component was lower than in the older group, but specificity was equal. The exception was bacteria on microscopy, which was equally sensitive but less specific than in the older group. Test of cure for bacterial UTI were uniformly negative.

Conclusions: Urine culture should remain the standard to diagnose UTI in neonates. UA is helpful but not sensitive enough to rule out UTI. Test of cure after bacterial UTI is not necessary if sensitivities are known. Reflux after the first UTI was uncommon in our group of infants; this supports the recommendation to omit routine VCUG. Renal ultrasound abnormalities were common in our population, and ultrasound did not reliably identify infants with reflux.

OSTEOPOROSIS AND BONE MINERAL DENSITY ARE ASSOCIATED WITH AORTIC VALVE CALCIFICATION: THE AGE, GENE-ENVIRONMENT SUSCEPTIBILITY (AGES)-REYKJAVIK STUDY

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Purpose of Study: Aortic valve calcification (AVC) is a marker of atherosclerosis, and occurs in the majority of subjects with osteoporosis. Studies in populations with high osteoporosis prevalence, like Iceland, may provide a clearer understanding of the pathogenesis of AVC.

Methods Used: Baseline data from the age 70-84 participants from the AGES-Reykjavik Study was analyzed. AVC was defined as score ≥ 1.75 on the backscatter image of the aortic valve. The age, gene-environment (GxE) interaction model was used to examine the interaction between age, sex, 45 single nucleotide polymorphisms (SNPs), and bone mineral density (BMD). The most significant SNPs were further analyzed in a Mendelian randomization framework, using the instrument variable for SNPs in the neighboring gene, lipoprotein lipase.

Summary of Results: A total of 17,444 participants were included. AVC was present in 1,757 participants (10.1%). Age, sex, and SNPs were significantly associated with AVC. The most significant SNPs were further analyzed in a Mendelian randomization framework, using the instrument variable for SNPs in the neighboring gene, lipoprotein lipase. The most significant SNP in the Mendelian randomization framework was a SNP in the neighboring gene, lipoprotein lipase. The results suggest that AVC is associated with osteoporosis, and that the pathogenesis of AVC may be related to the pathogenesis of osteoporosis.
Purpose of Study: There is growing recognition that calcium and bone homeostasis contributes to vascular calcification, but the association between bone mineral density (BMD) and aortic valve calcium (AVC) is unknown.

Methods Used: We studied 5764 participants of the Reykjavik Study (born 1907-35) studied at midlife (1967-96), and later phenotyped at AGES-Reykjavik exam 1 (2002-06) and 2 (2007-11). Demographics and risk factors were assessed at midlife and follow up exams, which also included computed tomography (CT) scanning. AVC was measured from CT scans using Agatston methodology. Vertebral trabecular (vt) BMD was assessed using quantitative CT, and T-scores calculated using NHANES reference standards. Subjects >65 years at midlife exam, statin users, and those with vBMD z-scores >5 or GFR <15 ml/min/1.73 m2 were excluded. Multi-variable logistic and linear regression analyses were performed.

Summary of Results: N=200 subjects (58% F; age 76±6 years) met inclusion criteria for midlife and exam 1 analyses. Over a median of 26 (range 11-36) years, each 1 cm loss of height was associated with a 1.07 (95% CI: 1.02-1.12, p=0.001) increased odds of AVC and a 0.10 (95% CI: 0.06-0.14, p<0.0005) increase in log(AVC score). At exam 1, osteoporosis (vBMD T-score<-2.5) was present in 19% of women and 3% of men, while 42% had AVC. After adjustment for age, gender, body size and cardiovascular risk factors, osteoporosis was associated with a 1.25 (95% CI: 1.03-1.53; p=0.03) higher odds of AVC, but was not associated with AVC severity (p=0.44). Among n=2793 with exam 2 AVC scores, exam 1 vBMD T-scores were inversely associated with AVC progression over a median 5.3 year follow up among women (p=0.01) but not men (p=0.82).

Conclusions: Loss of height from midlife, a marker of osteoporosis, is associated with the presence and severity of AVC in older age, while vBMD is associated with AVC on both a cross-sectional and prospective basis. These findings suggest a mechanistic link between calcium loss and valvular calcification, and perturbations in bone homeostasis, increased shear forces due to altered thoracic aorta geometry, or other potential mediators merit further investigation.

177

A "DIABETOGENIC" DIET INDUCES INSULIN RESISTANCE AND CARDIOMYOPATHY IN BTBR ob/+ MICE

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Purpose of Study: Diabetes is associated with a 2- to 3-fold risk in heart failure due to altered thoracic aorta geometry, or other potential mediators merit further investigation.

Summary of Results: We hypothesized that feeding DD to BTBR ob/+ mice would induce cardiomyopathy similar in degree to that of BTBR ob/ob mice in chow-fed BTBR mice (24-25% in heart weight, or b) feeding a "diabetogenic" diet (DD) to wild-type BTBR mice (17% in heart weight). Leptin haploinsufficient, BTBR ob/+ mice do not develop cardiomyopathy on a Chow diet, but we hypothesized that feeding DD to BTBR ob/+ mice would induce cardiomyopathy similar in degree to that of BTBR ob/ob mice.

Methods Used: At age 4 weeks, female BTBR ob/+ mice were placed on Chow diet (n=13) or DD (59% of calories from fat, 26% of calories from sucrose, n=9). Oral glucose tolerance tests (OGTTs) and fasting serum glucose levels were obtained every 4 weeks until sacrifice at 16 weeks on diets. Summary of Results: As compared to those fed Chow, DD-fed BTBR ob/+ mice had impaired glucose tolerance by 8 weeks on diets (P<0.001), and higher fasting glucose levels by 8 weeks on diets (177±4 vs. 211±4 mg/dL, P<0.0001). At 16 weeks on diets, differences persisted between Chow- and DD-fed groups for glucose intolerance (P<0.0001) and fasting glucose levels (196±4 vs. 236±11 mg/dL, P<0.0013), and body weights were 30% higher in DD-fed BTBR ob/+ mice (P<0.0001). DD-fed mice had cardiac hypertrophy, with a 22% increase in heart weight (P=0.0001) at necropsy and a 24% increase in LV mass index (P<0.0001) by echocardiography. Echocardiography also showed that DD-fed BTBR ob/+ mice had both impaired systolic function (23% increase in fractional shortening, P<0.0001), and impaired diastolic function (30% increase in Ea/Aa ratio, P=0.001).

Conclusions: Thus, 16 weeks feeding of a "diabetogenic" diet to BTBR ob/+ mice resulted in a 22% increase in cardiac hypertrophy, as well as echo-cardiographically detectable decreases in both systolic and diastolic function. Thus, diabetogenic diet-fed BTBR ob/+ mice represent a straightforward and efficient tool for studying the pathogenic mechanisms underlying cardiomyopathy in insulin resistance and diabetes.

178

HUMAN LEUKOCYTE SENSITIZATION IN HYPOPLASTIC LEFT HEART SYNDROME PATIENTS RECEIVING EARLY PALLIATIVE SURGERY WITH AND WITHOUT GRAFT TISSUE

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Purpose of Study: Patients born with Hypoplastic Left Heart Syndrome (HLHS) require prompt surgical palliation in order to sustain adequate systemic blood flow, and many eventually require cardiac transplant. The standard for surgical palliation is the Norwood surgery, which often involves the use of homograft tissue, and less frequently, bovine pericardium or synthetic CorMatrix ECM®. When exposed to non-self human material such as homograft tissue, patients can develop antibodies to human leukocyte antigens (HLAs). This so-called "HLA sensitization" often complicates and sometimes precludes future heart transplantation. A surgical alternative to the Norwood procedure, which does not involve a homograft, and thus HLA-antibodies are unlikely to develop. The goal of this study was to compare HLA-antibody levels between patients who had undergone a Norwood surgery versus a hybrid procedure.

Methods Used: In this retrospective cohort study, HLHS patients were categorized into 3 groups: Norwood (n=13), Norwood with Bovine pericardium or CorMatrix (group 2, n=6), and Hybrid (group 3, n=21). HLA class I and II antibody levels were collected from the latest available Panel Reactive Antibody (PRA) test. Conforming to current clinical practice, patients were defined as HLA sensitized if their HLA antibody levels measured by PRA were >10% HLA sensitization was compared between the 3 groups with the Fischer's Exact test.

Summary of Results: Group 1 had a significantly higher proportion of HLA-sensitized patients than group 3 (HLA class I: 38.5% vs 0%, p=0.005; HLA class II: 46.2% vs 4.8%, p=0.007). Group 2 was limited to 6 patients and only 1/6 was HLA-sensitized, not statistically significant, compared to group 1 and 3.

Conclusions: The Norwood with homograft group had a significantly larger proportion of HLA-sensitized patients than the Hybrid group. This increases the complication risk of future heart transplantation, and may lead to worse post-transplant outcomes. Further analysis of post-transplant outcomes for HLHS patients, palliated with these 3 surgical methods, will be conducted to guide their method of initial surgical palliation in the immediate newborn period.

179

ABNORMAL ABDOMINAL AORTA HEMODYNAMICS ARE ASSOCIATED WITH NECROTIZING ENTEROCOLITIS IN INFANTS WITH CONGENITAL HEART DISEASE

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Purpose of Study: Necrotizing enterocolitis (NEC) generates significant morbidity and mortality in infants with congenital heart disease (CHD). Patients with hypoplastic left heart syndrome (HLHS) have a NEC incidence as high as 20%, associated with an increased mortality odds ratio of 5.66. While the shunt physiology of HLHS theoretically increases the risk for gut hypoperfusion, shunt type does not affect NEC incidence. Similarly, there are many infants with other forms of CHD who develop NEC in the absence of decreased cardiac output or a diastolic run-off lesion. We hypothesized that additional risk factors beyond diastolic run-off contribute to gut hypoperfusion and may be detectable by analyzing abdominal aorta blood flow.

Methods Used: We retrospectively analyzed abdominal aorta Doppler pulsed-wave and spectral waveforms in two cohorts of patients with CHD. The first group included all patients who underwent Norwood palliation for HLHS at our institution from January 2007 to January 2012. The second group included all recorded cases of NEC in patients with CHD over the first 4 months of 2012 with age and anatomy matched case controls. We defined NEC based on modified Bell's criteria of stage IB or higher.

Summary of Results: 67 patients underwent Norwood palliation during the study period. Of the 63 who survived to the initiation of feeds, 11 (17.4%) developed NEC. Those with NEC had a lower pulsatility index compared...
to the rest of the cohort (2.21 ±0.28 vs. 3.05 ±0.78, p=0.01). In our second group, there were 7 cases of NEC. The cardiac diagnoses included HLHS (3), critical aortic stenosis (1), double inlet left ventricle (1), tetralogy of Fallot with absent pulmonary valve (1) and anomalous right coronary artery (1). Similar to the HLHS cohort, the average pulsatility index was lower in the NEC patients compared to age and anatomy matched controls (1.72 ±0.20 vs. 2.66 ±0.57, p=0.01).

Conclusions: Abdominal aorta Doppler pulsations are abnormal in patients with CHD whose peri-operative course is complicated by NEC. Further investigation is warranted to determine if this is secondary to changes in the mesenteric and systemic vasculature or subclinical changes in myocardial performance. Increased understanding may lead to earlier detection and prevention of gastrointestinal complications in CHD.

180
CONTEMPTON: STATUS 2 PATIENTS DO NOT NEED TO UNDERGO HEART TRANSPLANTATION
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Purpose of Study: Status 2 patients awaiting heart transplant are known to be stable on medical management usually waiting at home. Heart failure medical therapy has improved dramatically over the past several years and outcome has been improving. There is much contention as to whether these status 2 patients should even undergo heart transplant. We reviewed our single center experience with standard heart failure care to assess whether status 2 patients outcome was similar to those status 2 patients who underwent heart transplantation.

Methods Used: Between January 1, 1994 and September 30, 2007, 304 patients were evaluated for heart transplantation. Only those patients who were listed as status 2 at the time of listing were included in this study. Patients must have survived for 1 year after listing to be entered into this study. Patients were divided into those who were transplanted and those who were not during the 5-year followup of this study. Subsequent 5-year outcomes included survival and major adverse cardiac events.

Summary of Results: The status 2 patients who did not undergo heart transplant had similar subsequent 5-year survival to those status 2 patients who underwent heart transplantation (80% vs. 74%, p=0.337).

Conclusions: Status 2 stable heart failure patients awaiting heart transplant appear to have comparable outcome to those status 2 patients that undergo heart transplant. A randomized trial for status 2 patients awaiting heart transplantation is warranted.

181
THE USE OF A BEDSIDE GLUCOSE MONITOR IN HYPERINSULINEMIC EUGLYCEMIC CLAMPS
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Purpose of Study: Insulin resistance (IR) is common in type 1 (T1D) and type 2 diabetes mellitus (T2D) and predicts increased cardiovascular disease risk. The increasing obesity rates in youth worsen IR, making assessment of IR increasingly important. The current gold standard for assessing IR is a hyperinsulinemic euglycemic clamp. Blood glucose levels are typically measured at the bedside every 5 minutes for 3-5 hours by a Yellow Springs Instruments® glucose analyzer (YSI), which requires laboratory personnel, extensive warm-up and calibration, 0.5ml of blood/sample, a centrifugation step, and 2-3 minutes/sample to obtain results. The hospital-grade glucose meter Stat Strip® (Nova Biomedical) is advertised as highly accurate, fast (6 seconds/sample), more economical, portable and uses whole blood (1 drop), making it an attractive alternative for clamp studies. We hypothesized that the Stat Strip® could be used to measure glucose levels more easily and efficiently but just as accurately as the YSI.

Methods Used: We compared Stat Strip® vs. YSI, in the setting of ten 3-stage hyperinsulinemic euglycemic clamps (10, 16, 80 μm2/min insulin) in a variety of adolescents (obese, T1D, T2D and normal controls). Glucose levels were maintained at 95 mg/dl by titrating a 20% dextrose infusion based on q 5-10 min YSI-determined IV glucose readings. One half of each blood sample was centrifuged at the bedside and plasma glucose analyzed by YSI in duplicate. The second half of the blood sample was used to simultaneously determine whole blood glucose by Stat Strip® in triplicate.

Summary of Results: The averages of the two machines were highly correlated (r=0.902). There was a slight expected bias of the Stat Strip® to the YSI, in the setting of ten 3-stage hyperinsulinemic euglycemic clamps (10, 16, 80 μm2/min insulin) in a variety of adolescents (obese, T1D, T2D and normal controls). Glucose levels were maintained at 95 mg/dl by titrating a 20% dextrose infusion based on q 5-10 min YSI-determined IV glucose readings. One half of each blood sample was centrifuged at the bedside and plasma glucose analyzed by YSI in duplicate. The second half of the blood sample was used to simultaneously determine whole blood glucose by Stat Strip® in triplicate.

Conclusions: Use of the Stat Strip® could help improve the insulin clamp technique, especially in pediatrics where blood volume and speed of obtaining results are critical. Additional data are required to extend applications to non-euglycemic conditions.

182
BETA-CELL FUNCTION IS IMPAIRED IN YOUTH TREATED WITH SECOND-GENERATION ANTIPSYCHOTICS
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Purpose of Study: Second-generation antipsychotics (SGAs) are commonly prescribed to youth, but are associated with metabolic effects including weight gain and diabetes. The mechanisms underlying the development of diabetes are not clear. The purpose of this study was to compare glucose homeostasis, insulin sensitivity, insulin secretion, and overall β-cell function in risperidone-treated, quetiapine-treated and SGAs-naïve youth with mental illness.

Methods Used: A cross-sectional study in which youth aged 9-17 years assessed within BC Children’s Hospital Mental Health Program to have ≥1 DSM-IV-TR diagnosis underwent a 2-hr oral glucose tolerance test. Blood was collected at 0, 15, 30, 60, and 120 min. Indices for insulin sensitivity (Matsuda index), insulin secretion (insulinogenic index), and β-cell function [insulin secretion-sensitivity index-2 (ISSI-2)] were calculated.

Summary of Results: A total of 18 SGAs-naïve, 20 risperidone-treated, and 16 quetiapine-treated youth participated. The three groups were similar for age, sex, ethnicity, BMI standardized for age and sex (zBMI), pubertal status, degree of psychiatric illness, psychiatric diagnoses, and other medications. The median treatment duration was 17 months (range 3-91) in the risperidone

162
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group and 10 months (range 3-44) in the quetiapine group. There were no differences in fasting glucose, insulin, lipid levels or Matsuda index between groups. None of the youth had impaired glucose tolerance. The quetiapine-treated group had lower insulinogenic index ($P < 0.01$) and lower ISSI-2 ($P < 0.01$) compared to the SGA-naïve group. Regression analysis in all youth revealed zBMI as the only significant predictor of Matsuda index ($\beta = -0.540$, $P < 0.001$). Quetiapine-treatment was negatively associated with insulinogenic index ($\beta = -0.426$, $P = 0.007$) and ISSI-2 ($\beta = -0.433$, $P = 0.008$).

**Conclusions:** Quetiapine-treatment in youth is associated with overall improved β-cell function, and specifically, lower insulin secretion. Prospective longitudinal studies are required to understand the progression of β-cell dysfunction following SGA-initiation.

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**CHILDHOOD OBESITY RATES IN THE LOW INCOME POPULATION OF SAN BERNARDINO**

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**Purpose of Study:** Childhood obesity is a major problem in San Bernardino, particularly among the low-income population served by Social Action Community Health Systems (SACHS), a low-income clinic that serves a community in which 35.2% of minors live below poverty level (U.S. Census Bureau). In this study, we estimated age-related prevalence of overweight and obesity among children, age 2-15, visiting SACHS to assess the need for and to develop age-specific interventions for this high-risk population.

**Methods Used:** We reviewed the charts of 893 children, age 2-15, who visited SACHS from April 1, 2011 to January 31, 2012. Height and weight from their latest visit were recorded without identifiers. BMI-for-age percentiles were calculated on the CDC website. Three age groups (preschool, elementary, and preteen) were defined to represent children with age-specific lifestyles requiring different interventions. Estimates of the prevalence of overweight and obesity (BMI ≥85%) were obtained for each age group, along with confidence intervals, the relative prevalence between groups, and associated chi-squared tests of independence.

**Summary of Results:** Each age group consisted of about a third of the total children in the study, which conveys a lower rate of inclusion in older age groups. Overall, 34% of the study patients were overweight or obese, with a marked increase from 21% at preschool age to 34% at elementary age and 52% at preteen age. This corresponds to a 1.6 and 2.4 higher prevalence at elementary and preteen ages, respectively, than at preschool age ($p < 0.000$).

**Conclusions:** One third of children, age 2-15, who visit SACHS are overweight or obese, and this prevalence more than doubles from preschool to preteen age. These findings not only highlight the magnitude of the problem in this population but also the need to develop age-specific treatments and preventions as early as possible.

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**FITNESS CAMP: PART OF A SOLUTION TO CHILDHOOD OBESITY?**

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**Purpose of Study:** Childhood obesity is a national health epidemic. In the U.S., 17% of children and adolescents are overweight or obese. This study aimed to determine whether a free one-week fitness day camp for overweight children from low-income families could improve health knowledge and change health attitudes.

**Methods Used:** Physicians and school nurses selected overweight children in San Bernardino County to attend a week-long fitness day camp. The camp consisted of exercise, health education, and healthy meals. Participants completed pre and post camp true/false question surveys. Health Knowledge Surveys (HKS) involved questions regarding health information; exercise requirements, portion sizes, and the risks of being overweight. Attitudinal Surveys (AS) included questions regarding attitudes; importance of eating healthy, exercising, and needing to make lifestyle changes. We performed a t-test on the HKS questions and a chi-square test on the AS questions to assess change.

**Summary of Results:** Of the 115 children, 85 were overweight and 30 were normal/underweight. Results of the HKS: Pre camp, 61.83 ± 17 questions correct; post camp, 70.05 ± 15 questions correct; $p < 0.00027$. Results of the AS: No significant differences measured in the pre and post camp survey. The p-value approaches a significant value for one question, ($P < .0469$) “Do you think what you eat makes a difference in your health?” 50-90% of the children answered “yes” to some or all of the attitude questions on the pre-survey. These children again answered “yes” on the post-survey.

**Conclusions:** A one-week fitness camp is an appropriate intervention to improve children’s health knowledge. There were no significant attitudinal changes because the children already knew the importance of exercising, liking themselves and realizing the need to make changes to their diet and exercise habits. The significance of this camp was to give the knowledge “tools” necessary to make these changes. Since knowledge increased at the end of this camp, these week-long interventions could be an effective intervention for fighting childhood obesity.
INTERACTIVE NUTRITIONAL EDUCATION AT THE BOYS & GIRLS CLUB IN FERNDALE, WASHINGTON

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Purpose of Study: Obesity is endemic in the United States and an increasing problem worldwide. Childhood obesity leads to increased risk for T2DM, hypertension, and cardiovascular disease. It is linked to depression and low self-esteem in children. These issues are a major concern in Ferndale, Washington. The goal of the project was to create an interactive and reproducible nutritional curriculum for after school/summer programs like the Boys & Girls Club.

Methods Used: Key social service leaders provided input on the health concerns of Ferndale's diverse community. All interviewees identified obesity, T2DM and hypertension as the major health concerns. The Ferndale Boys & Girls Club director indicated their programs covered physical activity, but lacked healthy nutrition. Through collaboration, an hour and a half nutritional education program focused on 8-10 year olds was developed. The professional literature was reviewed for the best teaching methods indicated for the target population. MyPlate.gov was chosen for its user-friendly activity sources. The curriculum produced included: an interactive educational component, outdoor physical activity reinforcing discussion points, “snack art” with healthy foods, and nutrition computer games.

Summary of Results: 15 children attended the activity. All were female. Most were new to the nutrition field and its components, but had trouble identifying to which category food belonged. The range of activities maintained interest and covered concepts repetitively. “Food art” was a favorite and included a healthy snack, creativity, and category identification. Many children saved both their snack and designed plates. Most were eager to know when this session would recur.

Conclusions: Childhood obesity is a widespread problem that leads to devastating long-term health consequences. It will not disappear quickly, and it is important that children are educated in a multitude of ways how to make good choices about what they put in their body. Although children are not major contributors to household diet, they play a key role in directing family consumption. Positive feedback was received from participants, Boys & Girls Club administration, and the community. The program is inexpensive and reproducible if the club chooses to continue nutritional education.

UNVEILING DILLON'S DIABETIC PLATE: A COMMUNITY-BASED MEAL PLANNING PLACEMAT FOR THE DIABETIC POPULATION IN DILLON, MONTANA

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Purpose of Study: According to the County Health Rankings and Roadmaps, Beaverhead County is 12% below the national average for diabetic HgA1c screening. After sitting through multiple diabetic education classes in Dillon, it became evident that the diabetic community needed a method to simplify the management of their disease. The purpose of this project was three-fold: 1. To introduce a meal-planning program that allowed diabetics to eat similar amounts of carbohydrate at similar times each day, 2. to simplify meal planning with a placemat that was easy to see and remember, and 3. to offer ideas on exercise that were local and season specific.

Methods Used: The hospital dietician and cardiac rehabilitation nurse were consulted on diabetic meal and exercise recommendations. Informal interviews were conducted with diabetic patients to discuss their successes and failures with meal planning and exercise. A literature review was conducted to determine the success of the diabetic meal-planning method as well as the diabetes activity sources. The curriculum produced included: an interactive educational component, outdoor physical activity reinforcing discussion points, “snack art” with healthy foods, and nutrition computer games.

Summary of Results: 15 children attended the activity. All were female. Most were new to the nutrition field and its components, but had trouble identifying to which category food belonged. The range of activities maintained interest and covered concepts repetitively. “Food art” was a favorite and included a healthy snack, creativity, and category identification. Many children saved both their snack and designed plates. Most were eager to know when this session would recur.

Conclusions: Childhood obesity is a widespread problem that leads to devastating long-term health consequences. It will not disappear quickly, and it is important that children are educated in a multitude of ways how to make good choices about what they put in their body. Although children are not major contributors to household diet, they play a key role in directing family consumption. Positive feedback was received from participants, Boys & Girls Club administration, and the community. The program is inexpensive and reproducible if the club chooses to continue nutritional education.

CORRALLING YOUR CRAVINGS: PROMOTING FAST FOOD NUTRITION AWARENESS IN BUTTE, MT

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Purpose of Study: Fast food restaurants are a major source of meals for many people in Butte, MT. Such chains constitute 46% of all restaurants in the area, and many residents state they consume fast foods on a regular basis for reasons including convenience, lack of time to prepare meals, and cost. Fast food consumption is associated with adverse health outcomes such as increased risk for obesity. The purpose of this project was to provide education to residents regarding nutrition, methods of consuming healthier fast foods, and awareness of discrepancies in nutritional content between local chains.

Methods Used: Interviews were conducted with nutritionists and health care staff to determine effective methods of reaching fast food consumers in Butte. A literature review also revealed an interactive approach to be an effective method. A table containing displays of basic nutritional information, healthy vs unhealthy meal choices at chains in Butte, and an interactive game in which participants tried to rank common fast food items by nutritional content were presented at a local health fair. A handout containing nutrition basics, techniques for eating healthier, and nutritional information for each product in the game was distributed to each visitor.

Summary of Results: 28 adults visited the table and participated in the activities. Each took the informational handout and three additional visitors took a handout without participating. All participants were consumers of fast food. Few participants were able to correctly rank nutritional content, and most conveyed shock upon learning the actual nutritional content of fast food items. Many reported that they would consult the nutritional handout when experiencing their next fast food craving.

Conclusions: Fast food continues to be a major source of unhealthy meals and subsequent negative health outcomes for residents of Butte. Many participants reported a better understanding of fast food nutritional content after visiting the table. Although this was a start, there needs be a more far reaching method of disseminating information on making healthier fast food choices into the community. Requiring fast food establishments to openly display nutritional information might also assist in providing consumers with a more adequate understanding of their intake.

A NOVEL MECHANISM FOR THE GENETIC ORIGIN OF THE SEX CHROMOSOMES OF 48, XXXY SYNDROME

Tanda T1, Howell S1, Rinder H1, Hager K2, Hosono S2, Jennings K2, Tartaglia N1. The Children's Hospital Colorado, Aurora, CO and JS Genetics, New Haven, CT.

Purpose of Study: 48, XXXY syndrome is a sex chromosome aneuploid condition resulting from chromosomal nondisjunction. Previous studies evaluating the origin of the extra sex chromosomes in 48, XXXY syndromes indicate a paternal parent of origin of the extra sex chromosomes. However, this has only been reported in 6 cases. The purpose of this study is to determine the parent of origin of the extra sex chromosomes in a larger cohort of male patients with 48, XXXY syndrome.

Methods Used: DNA was collected by blood or buccal swabs from 45 participants with 48, XXXY. Eighteen X-linked markers were PCR amplified and the amplicons subjected to Pyrosequencing using DNA from all 48, XXXY males. The relative allele strength for each of the X-chromosome specific markers was scored as homozygous, heterozygous, or out of range. All Y chromosomes were presumed to be of paternal origin.
Summary of Results: Results showed that 43 of the 45 patients (96%) displayed heterozygosity for 4 of 12 of the 18 X chromosome markers. This indicates likely paternal inheritance of the extra sex chromosomes. Two of the 45 patients (4%) with 48, XXXY syndrome displayed homozygosity for all 18 markers used, indicating likely postzygotic nondisjunction. Maternal meiosis I or II nondisjunction during oogenesis combined with paternal nondisjunction events during spermatogenesis are statistically unlikely to be an etiology of 48, XXXY syndrome. Analysis of data from an additional cohort of 20 subjects with 48, XXXY including direct comparison with parental samples will be presented.

Conclusions: This study is the first to report 48, XXXY syndrome resulting from likely postzygotic nondisjunction. Future research will include genotype-phenotype comparisons in 48, XXXY patients with a paternal parent of origin versus those resulting from postzygotic nondisjunction.

190

DIAGNOSIS AND MANAGEMENT OF BOHRING-OPTIZ SYNDROME CAUSED BY DE NOVO ASXL1 MUTATIONS
Russell B1, Nasiak M2, Kramer N3, Johnston J1, Biesecker L2, Graham JM2.
1UC Irvine, Irvine, CA; 2Cedars Sinai Medical Center, Los Angeles, CA, and 3National Institute of Health, Bethesda, MD.

Purpose of Study: We define the characteristic features and management for Bohring-Opitz Syndrome (BOS), a rare genetic condition characterized by distinct facial features and posture, microcephaly, severe intellectual disability and feeding problems. Since being initially delineated in 1999, there are now approximately 30 published cases. In 2011, Holschon et. al. identified de novo nonsense mutations in ASXL1 in 7 out of 13 patients with BOS. Previously, somatic mutations in ASXL1 have been detected in myeloid malignancies and bladder cancer, suggesting ASXL1 might be involved in tumor suppression.

Methods Used: We report two previously unpublished patients with BOS and novel de novo frameshift mutations in ASXL1. One patient developed bilateral Wilms tumor, a tumor that is rare in an infant who has significant feeding problems.

Summary of Results: We review these two new cases and compare them with previous cases to broaden diagnostic criteria and suggest a tumor surveillance protocol. The only previously reported cases of malignancies in BOS patients are a solid tumor in a patient without an ASXL1 mutation and an untested patient who developed medulloblastoma at age 5 years. Both our patients are normocephalic with varied feeding issues and distinctive personalities (interactive, happy, and curious).

Conclusions: With a malignancy potential for ASXL1 mutations now apparent, tumor surveillance for BOS patients should be considered for disease monitoring and management. Diagnostic criteria may also need to be broadened to help identify previously undiagnosed cases.

191

STATE HEALTH DEPARTMENTS HANDLING OF SICKLE CELL TRAIT RESULTS IDENTIFIED THROUGH THE NEWBORN SCREENING PROGRAMS
Tuaflo KR1, Ezeanuho E1, Hunt A1, Shabani S1, Whitten-Shurney W1.
1University of Nevada School of Medicine, Las Vegas, NV and 1Children’s Hospital of Michigan, Detroit, MI.

Purpose of Study: Newborn screening (NBS) programs for sickle cell disease were designed to identify individuals who are homozygous for the sickle cell gene and its variants (SS). Individuals who are heterozygous for sickle cell gene (AS) are also identified through this screening program, though this was not part of the original intent. Currently, no national guidelines exist on how to address patients with an AS result obtained through NBS. We sought to determine how individual states deal with results of individuals with AS identified through the NBS programs.

Methods Used: A 3-item questionnaire was designed and sent to all 50 states’ NBS programs by email to determine who performs the NBS, how results in a database could assist with the effort to make individuals with AS aware of their test results without the extra cost of testing.

Conclusions: Although all NBS programs identify patients with AS, follow-up is inconsistent. Uniform guidelines on handling results of individuals with AS identified through NBS programs is needed. Availability of these results in a database could assist with the effort to make individuals with AS aware of their test results without the extra cost of testing.

192

DIAGNOSIS AND SURGICAL TREATMENT OF SCOLIOSIS IN DUCHENNE AND BECKER MUSCULAR DYSTROPHY
Shatyer M1, Andrews J1, Meaney FJ1, Romitti PA2, Cunniff C1.
1University of Arizona College of Medicine, Tucson, AZ and 2University of Iowa College of Public Health, Iowa City, IA.

Purpose of Study: To describe ambulation status and age at diagnosis of scoliosis and its surgical treatment in a population-based sample of boys with Duchenne and Becker muscular dystrophy (DBMD) and to analyze differences in race/ethnicity and socioeconomic status (SES) between those who underwent scoliosis surgery and those who did not.

Methods Used: The study cohort included 363 males, all with DBMD and scoliosis and ascertained through the MD STARnet, a population-based surveillance system that identified all individuals with DBMD born from 1982 through 2009 and residing at any of 5 U.S. surveillance sites when ascertained. Scoliosis was defined as a Cobb angle of ≥10°. Descriptive statistics for onset of scoliosis included median age, age range and the percentage that had scoliosis surgery. Chi square and Student’s t tests analyzed differences in race/ethnicity and SES by receipt of scoliosis surgery. SES was measured as percent of residents below poverty by census tract. The follow up period was January 1982 through April 2009.

Summary of Results: The median age of scoliosis diagnosis was 12.7 years (range: 6.3-19.8 years). When scoliosis was diagnosed, 65.8% had ceased ambulation. Scoliosis surgery was performed in 45.2% (n=164). For those with curves of 20° to 40°, 48.4% (59/122) underwent surgery, and for those with curves >40°, 64.1% (91/142) underwent surgery. Regardless of curvature, the percentage of individuals that underwent surgery did not differ by race/ethnicity or SES from those who did not undergo surgery.

Conclusions: The median age of scoliosis diagnosis in males with DBMD coincides with the period in the natural history of DBMD when they require full time wheelchair use. However, about 1 in 3 will develop scoliosis while they are still ambulating. Current recommendations for scoliosis surgery are that it be performed when the Cobb angle is 20° to 40° and cardiopulmonary function is not compromised, but in the current investigation about 55% (91/164) of those who underwent surgery did so when scoliosis was >40°. The decision to undergo surgical correction for scoliosis in individuals with DBMD is likely to be complex and involve many factors in addition to race/ethnicity, SES, and scoliosis severity.

193

HOMOZYGOUS WNT10A MUTATION IN A PATIENT WITH ISOLATED OLIGODON'TIA
Niaki M1, Kwan A1, Bernstein JA1, Mues G2. 1Stanford University, Stanford, CA and 2Baylor College of Dentistry, Dallas, TX.

Case Report: Oligodondontia has been recognized as a dominant trait associated in a minority of cases with mutations in PAX9, MSX1, and AXIN2. Recently mutations in WNT10A have been found to explain over half of isolated oligodontia cases. Previously this gene was known for its role in the syndromes odontoenychodental dysplasia (OMIM: #257980) and Schopf-Schulz-Passarge (OMIM: #224750). We report a case demonstrating the association of WNT10A and isolated oligodontia.

A 10 year old male initially presented at age 7 after dental x-rays demonstrated the absence of 14 secondary teeth. There was no reported family history of hypodontia. Physical exam was consistent with isolated oligodontia.

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His primary teeth demonstrated normal morphology. Examination of the hair, nails, and skin was unremarkable. History of sweating as well as normally shaped teeth made the diagnosis of ectodermal dysplasia less likely. Eye examination was also negative.

Sequencing of DLX1, DLX2, BARX1, EDA, GLI2, GLI3, and WNT10A was performed on a research basis. A homozygous mutation in the WNT10A gene predicted to result in F228H was identified. No abnormalities were detected in the other genes sequenced.

WNT10A mutations have been associated with syndromic oligodontia. Recently, work by van den Boogaard has identified both dominant and recessive mutations in this gene in isolated oligodontia. Interestingly, the homozygous mutation seen in our patient was also observed in multiple individuals in the cohort of van den Boogaard suggesting a possible genotype-phenotype association.

Molecular testing is increasingly useful in the evaluation of individuals with hypo/oligodontia. Testing may clarify the mode of inheritance in simplex cases. Additionally, as AXIN2 related oligodontia has been associated with cancer predisposition patient management may also be influenced by the results of testing. Testing for mutations in WNT10A should be considered in families with oligodontia.

194

ANALYSIS OF THE PRDM9 GENE SHOWS LARGE AMOUNTS OF DIVERSITY AND POINTS TOWARD POTENTIAL SPECIATION MECHANISM IN ANCIENT PRIMATES

Roach D, Schwartz J, Shendure J. University of Washington, Seattle, WA.

Purpose of Study: Genes that cause hybrid sterility between species have the potential to reveal important insights into reproduction and the evolutionary mechanisms that drive speciation. Improving our knowledge of speciation mechanisms will better our understanding of genetic causes of sterility in humans. PR domain containing 9 (PRDM9) is a gene involved in meiotic recombination that was recently identified as both the first hybrid sterility gene and a genetic cause of sterility in some males. Despite its importance, relatively little is known about the diversity present at the population level in primates. This is due to the presence of a ~1.5 kb, highly repetitive zinc finger (ZF) domain that makes sequencing difficult on next generation platforms. In this study we developed methods to sequence this ZF domain to better interrogate the diversity contained within primate populations.

Methods Used: Genomic DNA was obtained from 44 western, central, and eastern chimpanzees as well as two bonobos. The region of interest was PCR amplified and purified using gel electrophoresis, which allowed us to separate alleles of different lengths. We then developed a nested sequencing approach utilizing four unique primers and the Sanger sequencing protocol. The four separate reads were then manually stitched together to give a consensus sequence of the entire gene.

Summary of Results: Within this cohort, we have identified 27 novel alleles ranging in abundance from ~1% to 20% and have found substantial diversity amongst alleles. Surprisingly, there was no allelic overlap between chimpanzees, bonobos, or humans (from reference sequences), and no common zinc fingers between humans and the other primates.

Conclusions: There is significant diversity both within and between primate populations, lending credence to the hypothesis that this gene can lead to speciation. We are currently developing an in vitro assay to elucidate the function of all the ZF alleles we have sequenced to date, which will improve the power of current computational prediction algorithms. As we continue to ascertain functional aspects of the ZF domain, we hope to illustrate specific instances of hybrid sterility and the mechanism for sterility within individual humans.

195

VALOSIN CONTAINING PROTEIN ASSOCIATED DISEASE PROGRESSION AND LETHALITY IMPROVES WITH AN INCREASED-FAT DIET IN A MOUSE MODEL

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Purpose of Study: Mutations in the valosin containing protein (VCP) gene causes diseases with varied manifestations which can include inclusion body myopathy, Paget’s disease of bone, frontotemporal dementia and amyotrophic lateral sclerosis. Currently there is no known effective treatment for patients with myopathies caused by mutations of this gene. The most common mutation resulting in disease processes in the VCP gene is the R155H mutation. Mouse models of this mutation show manifestations similar to humans. Compared to the heterozygous mouse model, the homozygous mutation in the mouse model results in a more severe disease and lethality. We discovered that providing a high fat diet to pregnant heterozygous dams resulted in a reversal in the lethality and a slower disease progression of the homozygous offspring.

Methods Used: We investigated the effects of a high fat diet regimen on the disease progression for homozygous versus wildtype mice using immunohistochemistry, myopathic staining and western blots.

Summary of Results: Examining the quadriceps of homozygous mice with H&E stain and IHC with autophagy markers anti-LC3 and p62 demonstrated that with a high fat diet autophagy flux decreased leading to a slowing of disease progression and reversal of lethality.

Conclusions: The finding that an increased fat diet can reverse lethality and slow disease progression in the homozygous mouse model suggests that polysaturated lipid supplementation can serve as a potential therapeutic strategy for patients with disease caused by mutations in the VCP gene.

Neonatology – General II

Concurrent Session

12:30 PM
Friday, January 25, 2013

196

HYPOXIC ISCHEMIC ENCEPHALOPATHY IN THE COOLING ERA: SHORT TERM OUTCOMES IN THE STATE OF CALIFORNIA

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Purpose of Study: Hypothermia (HT) therapy is the standard of care for term newborns with hypoxic ischemic encephalopathy (HIE). Our objective was to characterize the short-term outcomes of HIE in California.

Methods Used: We linked the California Perinatal Quality Care Collaborative (CPQCC) and California Perinatal Transport System datasets. Inclusion criteria were gestational age (GA) >/ = 35 weeks, CPQCC HIE diagnosis, and birth between January 2010 to December 2011. The primary outcome of death prior to hospital discharge was compared between HT (active cooling in the NICU) vs. normothermia (NT, never cooled or passively cooled only). Multivariable logistic regression accounting for HIE severity, Apgar score and GA was used to estimate odds ratios (OR) and 95% confidence intervals (CI).

Summary of Results: There were 284 cases of HIE in the year 2010, of which 58% received HT, and 314 cases in 2011, of which 70% received HT. There were no sociodemographic differences between infants in the HT vs. NT groups. HT was associated with delivery room interventions: endotracheal ventilation, epinephrine, and compressions, (p < 0.0001); HIE severity: severe vs. mild (OR 2.9, CI 1.9-4.6), moderate vs. mild (OR 3.4, CI 2.3-5.2), and lower 5 (AP5): 3.5 (SD 2.1) vs. 5.1 (SD 2.5), (p < 0.0001), and 10 (AP10) minute Apgar score: 4.7 (SD 2.2) vs. 5.7 (SD 2.1), (p < 0.0001). There were 94 (10%) deaths: 84% in severe HIE, 13% moderate, and 3% mild, with no difference between HT and NT. Death was associated with Apgar score: AP5 of 0-3: 22%, 4-6: 10%, 7-9: 10%, (p < 0.0001); AP10 of 0-3: 31%, 4-6: 14%, 7-9: 6%, (p < 0.0001). The need for mechanical ventilation was associated with HT (p < 0.0001) and HIE severity (p < 0.0001).

Conclusions: This is the first statewide database study characterizing outcomes for term infants with HIE in the hypothermia era. HIE severity remains receive hypothermia in spite of its proven benefit. Although this study differs from published trials in that HT was not randomized or uniformly applied, our findings highlight an opportunity to identify practice site variation and quality improvement interventions, to assure consistent evidence-based care of term infants with HIE, and selection of those qualified for hypothermia therapy.

NEUROCOGNITIVE OUTCOMES AT 18-22 MONTHS ARE IMPROVED IN FORMER PRETERM INFANTS ADMINISTERED DARBEPOETIN OR ERYTHROPOIETIN

Ohls R, Kamath-Rayne BD,3 Christensen R 2, Wiedmeier S 4, Rosenberg A 5, Lowe J 1
1Univ New Mexico, Albuquerque, NM; 2Cincinnati Children’s Hospital, Cincinnati, OH; 3University of Colorado, Denver, CO; 4Intermountain Health Care, SLC, UT and 5University of Utah, SLC, UT.

10-2310UM/JM/00136137d3/asf on December 4, 2015. Downloaded from jive.com on December 4, 2022 by guest. Protected by copyright.
Purpose of Study: Erythropoiesis stimulating agents (ESAs) darbepoetin alfa (Darbe) and erythropoietin (Epo) have shown promise as neuroprotective agents. We previously reported decreased transfusions and donor exposures in preterm infants randomized to ESAs compared to placebo/controls (PC). We evaluated infants at 18-22 months and hypothesized that those previously randomized to ESAs would have improved neurodevelopmental outcomes compared to PC.

Methods Used: Infants (500-1,250 grams, 48 hours of age) were randomized in masked fashion to Darbe (10 mcg/kg, 1×/wk SC), Epo (400 units/kg, 3×/wk SC) or PC, dosed through 35 weeks postconceptual age. All infants received supplemental iron, folate, and vitamin E, and were transfused according to a restrictive transfusion protocol. Infants were evaluated at 18-22 months corrected age using the Bayley Scales of Infant Development (BSID-III). Object permanence (OP, a measure of early working memory) was calculated from the BSID-III. Anthropometrics and assessment of cerebral palsy (CP), blindness and deafness were determined.

Summary of Results: Of the original 102 infants enrolled (946±169 grams, 27.7±1.8 weeks gestation), 7 died prior to discharge and 14 infants were lost to follow-up. The 81 infants evaluated (28 Epo, 27 Darbe, 26 PC) were comparable among groups for age at testing, birth weight and gestational age. After adjustment for gender, analysis of covariance resulted in significant differences among groups: cognitive scores were similar for Darbe (97±8, mean SD) and Epo (98±14) compared to PC (89±14, p=0.02 vs ESA recipients) as was receptive language (p=0.05). OP was higher for the Darbe group compared to the Epo group (p=0.05); both Epo and Darbe groups were significantly higher than the PC group (p=0.01). None in the ESA groups had CP, compared with 5 in the PC group (p=0.002). No differences among groups were noted in blindness or deafness.

Conclusions: Infants previously receiving ESAs showed improved cognitive outcomes compared to PC at 18-22 months. ESAs may prove beneficial in improving long term outcomes of preterm infants (NCT 00334737; NCT 01207778).

198

NEURODEVELOPMENTAL OUTCOMES AFTER TREATMENT WITH ERYTHROPOIETIN IN A PILOT TRIAL FOR PERINATAL HYPOXIC-ISCHEMIC ENCEPHALOPATHY

Rogers EE1, Glass HC2, Bonifacio SL1, Chang T1, Mayock D1, Durand DJ1, Song D1, Ballard RA1, Wu YY1,2, UCSC, San Francisco, CA; 1UCSF, San Francisco, CA; 1Children’s National Medical Center, Washington, DC; 1University of Washington, Seattle, WA; 1Children’s Hospital and Research Center Oakland, Oakland, CA and 1Santa Clara Valley Medical Center, San Jose, CA.

Purpose of Study: Perinatal hypoxic-ischemic encephalopathy (HIE) leads to death or moderate to severe disability in 45-55% of cases. Animal models suggest high dose erythropoietin (Epo) is neuroprotective for perinatal HIE. In a multicenter dose escalation study of Epo for HIE, Epo was found to be well tolerated by infants undergoing therapeutic hypothermia. We describe the neurodevelopmental outcomes of children who received Epo and hypothermia for HIE in this trial.

Methods Used: Infants who meet criteria for therapeutic encephalopathy for HIE are standardized after discharge in each of the participating institutions either in high risk infant follow up, neurology, or combined clinics. Information was gathered regarding motor delay, abnormal tone on neurologic examination, language delay, and need for rehabilitation services.

Summary of Results: There were no deaths in our cohort. Brain MRI at median 6d (range 4-13) was abnormal in 11 patients whereas a normal brain MRI was seen in 13 (54%). Clinical outcomes data was available in 23 of 24 infants (96%), at mean 11.2 months of age (range 3-19). Significant motor abnormalities were seen in 4 patients (17%); all had MRI evidence of brain injury. Seven additional infants with watershed distribution brain injury had no significant neurodevelopmental concerns at mean 11.7 months (range 6-15). No language delays were seen at time of follow up.

Conclusions: Infants enrolled in this small multicenter pilot trial exhibit a relatively low rate of neurodevelopmental abnormalities compared to trials of hypothermia alone for HIE. Longer term follow up is important and ongoing. Epo plus hypothermia appears to be a safe treatment for HIE.

199

NON-INVASIVE REGIONAL BRAIN TEMPERATURE MEASUREMENTS DURING AND AFTER HYPOTHERMIA THERAPY IN INFANTS WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY

Wu T1, McLean C1, Bluml S2, Friedlich P1, Seri I1, 1Center for Fetal and Neonatal Medicine, USC Division of Neonatal Medicine, Children’s Hospital Los Angeles and LAC+USC Medical Center, Los Angeles, CA and 2Division of Radiology Keck School of Medicine, University of Southern California, Los Angeles, CA.

Purpose of Study: To determine brain temperature during and after hypothermia therapy in infants with hypoxic-ischemic encephalopathy.

Methods Used: Infants with hypoxic-ischemic encephalopathy (HIE) admitted to Children’s Hospital Los Angeles for hypothermia therapy (HT) from April to September 2012, were enrolled into the study. Patients were categorized by the severity of HIE based on Sarnat staging and amplitude-integrated EEG findings. Magnetic resonance imaging (MRI) scans were obtained during follow up. After HT for each patient, Regional brain temperatures (left thalamus, right basal ganglia, and bilateral parietal-occipital grey matter) were derived from analysis of chemical shift differences of metabolites on MR spectroscopy. Brain temperatures during and after HT were compared using paired t-test. Percent difference between brain and rectal temperature was calculated.

Summary of Results: A total of six patients (4 mild, 1 moderate, and 1 severe HIE) were enrolled. All patients had a significant difference between mean brain temperature during and after hypothermia therapy (34.3±1.4°C vs. 36.9±1.3°C, p <0.001). The dissociation between brain and rectal temperature was wider in the patient with severe HIE (7.9% difference) compared to patients with mild and moderate HIE (2.5% difference), although not statistically significant.

Conclusions: Brain temperature in neonates with HIE during and after HT was significantly different. This study provides a novel method to non-invasively assess regional brain temperature in newborns with HIE undergoing HT. More patients with severe HIE are needed to assess the magnitude of brain-rectal temperature dissociation among severely encephalopathic patients.

200

ABSENCE OF CEREBRAL AUTOREGULATION IN THE PRETERM LAMB AFTER PRETERM DELIVERY

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Purpose of Study: Cerebral vessels compensate for increases and decreases in arterial pressure by changing resistance, resulting in relatively constant blood flow across a range of pressures. This phenomenon is called autoregulation and has been demonstrated in adults, newborns, and even in fetal sheep in utero as young as 92 days of gestation (term 147). In contrast, clinical studies of preterm infants suggest that autoregulation is absent. This study tests the hypothesis preterm fetal lambs will demonstrate cerebral autoregulation following cesarean delivery and resuscitation.

Methods Used: Premature lambs 127-132 d (n=6) delivered by cesarean section and studied within 6 hours of birth and 2-week-old lambs delivered naturally (n=6) were anesthetized and mechanically ventilated. Arterial PCO2 and PaO2 were maintained in normal range. Cerebral blood flow (CBF) was monitored using laser Doppler flowmetry probes inserted in right and left cerebral cortices. Mean arterial blood pressure (MAP) was experimentally adjusted from 20 to 140 mmHg by mechanical and pharmacological methods.

Summary of Results: In preterm lambs, CBF changed in direct proportion to MAP across all ranges of pressures studied, demonstrating a lack of autoregulation. In contrast, 2-week old lambs demonstrated no significant change in CBF at mean arterial blood pressures ranging from ~50 to as high as 165 mmHg.

Conclusions: Cerebral autoregulation is absent in preterm lambs immediately following cesarean delivery and resuscitation.
NEUROPROTECTIVE EFFECTS OF NITRITE AGAINST HYPOXIC ISCHEMIC BRAIN INJURY IN NEWBORN RAT PUPS

Truong HN1, Wolfe C1, Hartman RE2, Obeida A1, Blood AB1.1Loma Linda University, Loma Linda, CA and 2Loma Linda University, Loma Linda, CA.

Purpose of Study: Nitrite, an anion normally present in blood at mid-nanomolar concentrations, can be reduced to NO under hypoxic conditions. Increased blood nitrite concentrations have been associated with improved outcome in a number of adult animal models of ischemia/reperfusion injury, and with improved exercise performance in humans. The current study was designed to determine the effects of nitrite on hypoxic ischemic brain lesion size and neurodevelopmental outcome in a newborn rat pup model of hypoxic/ischemic brain injury.

Methods Used: Ten-day-old Sprague-Dawley rat pups underwent hypoxic ischemic brain injury using the Rice-Vannucci model. Five minutes prior to the hypoxia, rat pups were injected intraperitoneally with either nitrite (0.165, 8.25, or 82.5 mg/kg) or saline. Magnetic resonance imaging was performed at 1, 7 and 40 days after the hypoxic ischemic injury. Behavioral testing (rotarod, zero maze, and water maze) was performed at 1 month of life to assess learning, memory, and balance.

Summary of Results: There was no significant difference in overall brain lesion size between nitrite (n=21) and control (n=21) rats on Days 1, 7, or 40. However, nitrite-treated rats demonstrated significant improvement in brain lesion size at day 7 and day 40 compared to day 1 and compared to controls. Despite this difference, behavioral testing detected no significant differences between nitrite and control groups.

Conclusions: Nitrite treatment enhances recovery from hypoxic ischemic injury, but our study does not demonstrate protection against neurocognitive deficits.

202

EARLY POSTNATAL WEIGHT GAIN AS AN ACCURATE PREDICTOR FOR THE DEVELOPMENT OF RETINOPATHY OF PREMATURITY

Weiner A1,2,3, Binwale M1,2, Barton L1,3, Ramanathan R1,2,3, Sardesai S1,3, Cayabyab R1,3,1LAC+USC Medical Center Keck School of Medicine, Los Angeles, CA; 2Children’s Hospital Los Angeles, Los Angeles, CA and 3Good Samaritan Hospital, Los Angeles, CA.

Purpose of Study: CurrentROP screening guidelines are based on birth weight and gestational age. Postnatal weight gain has been shown to accurately predict the development of advanced stages of ROP with an online tool called WINROP (Weight, IGF-I Neonatal Retinopathy of Prematurity). The purpose of this study was to validate the reliability of early postnatal weight gain as an accurate predictor ofROP Stage 3 or greater in a large US cohort with ethnic diversity.

Methods Used: Records for infants <32 weeks gestation, born at LAC+USC Medical Center NICU between 1994 and 2006 were evaluated. Weekly weights from birth to 36 weeks post menstrual age were entered into the WINROP computerized tool. This tool gave one of three alarms when the rate of weight gain recorded fell below the value of a control group: (1) no alarm indicating the infant was not considered at risk for developing ROP; (2) a low-risk alarm indicating an infant at minimal risk for developing severe ROP or (3) a high-risk alarm indicating an infant at an increased risk for developing Stage 3 ROP or greater. The stage of ROP for each infant as recorded by an ophthalmologist was then compared with the alarms given based solely on rate of weight gain from the WINROP tool.

Summary of Results: To date there have been 170 infants entered into the WINROP data collection tool. Of those infants who developed ROP Stage 3 or greater, the WINROP data collection tool detected 25/25 (100%) based solely on rate of weight gain, even before their first eye examination. Of those infants who developed Stage 2 ROP (n=20), 100% have been identified as high risk utilizing the computer based tool. Of the 35 infants who developed Stage 1 ROP, 37 of 39 (95%) were accurately identified.

Conclusions: Postnatal weight gain in our ethnically diverse population appeared to be an accurate predictor of those infants who developed Stage 3 ROP or greater with a sensitivity of 100%. The WINROP tool also identified with high accuracy those infants who did not developROP that required treatment.

203

DOPAMINE RESISTANT HYPOTENSION AND RETINOPATHY OF PREMATURITY

Catenacci M1, Miyagi S2, Wickremasinghe A1, Lucas S2, De Alba Campomanes A1, Good W1, Clyman R1.1UCSF, San Francisco, CA; 2UCSF, San Francisco, CA and 3UCSF, San Francisco, CA.

Purpose of Study: Immature gestation is the most consistent predictor of severe ROP (> stage 3 or stage 2 with plus disease). Although hypotension has been identified as a predictor ofROP, no studies have examined the relationship between the etiology and severity ofhypotension and subsequent development ofROP.

Methods Used: Infants (~27-6/7 weeks gestation, n=242) were observed for hypotension (mean blood pressure = [(postconceptual age (in mm Hg)) - (3 to 4 mm Hg)]) and treated with a standardized hypotension-treatment protocol. The etiology of hypotension was classified as: (a) culture-positive infection and/or necrotizing enterocolitis, (b) PDA ligation, and (c) “idiopathic” (no cause identified other than prematurity); and as being dopamine-responsive or dopamine-resistant. Dopamine-resistant hypotension was defined as hypotension that required dopamine (>18 mcg/kg/min) plus hydrocortisone. Eye exams were performed until ROP resolved or the retina matured. Multivariate logistic regression analysis examined the effects of etiology and severity of hypotension on the incidence of severe ROP.

Summary of Results: 39% of the infants developed dopamine-responsive hypotension; 25% developed dopamine-resistant hypotension (due to infection/ NEC (3%), ligation (5%), or “idiopathic” (17%)). Severe ROP developed in 19% of the infants. Only infants with “idiopathic” dopamine-resistant hypotension...
hypotension were at significant risk of developing severe ROP ((65% de-
veloped severe ROP; Odds ratio: 10 (95% CI: 4.28)). Infants who developed
“idiopathic” dopamine-resistant hypotension after age 14 days were at in-
creased risk of developing severe ROP compared to those who developed it
in the first 2 weeks of life.

Conclusions: “Idiopathic” dopamine-resistant hypotension is an early,
strong predictor of severe ROP. Both the adjusted odds ratio and the pre-
dictive significance of other known risk factors (like gestational age) are
significantly weaker by comparison. We speculate the postnatal inflammatory
state that plays a role in dopamine-resistant “idiopathic” hypotension also
contributes to the development of severe ROP and may explain the associa-
tion between altered vascular tone and abnormal retinal development.

Pulmonary and Critical Care I
Concurrent Session
12:30 PM
Friday, January 25, 2013
204
THE IMPACT OF PERIOPERATIVE MEDICINE ROTATION
IMPLEMENTATION ON ICU OUTCOMES
Linda University, Loma Linda, CA.
Purpose of Study: As the role of the anesthesiologist broadens in peri-
operative care, adjustments to residency program curriculums are expected.
ACGME anesthesiology program requirements have proposed increased res-
ident training in non-operating room rotations. A focused rotation that gives
residents continuity of patient care and enhances perioperative knowledge
would allow for development of true perioperative physicians and, in theory,
better patient outcomes. We implemented a structured two-month resident
rotation in clinical perioperative medicine in December of 2009, based in a
5 OR, 8 ICU bed facility with a dedicated preanesthesia consultation and
education clinic that is part of our campus. The purpose of this study was to
determine if the implementation of the perioperative medicine rotation re-
sulted in decreased ICU average length of stay.

Methods Used: ICU Case Mix Index, average length of stay and resident
experience data were collected and compared in a month-matched fashion for
the year prior to and after implementation. APACHE II scores and predicted
death rates were retrospectively calculated. Data was compared using the
Mann-Whitney test with p<0.05 considered significant.

Summary of Results: The average length of stay was longer in the year
prior to than after implementation of the dedicated perioperative medicine
rotation (Table). The ICU patient population had similar severity of illness
indicated by APACHE II scores, predicted mortality and case mix index.

Conclusions: The implementation of a comprehensive anesthesiology peri-
operative medicine rotation was effective in reducing ICU average length of stay
while managing patients with similar severity of illness. These results dem-
onstrate a positive impact on patient care and cost management and may result
from anesthesiologists’ management of patients’ perioperative courses. The
rotation itself also provides patient continuity for resident physicians, leading
to added education and experience benefits. This rotation may provide a model
for structuring future anesthesiology resident training in perioperative medicine.

Results: Shown as Mean, 95% confidence interval

<table>
<thead>
<tr>
<th></th>
<th>Average ICU Length of Stay Days</th>
<th>Case Mix Index</th>
<th>APACHE II</th>
<th>Predicted Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to Implementation</td>
<td>5.1, 4.3, 5.9</td>
<td>2.3, 2.1, 2.6</td>
<td>18.6, 17.9, 19.4</td>
<td>54.2, 32.1, 34.6</td>
</tr>
<tr>
<td>After Implementation</td>
<td>3.6, 2.5, 3.3</td>
<td>2.4, 2.1, 2.7</td>
<td>20.3, 18.6, 20.3</td>
<td>56.1, 33.3, 38.8</td>
</tr>
<tr>
<td>p-value</td>
<td>0.0004</td>
<td>0.50</td>
<td>0.06</td>
<td>0.06</td>
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</tbody>
</table>

205
VALIDATION OF A TOOL FOR PROMOTING
SELF-MONITORING AND SELF-MANAGEMENT
IN CHILDREN WITH ASThma
Fassl B 1, Nkoy F 1, Stone B 1, Maloney C 1, Schatz M 2. 1University of Utah,
Salt Lake City, UT and 2Kaiser San Diego, San Diego, CA.
Objective was to validate a new self-monitoring tool (Asthma Symptom
Tracker--AST) developed to 1) engage children and/or their parents in weekly
self-monitoring of chronic asthma and 2) support care providers in assess-
ing the effectiveness of asthma.

Methods Used: Prospective cohort study in children 2-18 years admitted
to a tertiary care children’s hospital for asthma between 03/02/2011 and 01/
31/2012. The AST was validated by: 1) correlating weekly AST scores with con-
current asthma control questionnaire (ACQ) scores (criteria va-
lidity), 2) comparing longitudinal changes in AST and ACQ scores (re-
sponsiveness), and 3) testing the association between AST scores with quic-
ker reliever use and readmission between frequent and non-frequent users (dis-
criminant validity). We surveyed parents/patients for their satisfaction with
the AST at the end of the 6-month follow-up period. During hospitalization,
a research nurse obtained baseline AST and ACQ scores; weekly scores were
sent to the research team. Concurrent ACQ assessments were obtained by
phone during the first month. Asthma readmission data was obtained elec-
tronically. Analysis included Chi-square tests and logistic regression.

Summary of Results: 51% (136/266) of patients were enrolled:1552 in-
dividual self-assessments were completed. The correlation between weekly
AST and ACQ scores was strong (r=0.89, p<0.01). AST scores showed longi-
tudinal variation similar to ACQ scores. Patients with poorly controlled asthma
reported more use of quick relievers than well- and well-controlled patients:
81%, 26%, and 0.3% (p<0.01). There were 13 (9 ED and 4 inpatient) read-
missions within 6 month among enrollees: 8% (1 patient) in frequent vs. 92%
in non-frequent users (p<0.01). Frequent use of the AST was associated with
reduction in readmission (p<0.01). 36 patients completed a satisfaction sur-
vey and reported high satisfaction (97%) with the AST and improved (88%)
asthma self-management skills.

Conclusions: The AST is a valid, user friendly and highly rated tool by
parents that can be used to improve asthma ambulatory care in children.

206
LUNG TRANSPLANTATION FOR PULMONARY
HYPERTENSION SECONDARY TO HIV
Kern RM, Blanc PD, Hays S, Kukreja J, Leard L, Golden J, Kleinhenz M,
Singer JP. University of California San Francisco, San Francisco, CA.
Case Report: HIV seropositivity is generally considered a contraindi-
cation to lung transplantation (LT) given concern over disease progression
with further immunosuppression. To date, an isolated case-report of LT
performed in an HIV+ patient for cystic fibrosis reported excellent outcomes
post-LT with no HIV related complications or rejection at 2 years. We report
a case of LT in an HIV+ patient with a complicated post-LT course. Pul-
monary hypertension (PH) due to HIV was diagnosed in a 40 year-old woman.
Despite aggressive therapy (intravenous treprostinil; oral bosentan and sil-
odrain) for severe PH, she was unable to tolerate her current regimen.
HIV reactivation does not appear to be a concern for this patient. Her periop-
ervative course was complicated by severe (grade 3) primary graft dysfunction and the first post-
LT year by pulmonary emboli and 3 episodes of acute allograft rejection. The
rejection was recalcitrant to standard pulsed corticosteroid treatment and was
ultimately treated with Thymoglobulin. Her CD4 decreased from 1053 to 250
soon after Thymoglobulin and to 183 5-months later, but the viral load re-
ained undetectable. In the second post-LT year the patient contracted re-
spiratory syncytial virus requiring treatment with corticosteroids, inhaled
ribavirin and intravenous immunoglobulin. By post-LT year 2, she had de-
veloped severe (grade 3) chronic allograft dysfunction, with an FEV1 of
0.67L (23% predicted). To date, the patient has survived 3 years post-LT but
with severely limited function. In summary, this is only the second reported
case of LT in an HIV+ patient. Frequent acute rejection has been reported
in HIV+ kidney transplant recipients; HIV reactivation does not appear to be
a part of that clinical picture. Our experience suggests a similar pattern may
characterize LT, but more data are needed. Given the growing population of
HIV+ patients with advanced lung disease and the resource-intensive nature of
LT, clinically important questions remain to be answered.
SLEEP-RELATED QUALITY OF LIFE AND PHYSIOLOGIC PARAMETERS IN VETERANS WITH EARLY AMYOTROPHIC LATERAL SCLEROSIS

Farshidpanah S1,2, Klein WF3, Fargo R2, Dandamudi N2,1, Loma Linda University Medical Center, Loma Linda, CA and 2Loma Linda VA Healthcare System, Loma Linda, CA.

Purpose of Study: Amyotrophic lateral sclerosis (ALS) is the most common form of progressive motor neuron disease in adults. Regardless of time or type of presentation, paralysis is progressive and leads to death due to respiratory failure within 2-5 years. Furthermore, sleep disordered breathing may occur early in ALS and often precedes clinical evidence of respiratory muscle dysfunction.

Methods Used: United States veterans with a confirmed diagnosis of ALS who are free of any respiratory compromise, were referred to us by the ALS support staff. Full pulmonary function testing (PFT) including spirometry and DLCO with room air arterial blood gas (ABG) were performed. The Pittsburgh Sleep Quality Index (PSQI) was used to evaluate night-time complaints and the Epworth Sleepiness Scale (ESS) captured daytime symptoms in patients at risk for sleep disturbance. The functional disability assessment was made using the ALS Functional Rating Scale-Revised (ALSFRS-R).

Summary of Results: Nine male veterans with mean age of 69.3±6.4 years were recruited from diagnosis to study enrollment was 356 days (interquartile range: 269-427). Patients had a mean FEV1 of 1.98±0.47L which was 59%±17% of predicted (FEV1%). A mean FVC of 2.56±0.92L represented 58±19% of predicted (FVC%). The mean FEV1/FVC was 78±8%. Measurements of mean pH (7.43±0.02), mean pCO2 (39.5±4.9mmHg) and mean pO2 (75.4±11.9mmHg) were all within normal limits. The median PSQI was 4 (2.6-5) and 2 patients (22%) had PSQI >5. Median ESS was 4 (2.5-5.5) with 1 patient (11%) reporting borderline sleepiness with ESS of 10. The median ALSFRS-R was 34 (23.3-38) with 4 patients (44%) classified as mild impairment (ALSFRS-R 37-48) and 5 patients (54%) as moderate impairment (ALSFRS-R 25-36). We found a correlation between the ESS and pCO2 (r=0.74, p=0.04), as well as the PSQI total score and pH (r=0.92, p<0.001).

Conclusions: As expected, patients in the early stages of ALS are not hypocapnic and demonstrate a restrictive pattern on PFT. Self-reported sleep problems (as measured by surveys) may correlate with physiologic parameters. It will be imperative to follow this study with full polysomnography to evaluate sleep characteristics and assess for possible sleep-related breathing disturbances.

CEREBRAL AIR EMBOLISM AFTER PERCUTANEOUS LUNG BIOPSY: A DREADED COMPLICATION

Farshidpanah S1, Dinh V A2,3, Lo T1,1, Loma Linda University, Loma Linda, CA; 2Loma Linda VA Healthcare System, Loma Linda, CA and 3Loma Linda University, Loma Linda, CA.

Case Report: Percutaneous lung biopsy is a commonly performed procedure and is seldom complicated by systemic air embolism. Despite its rare incidence (0.02-0.07%), it can be associated with long-term morbidity and mortality. If suspected, emergent computed tomography (CT) scanning should be considered and hyperbaric oxygen therapy (HBOT) promptly initiated. We present a case of simultaneous aortic and cerebral artery air embolism successfully treated with HBOT.

A 79 year old female with a history of breast cancer from an outside facility underwent a CT-guided percutaneous needle biopsy of a suspicious right lower lobe lesion. Immediately after the biopsy, she became bradycardic and confused. A CT scan of head and chest revealed “multiple air-filled serpiginous structures consistent with air emboli into the left cerebral hemisphere” (Fig. A). A right-sided pneumothorax was present and a significant amount of air was seen in the ascending aorta (Fig. B). She subsequently became confused, agitated and complained of generalized body pain. Physical examination was unremarkable except for mild weakness and focal seizure-like activity in her right arm. Her labs were normal and vitals remained stable. Oxygen via non-rebreather mask only minimally improved her symptoms. She was then transferred to our hospital for HBOT. A right-sided chest tube was placed and United States Navy Table 6 protocol was used with complete resolution of her presenting symptoms.

Clinicians need to recognize air embolism as a rare but serious complication of percutaneous lung biopsy. HBOT remains the definitive therapy and should be initiated promptly. It is prudent for interventionalists to understand the principles of HBOT and remain aware of available facilities in their local community.
Methods Used: Data abstraction from prospective and standardized monthly anemia protocol sheets from 18 PD patients. We considered only the 3rd month onward following initiation of the protocol in order to judge its effectiveness. Each patient contributed a mean of 12.7 values, range 4 – 28. Data is reported on 15 patients; three patients were excluded for non-adherence (1) or unremitting inflammatory conditions (2) during therapy.

Summary of Results: See Table. NOTE: 2 pts received PRBC while on the protocol due to blood loss post transplant nephrectomy & during chemotherapy for hepatoblastoma. Only 3 formal decisions were required by the nephrologist in order to decide on dosing of ESA or Iron outside the protocol. Many of the hemoglobin values that fell BELOW the target of 110 g/L were coincident with recent or current infections and or hospitalizations.

Conclusions: 47% of monthly Hgb values were in target (consistent with values from the literature) using only 50% (approximately 120 U/KG/WK) of EPO equivalent dose as would be expected from the 2011 NAPRTCS report (Mean EPO dose on PD ~ 200-250 U/KG/WK): note the conversion of Darbo : Epo was performed at 1 mcg : 240 IU. Very few hemoglobin values exceeded the upper target of 130 g/L (6%). The protocol also allowed for the majority of ferritin and TSAT values (58% and 66%) to remain within the desired ranges by use of only 4 mg/kg/day of elemental iron given orally. Given current concerns regarding the risks of significantly elevated hemoglobin values, use of high doses of erythropoietic salvage agents and or iron therapy we feel this protocol, when delivered consistently by a dedicated PD nurse offers a clear and consistent approach and results that are unlikely to place the patient at risk of excessive doses of any of these products.

Targets as per KDQCC 2006/7

<table>
<thead>
<tr>
<th>Metric</th>
<th>N</th>
<th>Mean (SD in MED)</th>
<th>IN TARGET (R)</th>
<th>ABOVE/ BELOW TARGET</th>
</tr>
</thead>
<tbody>
<tr>
<td>HGB [10.5-13.0 g/L]</td>
<td>160</td>
<td>11.14 (1.12)</td>
<td>47%</td>
<td>6%</td>
</tr>
<tr>
<td>FERRITIN [100-500 NG/ML]</td>
<td>176</td>
<td>156 [126 / 190]</td>
<td>59%</td>
<td>2%</td>
</tr>
<tr>
<td>TSAT [20-50%]</td>
<td>27 [4 / 24]</td>
<td>67%</td>
<td>4%</td>
<td>38%</td>
</tr>
<tr>
<td>ELEMENTAL IRON [MG/KG/DAY]</td>
<td>81</td>
<td>4 [1.9 / 4]</td>
<td>2.3 - 5.9 [QIR 25-75]</td>
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<tr>
<td>DARBO DOSE [U/KG/WK]</td>
<td>90</td>
<td>0.56 [0.31 / 0.46]</td>
<td>0.35 - 0.72 [QIR 25-75]</td>
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</tr>
</tbody>
</table>

211 WATER SAFETY EDUCATION FOR THE YOUTH OF RED LODGE, MONTANA

Hartman MF. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Swimming pools and natural water settings serve as a source of recreation for children around the world. In Red Lodge and the surrounding area, children have ample access to public swimming pools, creeks, rivers, reservoirs, and mountain lakes. Youth can often be seen enjoying the swimming pool, fishing in Rock Creek, or boating at Cooney Reservoir during the summer months. The purpose of this project is to provide basic water safety education in order to decrease the risk of injury or death from water-related accidents in swimming pools and natural water settings.

Methods Used: Discussion with the directors of the Boys and Girls Club of Carbon County prompted my interest in water safety education as a need for the children in Red Lodge. Following a community exploration of the public swimming pool and the surrounding natural water settings, a review of the professional literature on water risk and safety was conducted. To relay this information to my target population, an interactive approach was taken: questions and answer style lecture with rewards for correct answers, demonstration of proper life jacket use, and an art contest where the children depicted one way to decrease the risk of water-related accidents. This small, yet effective intervention instilled a sense of respect for the dangers of water and a renewed excitement for safely enjoying aquatic activities.

212 BIKE SAFETY EDUCATION AND HELMET GIVEAWAY FOR PARENTS AND CHILDREN OF HAILEY, IDAHO

Bledsoe A. UW SOM, Seattle, WA.

Purpose of Study: Bicycling is a common form of transportation and recreation in Hailey, yet a huge proportion of children who bike fail to wear helmets. Hailey residents expressed concern over this lack of helmet use. Studies show that such interventions are most successful when education is coupled with helmet provision for children under 12. The event details were published in the newspaper and on flyers posted in town. For helmet acquisition, donations were sought through local bike shops and the transportation company. Other giveaways were used to provide an incentive for approaching the booth for education. A bike safety brochure was created and dispersed, and two educators spoke to parents about strategies to improve children’s helmet use and to children about bike safety tips and the medical reasoning for helmet use.

Summary of Results: 20 helmets were received through donation and all were given to children in need. At least 100 people stopped by the booth, and about 70 brochures were dispersed. Parents were receptive to information about improving children’s helmet use, and children were eager to learn about bike safety. Educators were very selective about who received donated helmets. The parents of children who received helmets expressed sincere appreciation, while the children were excited to start using their helmets.

Conclusions: The children of Hailey are especially susceptible to bike-related injuries due to the popularity of biking there, but many fail to wear helmets due to lack of education or financial circumstances. By combining education with helmet provision, this project made helmet use much more probable for at least 20 children. As laws requiring helmet use is proven to reduce head injuries in children, and Idaho has no such legislation, further efforts should focus on legislative interventions.

213 NUTRITIONAL EDUCATION FOR BREASTFEEDING WOMEN IN LIVINGSTON, MONTANA

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

Purpose of Study: Postpartum patients of Community Health Partners (CHP) in Livingston, Montana, often ask questions related to their nutrition while breastfeeding. The frequency of questions asked indicates a need for basic nutritional education for breastfeeding women. The purpose of this project was to increase awareness of nutritional recommendations, promote healthy eating, and clarify common misconceptions regarding nutrition during breastfeeding through a facilitated discussion among healthcare providers and postpartum women.

Methods Used: Pregnant and postpartum patients were interviewed to identify frequently asked questions regarding nutrition during breastfeeding. A literature review and an interview with the hospital dietician were conducted based on these questions. A “Nutrition during Breastfeeding” educational event at CHP was held, at which a cooking demonstration was performed and a nutritious lunch was served that exemplified a well-balanced meal. Recipes were provided to participants. Patient generated questions were addressed and answered during the event. A nutritional handout was developed and provided to participants.

Summary of Results: Four postpartum mothers, the clinic coordinator, a lactation consultant, and a local physician attended this event. In addition to conveying important nutritional information to postpartum women and clinic staff, the event initiated both mother-to-mother peer support and...
collaborative discussion among healthcare providers and mothers. Active participation, positive feedback and ongoing availability and usage of the nutritional handout all suggest successful results of this project.

**Conclusions:** Eating healthy, well-balanced diets can be a challenge for post-partum women busy caring for their infants. Despite common trends among questions generated by mothers regarding nutrition during breastfeeding, nutritional counseling is not often incorporated into patient visits. This interactive educational event demonstrated an easy, healthy, affordable meal while at the same time offered an opportunity for healthcare providers and post-partum mothers to discuss proper nutrition for breastfeeding women.

214

**ASSESSMENT OF BREASTFEEDING RATES BEFORE AND AFTER "BABY FRIENDLY" DESIGNATION AT PEDIATRIC CONTINUITY CLINIC, LAC-USC MEDICAL CENTER**

Laird M1, Kunza B1, Barton L2, Frantz K2, Vasan R1. 1Keck School of Medicine of USC, Los Angeles, CA; 2LAC+USC Medical Center, Los Angeles, CA.

**Purpose of Study:** LAC+USC Medical Center received a Baby Friendly Health Initiative (BFHI) designation in April 2012 from Baby Friendly USA. The BFHI is sponsored by UNICEF and WHO and involves implementing ten steps to increase exclusivity and duration of breastfeeding. These steps include training all health care staff in lactation management, restricting the distribution of formula and educating pregnant women on the techniques and benefits of breastfeeding. This study will assess the effectiveness of the BFHI by comparing rates of exclusive breastfeeding and prevalence of breastfeeding before and after receiving the Baby Friendly (BF) designation. We hope the implementation of the BFHI will have put us closer to meeting the Healthy Families 2020 objectives of having exclusive breastfeeding rates of 46.2% at three months, 25.5% at six months, and a prevalence of breastfeeding of 60.6% at three months and 34.1% at 12 months. The survey will inquire why mothers chose to stop exclusively breastfeeding, which will help us better address the barriers facing our patient population. Another aim of the survey is to elicit which BFHI components the mothers found most helpful in sustaining successful breastfeeding. Determining the most influential factors of the BFHI in increasing duration of breastfeeding will elicit what aspects other institutions should focus on implementing first.

**Methods Used:** A survey will be administered to up to 200 parents of infants up to 12 months of age as part of a routine history taking in the Pediatric Continuity Clinic (PCC). The survey asks when breastfeeding was ended, when breastfeeding of 60.6% at three months, 34.1% at 12 months. The survey will inquire why mothers chose to stop exclusively breastfeeding, which will help us better address the barriers facing our patient population. Another aim of the survey is to elicit which BFHI components the mothers found most helpful in sustaining successful breastfeeding. Determining the most influential factors of the BFHI in increasing duration of breastfeeding will elicit what aspects other institutions should focus on implementing first.

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**Conclusions:** Pending.

**Poster Session II**

**Gastroenterology**

2:30 PM
Friday, January 25, 2013

215

**VIRAL BREAKTHROUGH IN HEPATITIS C**

Ferguson JD, Zhou K, Bau S, Saab S. DGGOM at UCLA, Los Angeles, CA.

**Purpose of Study:** Despite improved virologic response with the addition of direct acting agents (DAA) to peginterferon and ribavirin treatment in chronic hepatitis C virus (HCV) genotype 1 infection, a subset of patients experience viral breakthrough while on therapy. Defining viral breakthrough and patient characteristics is important for ongoing and future HCV treatment.

**Methods Used:** Fifty-eight patients treated with either boceprevir or telaprevir between June 2011 and July 2012 were retrospectively evaluated for presence of viral breakthrough. Baseline HCV characteristics, time to viral breakthrough, and HCV resistance patterns were determined.

**Summary of Results:** Viral breakthrough was seen in 15.5% of patients treated. All patients with viral breakthrough were on telaprevir treatment. 8 out of 9 patients experienced breakthrough in the peginterferon and ribavirin (PR) only phase of treatment with mean time to breakthrough of 21.6 weeks (±6.5). Viral breakthrough was primarily seen in patients with genotype 1a, prior null response, advanced liver fibrosis and presence of resistant mutations at time of breakthrough.

**Conclusions:** A significant proportion of patients experience viral breakthrough after completion of treatment with direct acting agents (DAA). More frequent virologic assessments during the PR-only phase may be necessary to reduce cost and adverse effects of treatment.

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217

SITAGLIPTIN INDUCED HEPATIC NECROSIS: A CASE REPORT

Cruz VD, Ramos-Matos C, Davis A, Zetir M, Abel E. University of South Florida, Tampa, FL.

Case Report: Medications are often under recognized cause of acute hepatic injury and are typically a diagnosis of exclusion. We present a rare case of sitagliptin induced hepatic injury, with only one other case report found in the literature.

A 79-year-old male presents with diffuse abdominal pain, pruritis and worsening ascites for three months. On examination he was afebrile and noted to have scleral icterus, hepatomegaly and ascites. Initial chemistry metabolism panel revealed elevated liver functions tests, all of which were within normal limits before initiation of sitagliptin. Abdominal imaging showed an enlarged liver with a craniocaudal length of 23.7 cm. A liver biopsy was subsequently performed, showing organizing sub-massive hepatic necrosis. Unable to identify the cause of this necrosis, we revisited his medications. The patient was previously on sitagliptin in March through mid-June 2012, and presented in May with his current symptoms.

Drug induced liver injury is not very common in patients taking medications and are an important under recognized cause of acute liver injury. It is typically a diagnosis of exclusion, and should always be considered in the differential diagnosis of any patient presenting with either isolated deranged liver function tests in a healthy patient to acute liver failure. A detailed medical history should be elicited for any unknown cause of liver injury, as a variety of drug classes and toxins can be the culprit. While reviewing the literature, there has only been one reported case report for sitagliptin causing acute hepatic injury. For our patient, submassive hepatic necrosis was found without any ductal dilatation. The etiology of his impaired hepatic function is likely due to liver injury. With all other causes and medications ruled out and with his recent sitagliptin use, a diagnosis of exclusion points to sitagliptin as being the cause.

In summary, patients using sitagliptin should have their liver function assessed periodically. It should be discontinued at the onset of elevated liver enzymes, especially in cases of unknown hepatic injury.

Poster Session II
Genetics and Morphogenesis and Malformations

A COMPREHENSIVE SURVEY OF MUTATIONS IN THE OPA1 GENE IN PATIENTS WITH AUTOSOMAL DOMINANT OPTIC ATROPHY ‘PLUS’ PHENOTYPE

Ham M1, Smith M1, Osann K2, Kimonis V1. 1University of California, Irvine, Irvine, CA and 2University of California, Irvine, Irvine, CA.

Purpose of Study: Autosomal Dominant Optic Atrophy (ADOA) is a common neuro-optic disorder caused by a mutation in the OPA1 gene, with an estimated prevalence of 1 in 50,000 in the general population. Clinical anomalies include progressive bilateral vision loss, optic disc pallor, central vision loss, and impairment of color vision. Additionally, 10-20% of patients experience hearing loss and ataxia, and recent studies suggest disruption of cardioc and skeletal functions. The purpose of this study is to obtain a better understanding of the genotype-phenotype correlation of the various mutations in the OPA1 gene.

Methods Used: A methodical review of published OPA1 literature identified 405 individuals with confirmed OPA1 mutations, with descriptions of their visual and multi-systemic phenotypes. 117 of 405 (29%) reported extra-ocular symptoms. Statistical analysis was performed of the extra-ocular features using IBM SPSS Statistics v.20. Statistical significance was defined as a p-value less than 0.05 using Fisher’s exact tests.

Summary of Results: ADOA ‘plus’ individuals presented with the following symptoms: ataxia (22%), myopathy (21%), ophthalmoplegia (31%), neuropathy (29%), psychosis (9%), and sensorineural hearing loss (60%). Several genotype-phenotype correlations were observed. The ADOA classic group had a significantly greater prevalence of mutations in the GTPase and C-terminal coiled coil domain, while the ADOA ‘plus’ group was observed to have a greater prevalence of mutations in the GTPase and dynamin domain (p<0.001).

Within those with mutations in the GTPase domain, a greater prevalence of mutations in exons 8 and 9 were also observed in the classic ADOA group, while a greater prevalence of exons 14 and 15 mutations were observed in the ADOA ‘plus’ group (p<0.001). Interestingly, patients with maternally inherited OPA1 mutations were more likely to develop ‘plus’ symptoms (p=0.015).

Conclusions: This study provides novel data regarding genotype/phenotype correlations of ADOA relating to the domain involved. It also warrants looking for extra-ocular clinical features in ADOA patients, by performing additional neurologic and audiological evaluations.

218

A NOVEL STRATEGY TO IDENTIFY BIOMARKERS FOR PROSTATE CANCER

Scapa J1, Kerkoutian S2, Sun Y3, Zhang H2, Squires J3, Li X3, Goldstein A1, Wijek O1, Huang F2, 1David Geffen School of Medicine at UCLA, Los Angeles, CA; 2David Geffen School of Medicine at UCLA, Los Angeles, CA and 3Jonsson Comprehensive Cancer Center at UCLA, Los Angeles, CA.

Purpose of Study: Approximately 230,000 men are currently diagnosed with Prostate cancer (PC) and 30,000 die of PC annually in the US. Because of its high prevalence, it is recommended that routine screening for serum Prostate Specific Antigen (PSA) be started at age 50 although its value remains controversial. While PSA screening is over 90% sensitive in patients with PC, its specificity remains low. Patients with increased PSA are usually referred to a urologist for biopsy, since the majority of PC cannot be accurately diagnosed with radiological technologies. Among those biopsied, 75% are negative for cancer in elevated PSA patients, with the increase in PSA mainly due to benign prostatic hyperplasia or chronic prostatitis. However, approximately 25-33% of men with a negative biopsy have PC that was missed by tissue sampling. Hence, we focus on tumor-adjacent, histologically benign prostate tissue to identify biomarkers that can screen patients with negative biopsies containing normal prostate tissue for nearby PC or precancerous conditions. We hypothesize that there are specific gene expression changes in PC-adjacent, histologically benign prostate.

Methods Used: Using oligonucleotide microarray, we compared the gene expression of normal (non-cancerous), histologically benign PC-adjacent prostate tissue.

Summary of Results: Our microarray results show hundreds of genes that display at least a two-fold change in expression between normal and histologically benign PC-adjacent prostate tissue.

Conclusions: Histologically benign, PC-adjacent and normal prostate cells have distinguishable gene expression profiles that may serve as biomarker targets to develop immunohistochemistry or in situ hybridization laboratory tests that may predict the risk of PC in men with elevated PSA but negative biopsies.

220

MUTATIONS IN THE TETRATRICOPEPTIDE 19 GENE TTC19 ARE A RARE CAUSE OF LEIGH SYNDROME

Atwal PS, Schelley S, Ems GM, Stanford University, Stanford, CA.

Case Report: This is one of the few reported cases of a patient with Leigh syndrome shown to have mutations in the TTC19 gene. In order to increase our understanding of the molecular pathology of Leigh syndrome, we present a four-year-old boy with global developmental delay, language regression at 13 months and brain MRI showing T2 high signal lesions involving the putamen, caudate body and the brainstem that appear to be progressing.

Direct sequencing of Leigh syndrome nuclear gene panel was performed along with review of electronic chart and medical literature.

Molecular testing showed our patient is heterozygous for two previously undescribed mutations in the TTC19 gene, W186X (p.Trp186Stop) and c.964_a867delGGCT (p.Gly322MetfsX8), both of which are predicted to cause loss of protein function due to either protein truncation or nonsense-mediated mRNA decay. The mutation c.964_a867delGGCT causes a frameshift at glycine codon 322 (changing it to a methionine residue) and creates a premature stop codon at position 8 of the new reading frame. TTC19 is one of the few reported cases of a patient with Leigh syndrome shown to have mutations in the TTC19 gene. In order to increase our understanding of the molecular pathology of Leigh syndrome, we present a four-year-old boy with global developmental delay, language regression at 13 months and brain MRI showing T2 high signal lesions involving the putamen, caudate body and the brainstem that appear to be progressing.

With the recent development of the molecular laboratory, the use of whole exome or whole genome sequencing has become more common. The TTC19 gene is not included in most of these panels. Therefore, the use of targeted gene panels is important in the diagnosis of Leigh syndrome.

Leigh syndrome is a sub-acute, necrotizing encephalomyopathy with an estimated prevalence of 1:40,000 live births. It is characterized by an initial period of normal development during the first few months of life, after which...
children present with progressive delay or regression in psychomotor
development, nystagmus, ophthalmoparesis, optic atrophy, ataxia, dysphagia,
hyponxia and dystonia. The TCTC1 gene encodes tetratacitoideptide 19 (TCC19), a NCL assembly factor that is embedded in the inner mitochondrial
membrane. At present there have been five other cases identified as having a
truncating mutation in TCTC19, two of which were in one family. The phe-
notypic variation and clinical presentation of patients with TCTC19 mutations is
broad, with initial presentation from childhood to adulthood. In summary,
TCTC19 is one of a growing number of nuclear genes that affect mitochondrial
function and should be included in nuclear gene testing panels for the eval-
uation of patients with a Leigh syndrome phenotype.

PERIPHERAL NEUROPATHY, LEUKOENCEPHALOPATHY, AND CIRRHOSIS IN A 25 YEAR OLD WOMAN
Mendelsohn B, Seymour P. UC San Francisco, San Francisco, CA.
Case Report: Disorders of mitochondrial DNA maintenance are a diverse
set of conditions with a broad range of affected organ systems, ages of onset,
and rate of progression. We present a 25 year old young woman with
short stature and a progressive condition including, in order of symptomatic
appearance over 7 years: secondary amenorrhea, severe peripheral neu-
ropathy, leukoencephalopathy, a macrocynic anemia with thrombocytopenia,
diabetes mellitus, intermittent lacitic acidosis, and cirrhosis of the liver.
Her parents are second cousins, without a family history of similar disorders.
Diagnostic considerations are discussed with data obtained from MRI,
extromylogram and nerve conduction studies, nerve and liver biopsies, as
well as sequencing analysis for several genes involved in disorders of mito-
ochondrial DNA maintenance. Her symptoms are most consistent with the
adult-onset form of Navajo Neurohepatopathy, an autosomal recessive mi-
ochondrial DNA depletion syndrome caused by mutations in MPV17, a
mitochondrial inner membrane protein of unclear function.

POTENTIAL FOR CREATINE AS A THERAPY FOR HUNTINGTON’S DISEASE
Cantway C. University of Washington, Seattle, WA.
Purpose of Study: Huntington’s disease (HD) is an inherited progressive,
neurodegenerative disorder. The clinical manifestations of HD include impaired
motor function, diminished cognitive function, and psychiatric disturbances
that progress to dementia and death 15-20 years after the onset of symptoms. Be-
cause of the drastically impaired motor and cognitive functions of HD patients, it
is important to find a therapy that can either slow the progression of the
disease, or prevent the development of symptoms. Creatine, a molecule involved
in cellular energy regulation, has been studied in mice as a possible therapy for
HD. The goal of this literature review is to determine if creatine may be a possi-
ble therapy for human HD based on current human and mouse model studies.
Methods Used: 1 searched for studies investigating both the effects of
creatinine on HD model mice, and tolerability studies of creatine in humans.
Search criteria for mouse studies: randomized controlled trials using R6/2
or N171-82Q model mice, creatine as the only dietary supplement, surviv-
ability and rotarod performance as outcomes measured.
Search criteria for human studies: randomized controlled trials, partic-
ipants diagnosed with a neurodegenerative disease, creatine as the only dietary
supplement, creatine tolerability and tests for brain biomarkers affected by
creatinine as outcomes measured.
Summary of Results: The mouse model studies reviewed show that cre-
atinine supplementation increases survivability, motor performance, body and
brain weight, and decreases the amount of brain atrophy as compared to
unsupplemented transgenic mice. Creatine supplemented mice also showed
increased levels of NAA and ATP, markers of mitochondrial function.
The human studies reviewed show that creatine is tolerable at doses up to
30 grams per day. These studies also show that serum creatine levels,
creatinine brain concentrations, and NAA levels, a marker of mitochondrial
function, were elevated in creatine supplemented patients, whereas serum
80HG levels, a marker of oxidative damage, were decreased.
Conclusions: Various mouse model and human studies of HD have shown
that creatine supplementation has multiple beneficial effects on the pro-
gression of HD. These studies, combined with findings that long-term, high-
dose creatine use is safe in healthy individuals, indicates that creatine may be
a potential therapy for human HD.

CLEAN INTERMITTENT CATHETERIZATION (CIC) AS AN ALTERNATIVE DRAINAGE METHOD FOR HYDROCOLPOS IN PATIENTS WITH PERSISTENT CLOACA
Fostvedt S1, Grady R2, Amies Oelschlagel AX, Merguerian PA3, Avansino JR4.
1University of Washington School of Medicine, Seattle, WA; 2Seattle Children’s
Hospital, Seattle, WA. Purpose of Study: Persistent cloaca is a confluence of the genitourinary
tract and rectum into a common channel. Approximately 30% of these pa-
tients have hydrocolpos, an accumulation of fluid in the vagina. Drainage
with tube vaginostomy is favored in the literature but carries surgical risks
including infection, scarring, and adhesions. Clean intermittent catheteriza-
tion (CIC) is a less invasive method to treat hydrocolpos; however, it is
unclear whether CIC is associated with increased complications and renal
insufficiency. The purpose of this study was to compare CIC with other
Drainage methods (non-CIC).
Methods Used: A retrospective chart review was conducted for fifteen
females with hydrocolpos who were treated at our institution between 1994 and
2012. Patient characteristics, drainage complications, and functional outcomes
were summarized by frequencies, means, and standard deviations. These were
compared between patients managed with CIC and those managed with other
Drainage methods. The Fisher’s exact and independent two-sample t tests
were used for all analyses.
Summary of Results: Eight patients (53%) were managed with CIC and seven
(47%) with other methods. There was no significant difference be-
tween CIC and non-CIC patients in characteristics including weeks gestation
(36.3±3.4 vs 34.6±3.5, p=0.36), common channel length ≥3cm (43% vs
67%, p=0.59), and associated malformations (4.0±1.1 vs. 3.9±0.9, p=0.79).
CIC patients had a non-significant increase in hydrocolpos-associated com-
plications compared to non-CIC patients (2.4±1.2 vs. 1.4±0.5, p=0.08). There
was no significant difference between groups in renal outcomes including
creatinine (0.43±0.12 vs. 0.53±0.15, p=0.09), improvement of hydrone-
phrosis (4 vs. 6, p=0.28), and persistent functional issues (6 vs. 6, p=1.00).
Conclusions: Hydrocolpos-associated complications and renal outcomes
were similar in patients managed with and without CIC. Drainage of
hydrocolpos with CIC may be considered an alternative to other, more in-
vasive drainage modalities. Ultimately, a larger, multi-center study is neces-
sary to better understand the risks and benefits of CIC.

FIGHTING TUBERCULOSIS IN ARUA DISTRICT UGANDA USING INFORMATION AND COMMUNICATION TECHNOLOGY
Sarac R. University of Washington School of Medicine, Seattle, WA.
Purpose of Study: Tuberculosis (TB) is one of the leading causes of adult
deaths in Arua district. It is also the most common cause of death among
people living with HIV. A major contributor to late case finding and
high mortality is lack of accurate information about TB symptoms, modes
of transmission, and treatment. The goal of this project was to increase ac-
cess to TB information using the Information and Communication Tech-
nology (ICT) tools that already exist in the local communities.
Methods Used: Four staff members of NACWOLA, a local organization
working with HIV positive women, one physician from the Arua Regional
Referral Hospital, and a radio journalist from a local radio station, Radio
Pakis, were trained to record, maintain, and distribute spoken health educa-
tion content on flash drives that could be used with mp3-enabled radios.
Laptops and free standard software were used for recording and converting
the spoken content into mp3 format. A one page training manual was col-
mnated and distributed electronically. An hour long interactive
TB and TB/HIV health education program was recorded in the local Lugbara
language, featuring several HIV positive women asking questions of the
physician. The pre-recorded program will be played at the weekly NACWOLA
support group meetings and other community gatherings.

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Summary of Results: Twelve NACWOLA support groups with over 600 members received mp3 enabled radios and flash drives with the pre-recorded TB and TB-HIV health programs and were trained how to use them. Radio Pacis broadcasted a 6-minute piece on TB in all of Arua district using the excerpts of the recorded TB program, and has created a 15 minute feature presentation on TB in Lugbara to be broadcasted once a week for several weeks.

Conclusions: Radio is a major way of accessing information in village communities of Arua district and it can be utilized for increased access to health education. According to some support group members, bringing the voice of medical doctors, who are highly respected and admired, into village communities can lead to positive changes in health seeking behaviors. This suggests that a continuous delivery of accurate health education initiated by this project has a potential to significantly improve health outcomes in Arua district.

CLINICAL PRESENTATIONS AND TREATMENTS OF COCCIDIOIDOMYCOSIS OSTEOMYELITIS IN PEDIATRIC POPULATIONS OF THE SAN JOAQUIN VALLEY OVER THE LAST 10 YEARS


Purpose of Study: The purpose of this study was to retrospectively analyze primary and disseminated osteomyelitis due to coccidiodomycosis in the pediatric population. It is unclear which factors make certain ethnicities prone towards more devastating disease but it is important to address those at risk and consider extra surveillance that they may require. As of now there has not been much data on optimal management of coccidiodomycosis osteomyelitis based on differentiation of unifocal versus multifocal disseminated disease. Ridges are tailored specifically based on therapy failure without any clear distinction who will benefit most or how to approach patients in a systematic way.

Methods Used: A search of electronic medical records and patient charts was performed at Children’s Hospital of Central California consisting of patients diagnosed with coccidiodomycosis osteomyelitis over the last 10 years. Patient’s age, sex, race/ethnicity, county, laboratory & radiographic studies, treatment regimen, hospitalization duration, and disease outcomes were evaluated.

Summary of Results: Coccidiodomycosis osteomyelitis has an extensive disease duration in majority of the patients. It is important to make the distinction between unifocal versus multifocal osteomyelitis when initiating treatment. Certain patient populations, especially African Americans, require extra surveillance due to the severity of disease and poor response to typical treatments. Dissemination to the vertebrae is very common and is associated with a challenging disease course. Several patients have failed pharmacological therapy requiring extensive surgical debridement.

Conclusions: Coccidiodomycosis is an endemic disease of the southwestern United States which spans across central to southern California and includes the San Joaquin Valley. All age groups are affected with a prolonged course in many of the osteomyelitis pediatric patients. There is no established theory for disease prediction and not sufficient research has been performed in the pediatrics populations when it comes to establishing an effective treatment plan. Swift diagnosis with close pharmacological and frequently surgical interventions is essential in order to have favorable outcomes in this extremely devastating disease process.

INTRAUTERINE GROWTH RESTRICTION DECREASES GLUCOSE TRANSPORTER-1 AND ATP CITRATE LYASE MRNA LEVELS IN FEMALE NEWBORN RAT LUNG


Purpose of Study: Intrauterine growth restriction (IUGR) increases neonatal lung disease. In animal models, this predisposition to neonatal lung disease is accompanied by changes in glucose uptake in the lung. Lung glucose uptake is facilitated by the glucose transporter 1 (GLUT1). Cellular metabolism and utilization of lung glucose is reflected by enzyme ATP-citrate lyase (ACL), which converts glucose derived citrate into Acetyl CoA. However, it is unknown if lower lung glucose uptake in IUGR is associated with changes in the mRNA levels of GLUT1 and ACL. We hypothesize that IUGR will decrease GLUT1 and ACL mRNA levels in newborn rat lung.

Methods Used: IUGR was induced by bilateral uterine artery ligation in rat dams at E19 of gestation. Tissue of fetuses was collected at day 0 for real-time RT-PCR analysis of GLUT1 and ACL mRNA.

Summary of Results: Results are IUGR as % of sex-matched control ± SD. In female rat lung, IUGR decreased GLUT1 mRNA levels (77 ± 6%, p<0.05) and ACL mRNA levels (75 ± 10%, p<0.05). In male rat lung, however, IUGR did not significantly alter levels of either GLUT1 or ACL mRNA.

Conclusions: We conclude that IUGR sex-specifically affects GLUT1 and ACL mRNA levels in newborn rat lung. Future work will assess protein levels of GLUT1 and ACL, with the expectation that they will be similarly affected by IUGR. We speculate that, in female rat lung, decreased ACL mRNA is a response to decreased glucose uptake by the lung.

IUGR DOES NOT AFFECT DNA METHYLATION OF THE PPARγ PROMOTERS IN NEWBORN RAT LUNG


Purpose of Study: Intrauterine growth restriction (IUGR) impairs lung development. Lung development is, in part, regulated by expression of the PPARγ gene. Gene expression is influenced by epigenetics. Epigenetic modifications include DNA CpG methylation. Promoters with dense CpG regions are often unmethylated. Promoters with sparse CpG regions are often methylated, and that methylation is positively associated with expression. We showed in newborn rats, that IUGR decreases expression of PPARγ mRNA variants. These variants are transcribed out of two promoters of the PPARγ gene, a CpG dense and CpG sparse promoter. However, it is unknown if IUGR alters DNA methylation of PPARγ promoters in newborn rat lung.

We hypothesize that, in newborn rat lung 1) the CpG dense PPARγ promoter will be unmethylated and the CpG sparse promoter will be methylated, and 2) IUGR will decrease DNA methylation of the PPARγ CpG sparse promoter.

Methods Used: IUGR was induced by uterine artery ligation on day 19 of gestation in Sprague Dawley rats. PPARγ promoter methylation was quantified at regions within each PPARγ promoter using bisulfite modification and sequencing.

Summary of Results: The PPARγ CpG dense promoter was unmethylated in control or IUGR male or female rat lung. However, it is unknown if IUGR alters DNA methylation of PPARγ promoters in newborn rat lung.

Conclusions: In control rats, the PPARγ gene is characterized by an unmethylated CpG dense promoter and a methylated CpG sparse promoter. Despite IUGR-induced decreases in mRNA variants produced from these promoters, IUGR did not alter the levels of methylation observed at either promoter. We speculate that other epigenetic modifications along the PPARγ gene are also affected by IUGR and that in combination these changes contribute to the decreased PPARγ mRNA observed in newborn IUGR lung.

PREDICTORS OF NEONATAL NEUROLOGIC BIRTH DEPRESSION AND INTRAVENTRICULAR HEMORRHAGE IN PRETERM PREMATURE RUPTURE OF MEMBRANES

Hoover W1, Donnelly M2, Manco-Johnson M3, Winn V2, Armstrong-Wells J2,3,4. 1University of Colorado School of Medicine, Aurora, CO; 2University of Colorado School of Medicine, Aurora, CO; 3Hemophilia and Thrombosis Center, University of Colorado, Aurora, CO and 4University of Colorado School of Medicine, Aurora, CO.

Purpose of Study: Preterm birth is a major cause of adverse perinatal outcomes, including birth depression and intraventricular hemorrhage (IVH). Both birth depression and IVH contribute to lasting neurological disability,
However the role of maternal characteristics in contributing to these outcomes have not been well defined. We sought to determine predictors of these adverse outcomes in pregnancies complicated by early preterm premature rupture of membranes (PPROM).

**Methods Used:** We performed a retrospective cohort study of all singleton pregnancies with early PPROM (<32 weeks GA and delivery ≥22 weeks GA at University of Colorado Hospital (UCH) from 1/1/ 2007-12/31/2011. Cases (n=229) were identified, confirmed, and abstracted from the UCH Perinatal Database. Adverse perinatal outcomes were defined as Apgar of ≤7 at 1 and 5 minutes, or clinically significant IVH (Grade III or IV). To determine independent predictors of each outcome, we created a multivariate model including all univariate covariates with p-value of ≤0.10.

**Summary of Results:** Cohort demographics were representative of the Rocky Mountain Region. In our cohort there were no independent predictors of poor 1 minute Apgar. Female was the only independent predictor of poor 5 minute Apgar (OR=2.3 CI 1.06-5.28, p=0.04). When adjusted for non-white race, younger maternal age and increased BMI were independent predictors of clinically significant IVH (OR=1.4 CI 1.04-1.79, p=0.03; OR 1.2 CI 1.04-1.33, p=0.01, respectively).

**Conclusions:** In our cohort, female newborns had a 2-fold greater risk of poor 5 minute Apgar. Infants born to younger mothers or mothers with higher BMI appear to have increased risk for clinically significant IVH. Larger studies are warranted to examine the role of newborn gender, maternal age and race, and BMI with adverse neurological outcome in pregnancies complicated by early PPROM.

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**END-OF-LIFE DECISIONS ENTER A GREY ZONE AT THE EDGE OF VIABILITY**

Weiner JA, Kilbride H. Children’s Mercy Hospital & Clinics, Kansas City, MO.

**Purpose of Study:** Prematurity or complications of prematurity account for majority of infant deaths in the Neonatal Intensive Care Units (NICU). We examine trends in end of life care for preterm infants at differing gestational age. The purpose of the study is to determine circumstances and causes of deaths for preterm infants at a referral level NICU.

**Methods Used:** Retrospective descriptive study involving very preterm infants (<=32 weeks) that died in the NICU at a children’s hospital from January 1st, 1999 to December 31, 2008. Infants were categorized based on gestational age at birth. Level of stabilization was categorized using the criteria of Verhagen et al (J Peds, 2010). NICU deaths were further divided by gestational age. The primary outcome was level of clinical service provided at end-of-life (care withheld, care withdrawn, or CPR).

**Summary of Results:** Over 10 years, 414 infants died in the NICU, 35% were related to prematurity. Withdrawal of care was more common in infants 25-27 weeks and 28-32 weeks versus infants 22-24 weeks (62.5%, 55.9% vs. 43.8%). Infants 22-24 weeks were more likely to receive CPR and be unstable at the time of death (Table 1).

**Conclusions:** At the edge of viability, NICU deaths were more unstable and significantly more likely to receive CPR than other preterm infants. This suggest quality of life and medical futility enter a “gray zone” when dealing with the limits of viability. Differences in CPR for infants 22-24 weeks may represent selection bias. Those infants admitted to the NICU had parents who wanted “everything done”. These differences imply end of life care are viewed differently for preterm infants.

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**INCIDENCE OF BLADDER EVISCERATION IN NEONATES WITH GASTROCHISIS**

Dimond L1,2, Paquette L1,2, 1University of Southern California, Los Angeles, CA and 2Children’s Hospital Los Angeles, Los Angeles, CA.

**Purpose of Study:** Gastrochisis is a congenital condition in which portions of the GI tract herniate out through an abdominal wall defect, and are not covered by peritoneum or other membrane. Small bowel is most commonly found outside the abdominal cavity, with other organs eviscerating less frequently. The goal of this study is to assess the frequency of bladder evisceration in neonatal gastrchisis cases at CHLA, as well as to determine if bladder herniation is associated with additional urinary tract complications as opposed to normal bladder position.

**Methods Used:** This was a retrospective IRB-approved chart review. The NICCU Admission log was screened for all neonates with the diagnosis of gastrochisis cared for from 2003 to 2010. Once identified, those patients’ medical records were reviewed in the CHLA electronic medical record system. We reviewed the operative reports, physical exam notes, urine culture results during each child's first admission, and radiology reports during all admissions. Percentages of bladder herniation, UTI, and abnormal renal ultrasound were calculated.

**Summary of Results:** A total of 94 patients were included in the study. 7 of 94 children had an eviscerated bladder (7.4%). Of those, 2 (28.6%) had an abnormal renal ultrasound, and 1 (14.3%) had a UTI during the first hospital admission. The child with a UTI was not among those with abnormal ultrasounds. Among the 87 neonates without a herniated bladder, 13 (14.9%) had an abnormal renal ultrasound, and 16 (18.4%) had a UTI. Differences in rates of urinary tract complications were not significant between the eviscerated bladder and the normal bladder groups.

**Conclusions:** Bladder evisceration occurred in 7.4% of gastrochisis cases in our study. Although there was an increased risk of abnormal renal ultrasound with bladder herniation, interestingly, there was no increased risk of UTI, and these findings were not statistically significant. It appears that bladder evisceration confers no additional risk on neonates with gastrochisis, at least during the early years of life examined in this study.
LONG-TERM GROWTH OF SURVIVORS OF CONGENITAL HEART DISEASE

Aguilar DC, Raff GW, Griffin JJ. UCDMC, Sacramento, CA.

Purpose of Study: Long-term growth of survivors of congenital heart disease is poorly characterized, especially as it relates to the long-term effects on metabolic risk.

Methods Used: Cohort discovery extracted growth data of children with 3 common congenital heart diseases; Tetralogy of Fallot (TOF), transposition of great arteries (TGA) and VSD from the UCDMC electronic medical record, 34 with TOF, 35 with TGA and 163 with VSD were identified with measurements of body weight (BW) between ages 2y and 10y. A total of 2006 BW measurements (TOF = 371, TGA = 313, VSD =1322) were converted to gender-specific Z-scores using CDC growth chart.

Summary of Results: Body weight (BW) was significantly related to age at measurement (P < 0.0001), gender (P = 0.0034) and cardiac diagnosis (P < 0.0001). BW was significantly greater in those with TGA than those with VSD, who were greater than those with TOF (P < 0.0001 for all comparisons). BW Z-score was significantly affected by age (P < 0.0053), gender (P < 0.0001) and by diagnosis (P < 0.0001). There was a significant interaction between age and diagnosis (P < 0.0001), so the diagnoses were analyzed separately. TGA; BW Z-score was significantly greater than 0 but did not change with increasing age (P = 0.10). TOF; BW Z-score was significantly below zero during the period 2-10y, but increased significantly with increasing age. VSD; BW Z-score was significantly greater than zero during the period 2-10y, and continued to increase significantly with increasing age (P = 0.0048).

Conclusions: Patients with a history of TOF, TGA or VSD have abnormal metabolic risk and cardiovascular health merits further investigation.

Early Echocardiographic Predictors of Alveolar Capillary Dysplasia: A Case-Control Study

Arcimie R1, Stavroudis T1, Noori S1, Bhombi S1,2, Szmuszkovicz J2, Friedlich P1, 1Children’s Hospital Los Angeles, Los Angeles, CA and 2Children’s Hospital Los Angeles, Los Angeles, CA.

Purpose of Study: To evaluate early echocardiographic measures of pulmonary hypertension and refractory hypoxemia predictive of ACD.

Methods Used: A retrospective 1:1 matched case-control study at a quaternary hospital was conducted from 2000 to 2011. ACD patients were compared to patients with meconium aspiration syndrome and/or sepsis matched by gender, gestational age and birthweight. All patients were on ECMO and inhaled

Summary of Results: Extraction of great arteries (TGA) and VSD from the UCDMC electronic medical record, 34 with TOF, 35 with TGA and 163 with VSD were identified with measurements of body weight (BW) between ages 2y and 10y. A total of 2006 BW measurements (TOF = 371, TGA = 313, VSD =1322) were converted to gender-specific Z-scores using CDC growth chart.

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International Publication Trends in Plastic and Reconstructive Surgery

Mitchell E, Workman A, Gupta S. Loma Linda University, Loma Linda, CA.

Purpose of Study: As globalizing and worldwide economic development progress, the boundaries that previously prevented the exchange of goods, services, and information have blurred. The authors qualitatively observed this trend reflected in plastic surgery research, with more articles each year published outside of the USA and Europe.

Methods Used: A review of publications from 2001 to 2011 was conducted in the plastic surgery journal with the highest impact factor, Plastic and Reconstructive Surgery (IF=3.382). Articles were catalogued according to country of publication, subspecialty within plastic surgery (Craniofacial, Breast, etc.), and publication type (Original Article, Ideas and Innovations, etc.).

Summary of Results: Contrary to expectations, the percentage of contributions from the USA & Canada increased (from 54% in 2001 to 83% in 2011), while contributions from Europe, East & Southeast Asia remained the same or decreased. All other geographic areas were minor contributors.

Conclusions: The shift in contributor population in Plastic and Reconstructive Surgery occurred after 2006, the year the British Journal of Plastic Surgery expanded its readership to include international audiences and changed its name to The Journal of Plastic, Reconstructive & Aesthetic Surgery. Based on that trend, it is possible that JPRAS drew away a large number of international publications, transforming the most influential journal within plastic surgery into a primarily North American product.

Oral Vitamin Supplementation and Wound Healing: An Evidence Based Review of the Plastic Surgery Literature

Mitchell E, Workman A, Gupta S. Loma Linda University, Loma Linda, CA.

Purpose of Study: The role of nutrition in wound healing is particularly pertinent to plastic surgery. The success of every surgical procedure, whether outpatient or inpatient, depends on maximizing wound healing. The physiologic role of vitamins in wound healing has been studied extensively and can be found in most textbooks, yet few evidence-based studies within plastic surgery address the clinical impact of perioperative oral vitamin supplementation.

Methods Used: A review of the literature was conducted using search terms such as “vitamin,” “healing” and specific names of vitamins. Only articles that contributed new data were included in this review. All other review articles, safety reports and letters to the editor were excluded from this analysis.

Summary of Results: The reported effects of the vitamins included diverse and occasionally contradictory outcomes for the following parameters: contracture, wound tensile strength, antioxidant level and flap survival. The studies reviewed are demonstrated in the table below.

Conclusions: Based on studies of wound healing in patients with vitamin deficiencies, it is clear that nutritional status is a key component in wound
healing. At this time, it is unclear whether or not additional perioperative vitamin supplementation, beyond recommended dietary intake, increases clinical rates of wound healing. More research in this area is needed within the field of plastic surgery.

Studies within the field of plastic surgery concerning oral vitamin supplementation and wound healing.

<table>
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MEASUREMENT OF MOUTH OPENING IN A CANADIAN PEDIATRIC POPULATION

Liu H, Martens RK. BC Children’s Hospital, Vancouver, BC, Canada.

Purpose of Study: The goal of this study was to define the interincisal opening (IIO) in a pediatric population.

Methods Used: IIO was measured between the edges of the upper and lower right central incisors with the mouth maximally open in 926 eligible children between the ages of 1-18 at BC Children’s Hospital. Individuals with current or previous TMJ disease were excluded from the study.

Summary of Results: The mean and standard deviation of IIO for each age group of males and females, rounded down to the year, was calculated. The mean IIO at the adult end of our study was 52.8 mm and 49.4 mm for males and females, respectively. A scatter plot was created using the mean and two standard deviations representing the upper and lower limits of normal. The data fit a second order polynomial regression curve. The coefficient of determination for the lower limit of normal is 0.86 and 0.89 for males and females, respectively.

Conclusions: IIO increases with increasing age, and seems to plateau at about age 12. The mean IIO at the adult end of our test is 51 mm, similar to the literature value of 50.77 mm for adults. We hope the normal IIO of a pediatric population determined in this study will aid in the objective diagnosis of TMJ pathology.

DEFINING CRANIOSCOLIOSIS

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Purpose of Study: To define cranioscoliosis and establish precise diagnostic criteria for characterization and communication of the diagnosis and severity.

Methods Used: We examined the 3D photographs of 9 patients with one or more of the following diagnoses: cranioscoliosis, hemifacial microsomia, torticollis, microtia, or hemifacial hypertrophy. After aligning each photograph to normative landmarks, we measured the locations of 9 landmarks.
THE OPTIMAL DURATION OF ANTIBIOTIC PROPHYLAXIS IN PLASTIC SURGERY: A META-ANALYSIS OF 32 PUBLICATIONS

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Purpose of Study: Antibiotic prophylaxis administered perioperatively has been shown to decrease the risk for the core measure of post-operative surgical site infection, but specifics of use vary widely among different surgical specialties. The objective of this study was to perform a meta-analysis to determine the optimal duration of antibiotic prophylaxis in the field of plastic surgery.

Methods Used: A systematic literature review was conducted using various terms to locate studies of prophylactic antibiotic use in the field of plastic surgery. Studies included in the analysis were those with clearly recorded antibiotic dosage, duration, and incidence of surgical site infection. Studies were excluded if they included non-plastic surgery procedures or if they did not clearly fit our study parameters. 32 studies were identified. 12 of them involved head and neck surgery, 12 of them involved breast and body surgery, 7 of them involved hand surgery and 1 included multiple types of plastic surgery procedures. The data from each study was divided into one of four duration categories: no antibiotic prophylaxis, single-dose prophylaxis, 24-hour prophylaxis or extended course (24hr+) prophylaxis. The data was then statistically analyzed for each duration group.

Summary of Results: A Forest plot of each of the four categories was created and analyzed using the random effect model. The average percent of events per population for each category was as follows: no prophylaxis was 14.7%, a single dose prophylaxis was 7.7%, 24 hours prophylaxis was 14.1% and a 24 hour course of antibiotics. However, as the confidence intervals are wide and overlapping, these findings are not statistically significant. At this time, more research is needed to reach a better understanding of the value of antibiotic prophylaxis during surgery.

EFFECT OF PREOPERATIVE WASHES ON SURGICAL SITE INFECTION RATES

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Purpose of Study: Currently, surgical patients are asked to wash the surgical area at home, with an antiseptic solution. The goals of this research are: (1) determine what effect preoperative washes have onSSI rates and (2) stratify these effects based on patient population, surgical specialty, procedure, and wash protocol. Previous reviews have drawn conclusions from meta-analyses and randomized controlled trials, and looked at this question broadly. We will include other levels of evidence to gain a more comprehensive understanding, and determine the effect of washes onSSI rates in specific situations to allow for the formulation of more detailed treatment recommendations.

Methods Used: We are using the evidence review method outlined by the International Liaison Committee on Resuscitation. We are currently finishing a comprehensive literature review. Databases searched include EMBASE, PubMed, Medline, and CINAHL. Subject expert and librarian input was obtained regarding search terms and methodology. We are currently completing study selection. We will then determine levels of evidence for selected studies, perform a critical appraisal, and finally integrate our findings and formulate possible treatment recommendations.

SUMMARY OF RESULTS: Preliminary results show varying effects of preoperative washes onSSI rates between studies. Several reviews show no effect on SSI rate when preoperative washes were used, while some studies show a reduction in rates. Some data suggest that use of washes several days before and after the procedure is beneficial. Some evidence shows that preoperative washes affect SSI rates differently depending on the procedure.

Conclusions: As our research is still in progress, definite conclusions cannot yet be drawn. Generally, preoperative washes do not seem to impact SSI rates. This may be due to stringent infection control practices in the operating room, such that preoperative washes do not provide additional benefit. However, this may not necessarily be true in all patient populations, surgical specialties, or types of procedures, and may vary depending on the number and timing of washes. As we complete our research, we will draw conclusions as to the effect of washes in specific situations, as well as in general.

A RETROSPECTIVE COMPARISON OF TWO DIFFERENT CT URETERAL LENGTH MEASUREMENT TECHNIQUES

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Purpose of Study: Ureteric stents are frequently placed following ureteroscopy to ensure adequate ureteral drainage. Selection of the appropriate stent length is important as excess length may contribute to additional patient morbidity and may cause greater urinary symptoms. The purpose of this study was to compare two radiologic methods of ureter measurement with the actual ureteral length to determine whether CT measurement of the ureter would predict the actual ureteral length.

Methods Used: A retrospective review was performed of 90 ureteroscopy patients completed between April 2011 and September 2012. Ureteral length was determined using the preoperative CT scan by counting the number of axial slices and multiplying by the slice reconstruction thickness, and by measuring the estimated distance between the ureteropelvic and ureterovesical junction on the coronal reconstructions. These two estimates were then compared to the actual ureteral length measured endoscopically during ureteroscopy.

Summary of Results: Sixty patients were excluded because endoscopic ureteral length was not dictated on the operative report or outside CT images did not include slice thickness. Eighteen patients with endoscopically measured ureteral length had axial reconstruction and 21 had coronal reconstruction. There were 13 males and 8 females with an average age of 53 years (27-75). Average endoscopic ureteral length was 24 cm (20-26 cm). Average axial and coronal ureteral lengths were 22.2 and 21.4 cm, respectively. A significant difference was seen between axial and coronal measurements when compared with endoscopic measurements (p<:0.004 and p<:0.0001, respectively). Both axial and coronal measurements showed low correlation coefficients at 0.371 and 0.215, respectively.

Conclusions: CT underestimates ureteral length compared to endoscopic measurement by about 2cm. Even after accounting for this bias, there is weak correlation for CT ureteral length compared to endoscopic length. Further research is needed to find the most appropriate method for estimating length of the ureter.

REVERSED NEEDLE PASS CLEAR-CORNEAL OR LIMBAL INCISION SUTURING TECHNIQUE USING THE 3-THROW (1-1-1) ADJUSTABLE SQUARE KNOT

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Purpose of Study: A single radial suture is required for a corneal or limbal incision that does not seal despite stromal hydration. In the traditional
technique for placing this suture, the needle enters from the corneal side of the limbal incision and exits toward the scleral side and the suture is usually tied with a 3-1-1 surgical knot. We present an improved suturing technique in which the needle path is reversed.

The needle enters on the scleral side of the limbal incision, exits on the corneal side toward the apex, and is tied with an adjustable 1-1-1 knot.

**Methods Used:** In comparing suturing techniques, the ideal technique is one that avoids collapsing the anterior chamber so as to prevent possible endothelial trauma. The optimal technique is also fast, adjustable, and able to be buried.

**Summary of Results:** Compared with a traditional 3-1-1 knot, the new 1-1-1 knot technique offers significant advantages: It maintains chamber stability, allows suture tension adjustment, and promotes easy burial of the suture knot in the tissue while preventing suture breakage.

**Conclusions:** The reversed-needle pass combined with the 1-1-1 knot is a simple technique that offers simpler efficiency and significant advantages over the traditional 3-1-1 suturing technique.

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**Community Health II**

**Concurrent Session**

3:30 PM  
Friday, January 25, 2013

[243]

**I CARE TO KNOW: AN INNOVATIVE EDUCATION PROGRAM TO INCREASE HIV SCREENING AMONG ADOLESCENTS AGED 10-18 YEARS IN NIGERIA**

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1University of Nigeria School of Medicine, Enugu, Nigeria; 2las Vegas, NV and 3Year Of Ultimate Talents Harvest (YOUTH), Enugu, Nigeria.

**Purpose of Study:** We sought to develop an innovative program to increase knowledge and the proportion of adolescent aged 10-18 years who are aware of their HIV serostatus.

**Methods Used:** We designed a game show that utilizes questions in form of a quiz that assess knowledge of modes of acquisition of HIV, transmission, diagnosis, prevention methods, available treatment and services. (1) School administrators are approached to participate in the program. Following a video showing the program format, administrators explain the program to the parent-teacher-association and decide whether to participate.

**Summary of Results:** A group of 40 students based on peer recognition of ability to influence others are selected by the school (3) Informed consent are obtained from parents to allow selected students participate. Schools certify selected list of students. (4) Assent is obtained from students, pretest and posttest counseling is provided prior/after HIV testing to all participants by members of Support Group of PLWH and those identified with HIV are enrolled into care.

**Conclusions:** Eight participants are selected to represent each school in the Edutainment Game Show. Participants are asked to consume, according to their randomized assignment, according to their randomized groups, regular coffee or decaffeinated coffee for 5 days. The randomized, blinded beverage was consumed at two times during the day: in the morning between 6 am and 9 am and five hours later in the afternoon, between 11 am and 4 pm, respectively. On day 1, all participants were asked again to refrain from any caffeine consumption and remained on the same diet and fluid intake for the study for each participant. Day 15 concluded the study for each participant. Day 15 concluded the study for each participant. Day 15 concluded the study for each participant.

**Summary of Results:** The effect of caffeine on the urinary system by comparing urinary symptoms in healthy adults drinking caffeinated coffee to those drinking decaffeinated coffee in a randomized, controlled study.

**Methods Used:** A randomized, controlled, and double blinded study was performed. 35 healthy volunteers between the ages of 18 and 45 years were recruited for this study during a 4-month enrollment period between March 2012 and June 2012. Test subjects were randomly divided into two cohorts of coffee drinking: a caffeinated coffee and a decaffeinated coffee group.

Every participant conducted a 24-hour voiding log at the beginning of the study and started with a caffeine abstinence washout period for 5 days. On day 6, participants were asked to consume, according to their randomized groups, regular coffee or decaffeinated coffee for 5 days. The randomized, blinded beverage was consumed at two times during the day: in the morning between 6 am and 9 am and five hours later in the afternoon, between 11 am and 4 pm, respectively. On day 1, all participants were asked again to refrain from any caffeine consumption and remained on the same diet and fluid intake for the study for each participant. Day 15 concluded the study for each participant. Day 15 concluded the study for each participant. Day 15 concluded the study for each participant.

**Summary of Results:** The caffeinated group saw a significant increase in urinary volume. There was a delay effect noticed here in that the effects on urinary volume did not wear off until three days after the treatment concluded. The caffeinated group also showed a significant increase in urgency during the coffee stage. A lag effect was also noticed in terms of urgency. It took about five days to remove the effects of caffeine on urgency.

**Conclusions:** Improved knowledge of childhood nutritional needs and preparation of balanced diets from locally available food materials for caregivers of under-5 children is valuable in developing countries especially among caretakers of orphaned children who do not have the benefits of breast milk.

**Purpose of Study:** A significant number of newborns in Nigeria who survived their mother’s death during child birth are not breastfed. Because infant formulas are expensive, these infants are weaned and fed predominantly adult food at an early age. Understanding the nutritional value of various local foods will help caregivers provide a balanced diet for optimal growth and development. We sought to improve knowledge of food groups and preparation of balanced diets from locally available food products by community health workers in Enugu-Nigeria.

**Methods Used:** 50 community health workers selected from 10 local health centers completed a pre-training questionnaire to ascertain their knowledge base in identifying commonly available food groups and practices regarding child nutrition. Training comprised of didactic lectures on infant and child feeding habits, practical demonstrations on the preparation of balanced meals using locally available food products, nutritional assessment of children and methods of anthropometric measurements. We used a local cook to demonstrate how to mix and match different local food products to produce a balanced meal for children under the age of 5 years. Participants completed a post-training questionnaire.

**Summary of Results:** Pre-test score was 37.5%. A majority of participants (80%) stated that the first complementary food given is cereal pap. 27% (14/50) reported that food taboos exist in their communities. 27% (14/50) of the respondents indicated that there were foods (e.g. eggs) not given to children in their communities despite their nutritional values due to concern about introducing bad behaviors (e.g. stealing) to children. Post-test score averaged 85% revealing a marked improvement in knowledge.

**Conclusions:** Improving knowledge of childhood nutritional needs and preparation of balanced diets from locally available food materials for caretakers of under-5 children is valuable in developing countries especially among caretakers of orphaned children who do not have the benefits of breast milk.
BUILDING A TB SUPPORT AND ADVOCACY GROUP - VENTANILLA, PERU
Barnell J. University of Washington, Seattle, WA.

Purpose of Study: Tuberculosis is the leading cause of death of working-age men and women in Ventanilla, a rapidly growing shantytown north of Lima, Peru. Because TB incidence rates remain high despite a model TB control program, movement has been building to take the fight against TB from the clinic to the community by empowering people affected by the disease. This project aimed to empower TB patients, ex-patients, and contacts to form an officially recognized organization that supports, educates, and advocates for the TB-affected community in Ventanilla.

Methods Used: As part of a larger package of socioeconomic interventions developed by the NGO Prisma, two community workshops were organized for TB-affected families. A community needs assessment, literature review, focus groups, and semi-structured interviews with patients and health workers informed planning efforts. Workshops consisted of testimonials by representatives of TB support groups, health care personnel, and local community leaders. They also included group exercises to identify TB-related problems and develop potential solutions, a personal commitment activity, and a product fair to sell crafts made by participants. A follow-up workshop was held with TB advocates to plan next steps and set a timeline for electing leadership.

Summary of Results: 200 patients, ex-patients, and contacts participated in the workshops. Participants worked together in nine groups, identified over 100 TB-related problems in their communities, and generated solutions that could be achieved through organization. 87 participants made individual commitments to take action in the fight against TB, and 17 participants sold products, earning a total of $215. A committee of TB advocates (patients, ex-patients, and contacts) enthusiastically elected leadership at the end of August, initiated steps to register with the local government, and drafted short, medium, and long-term goals.

Conclusions: This project took important steps towards the creation of a formal organization and developed valuable connections with local community leaders. As the TB-affected community faces significant barriers to empowerment, sustained effort will be required to achieve a strong organization. Future success will depend on continued support and leadership by TB advocates and the Prisma team.

THE RELATIONSHIP BETWEEN PEAK INFLUENZA ACTIVITY AND ABSENTEEISM RATES IN PUBLIC SCHOOLS
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1University of New Mexico School of Medicine, Albuquerque, NM and 2Tri-Core Laboratory, Albuquerque, NM.

Purpose of Study: Influenza is a primary focus of public health efforts nationwide, as it contributes greatly to the morbidity and mortality of thousands. It is also a common reason for absenteeism within schools causing educational losses among children. Influenza's ubiquitous and lethal nature has prompted the CDC to recommend yearly vaccinations for all Americans 6 months and older with only a few exceptions. Additionally, a group of Japanese researchers found that Influenza-related mortality decreased by 3-4 times with obligatory vaccines, and when vaccines were no longer mandated the rates increased. Despite the availability of this preventative measure, vaccination rates remain low. This research was intended to demonstrate that influenza activity in an urban Southwestern city is related to community leaders. They also included group exercises to identify TB-related problems and develop potential solutions, a personal commitment activity, and a product fair to sell crafts made by participants. A follow-up workshop was held with TB advocates to plan next steps and set a timeline for electing leadership.

Summary of Results: Weeks in which there was prominent influenza activity also had significantly more absences than weeks without influenza activity. We also found that absences begin to rise before influenza in the community peaks.

Conclusions: This study demonstrates that there is in fact a relationship between high incidences of influenza and increased absences. This information provides added credence to the burdens of the disease and the benefits of vaccination to prevent such a phenomenon. Also of note is that children appear to have an important role of influenza transmission within the community.
PERCEPTUAL AND ADAPTIVE LEARNING MODULES PRODUCE LONG-TERM LEARNING OF PATTERNS IN DERMATOLOGY

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Purpose of Study: Current medical training relies on prolonged exposure and chance to bring a student into contact with various disease patterns. However, studies show that expertise depends heavily on implicit pattern recognition that is partially acquired through perceptual learning. Software programs called Perceptual and Adaptive Learning Modules (PALMs) have previously been shown to increase pattern recognition fluency. The purpose of this study was to determine the effect of PALMs on long-term memory of pattern recognition.

Methods Used: We created three PALMs that exposed medical students to a large number of dermatological images and required students to associate each image with its correct lesion morphology, configuration, or distribution. Each PALM, which was typically completed in less than 30 minutes, consisted of a pre-test, a learning module, and a post-test. The dermatology lesion morphology PALM, created one year previously, was used by the same group of medical students in their first and second years of medical school. Approximately half of the class completed this PALM in their first year.

Summary of Results: Comparing performance in years 1 and 2 revealed that morphology pre-test scores of second-year medical students who completed the morphology PALM one year previously were significantly higher than those of those who did not (P < 0.001; Effect size = 0.78). By contrast, there was no difference in performance between the two groups of students on the distribution or configuration PALMs. Interestingly, there was no correlation in performance for students among the three different PALMs.

Conclusions: Because student performance varied according to whether or not the PALM was used one year prior to the second administration of the module, this study indicates that patterns introduced in one brief session of repeated exposures to dermatology images can be retained for at least one year. Thus, PALMs appear to be effective and efficient programs for teaching basic visually-based dermatology educational components to medical students while yielding long-term memory of pattern recognition.

251

PERUVIAN COMMUNITY MEMBER’S KNOWLEDGE, ATTITUDE AND PRACTICE OF EMERGENCY MEDICAL CARE

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Purpose of Study: Unintentional and intentional injuries account for 10% of mortality worldwide and 15% of disability-adjusted life years. Age specific data for 10-24 year-olds show remarkable differences from the overall age statistics: injuries account for 40% of all deaths amongst both sexes and over half of all male deaths, with both figures being higher in developing countries such as Peru. Understanding how community members in Lima, Peru, access the emergency medical system to respond to injury is an important first step in reducing injury related morbidity and mortality in Lima.

Methods Used: A KAP (knowledge-attitude-practice) survey was designed to assess community members knowledge, attitude and practice with regards to medical emergencies. A two-stage cluster-sampling methodology as outlined by the WHO Guidelines for Conducting Community Surveys on Injury and Violence was used in conjunction with a “30 × 7” cluster sampling scheme to administer the survey. 30 clusters within the city of Lima, Peru were selected based off of probability proportional to size methodology and 7 households were randomly surveyed within each of the 30 clusters, for a total of 210 surveys, giving a confidence interval of +/- 10%.

Summary of Results: 63% of people surveyed did not know of a number to call in case of a medical emergency and 52% of people said that in the event of a medical emergency, they would take their family member directly to the hospital in a taxi or private car and not wait for an ambulance. 98% of people said that one should go to the hospital within an hour for a serious injury, but only 67% felt that an ambulance would arrive within the hour. Only 37% of people surveyed knew how to provide first aid, but 99% said that they would feel more comfortable if a neighbor was trained in first aid.

Conclusions: Emergency medical care in Lima is still in the development phase, with large gaps in the services available as well as in the public’s awareness of the existing services. Programs to improve the current system should focus on increasing the public’s knowledge of existing services as well as providing first-aid training for community members, especially in the peripheral low-income communities of Lima.

252

NUTRITIONAL CONTENT OF MEALS AT A PEDIATRIC HOSPITAL

Pierce MJ1, Banerjee S2. 1. UCSD, Fresno, Madera, CA; and 2. Children’s Hospital Central California, Madera, CA.

Purpose of Study: Inpatient hospital wards have many aspects of an obesogenic environment with decreased physical activity and access to high calorie foods and sugar-sweetened drinks. Our study proposed to investigate the nutritional content of meals served to children in a large free-standing children’s hospital in central California.

Methods Used: Daily menus were collected for one week on all patients ages of 2 to 20 years receiving regular or low-fat diet on the acute care floors of Children’s Hospital Central California in Madera, California. Menu item frequencies were calculated for breakfast, lunch, and dinner. Caloric content for all items was obtained from cafeteria information or online sources. Total macronutrient content including calories, grams fat, grams saturated fat, and total grams sugar were tabulated for each meal.

Summary of Results: 197 menus were collected including 71 breakfast, 103 lunch, and 23 dinner menus. Average caloric content for breakfast was 774 calories, which included 37 grams of fat, 17 grams of saturated fat, and 37 grams of sugar. Lunch averaged 707 calories, with 24 grams fat, 7.5 grams saturated fat, and 43 grams sugar. Dinner averaged 664 calories, with 22 grams fat, 7 grams saturated fat, and 31 grams sugar.

For the patients for whom all three meals were available, caloric content averaged 17.5% of the daily recommended value given by the United States Department of Agriculture (USDA).

The most commonly ordered items were beverages, with apple juice favored at breakfast and lunch and whole milk at dinner. Fried potatoes in the form of chips, french fries, and tater tots were among the top menu items for each meal.

Conclusions: Although this study only assessed food served through the cafeteria at meals, it strongly suggests that the food options provided to and chosen by inpatients at our hospital contribute to the obesogenic hospital environment. Issues identified included excessive provision of fruit juice and whole milk, which violates recommendations by the USDA and the AAP. Caloric content of meals far exceeded estimated daily values. Percentage values for fat and saturated fat were largely within recommended values, however all meals contained an excessive amount of calories from sugar. As a first step, we have proposed removing apple juice and whole milk on the regular menu.
253

BARRIERS TO CLEAR COMMUNICATION FOR PEDIATRIC PRIMARY CARE PROVIDERS WHEN USING PHONE INTERPRETERS: A FOCUS GROUP STUDY

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1USCF Fresno Medical Education Program, Fresno, CA and 2Childrens Hospital of Orange County, California, Madera, CA.

Purpose of Study: We are conducting focus groups with healthcare providers (HCP) and parents to investigate communication barriers and solutions when using phone medical interpretation in primary care. Our clinic is a pediatric resident continuity clinic that serves an ethnically and linguistically diverse, low-income population. The purpose of this abstract is to report our preliminary findings.

Methods Used: Focus groups of HCP and parents who have used phone interpreters are being conducted (4 groups each, 6 participants/group). Sessions explore participants’ perceptions of self-efficacy, facilitators, and barriers about using phone interpreters, and are facilitated by bilingual moderators in Spanish or English. Each group discussion lasts up to 1 hour, and participants complete a demographics questionnaire. Written notes document all comments and behaviors of the group. Notes are transcribed, coded, and analyzed to generate common themes within and between groups.

Summary of Results: One HCP group has been completed to date. Six female residents from the first and second year classes participated, ranging in age 25-30 years. Multiple issues were discussed a total 53 times. The proportion of issues related to phones not being available to capture body language (0.21) was discussed significantly more often than interruptions from phone disconnections (0.11, p<0.05), lack of phone availability (0.08, p<0.01), and incorrect information (0.04, p<0.001). Techniques commonly used by participants to overcome phone difficulties included: speaking slowly in short sentences, debriefing the interpreter about the patient situation before the encounter started, and using Google Translator.

Conclusions: Clear communication is crucial in a primary care setting that serves an ethnically and linguistically diverse, low-income population. The purpose of this abstract is to report our preliminary findings.

254

EFFECT OF PULMONARY REHABILITATION ON SLEEP AS MEASURED BY ACTIGRAPHY

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Purpose of Study: Chronic Obstructive Pulmonary Disease (COPD) is now the third leading cause of mortality. Sleep has profound adverse effects on respiration and gas exchange in patients with COPD. Patients with COPD have a longer time to sleep onset (latency), frequent arousals, frequent sleep stage shifts, and reduced sleep efficiency. Pulmonary rehabilitation (PR) is the standard of care for patients suffering from COPD. It improves dyspnea, exercise tolerance, and quality of life. Remarkably, the effect of PR on sleep has not been studied.

Actigraphy is a non-invasive alternative to polysomnography to study sleep. It allows objective assessment of sleep for extended periods with minimal inconvenience, and has become a useful tool to study sleep for intervention studies. The purpose of this study was to see if PR leads to improved sleep in COPD patients as measured by actigraphy.

Methods Used: This study was a prospective, observational, within-subject design. After informed consent, patients who were selected for our nationally accredited rehabilitation program had actigraphy done for 4 nights before and then after completion of the program. A repeated measures paired t-test was used to assess for difference in sleep parameters before and after PR.
comparing 2010-2011 and an individual letter to be shared with the personal physician was sent to each participant each year. Interpretation of results was included with recommendations when needed. Blood pressure (BP), body mass index (BMI) was recorded during and after annual health fairs. Risk factors were defined as follows: BP > 120/80, BMI > 25, HbA1c > 5.7 (15% 5-year diabetes likelihood), cholesterol > 200, Triglycerides > 150.

Summary of Results: Program participants numbered 999 in 2010 and 953 in 2011, with 883 participating in both years. This analysis is limited to the latter cohort. The group of workers with moderate (2-3) risk factors stayed at 58% of the cohort, while the low-risk fraction increased from 12 to 17%. The high-risk group decreased from 29 to 24%. The cohort experienced a 50% drop in workers with hypertension but the respective roles of life-style change versus medication were not evaluated.

Conclusions: Substantial improvements in risk factors occurred over one year of comparison in a workplace health promotion program with over 90% participation, likely due to monetary incentives. Sustainability of the improvements and their possible impacts on morbidity remain to be learned.

| Numbers of Participants with Risk Factors (Range, 0 to 5) |
|-------------|-------------|-------------|-------------|-------------|-------------|
| 2010        | 0           | 1           | 2           | 3           | 4           | 5           |
| 2011        | 19          | 91          | 216         | 302         | 178         | 75          |

257  
MALARIA EPIDEMIOLOGY IN THE ILLEGAL MINING CAMPS OF MADRE DE DIOS, PERU
Manning P, Vo H, Vinetz J. University of California, San Diego, La Jolla, CA.

Purpose of Study: This project focuses on assessing the prevalence of asymptomatic and symptomatic parasitemia in the mining camp population of Delta Uno located in Madre de Dios, an endemic region with high focal transmission that has largely been unstudied. While the region of highest malaria incidence in Peru is in the northeastern state of Loreto, Plasmodium vivax is the sole cause of malaria in the mining camps in southeastern Peru. Despite having a lower rate of transmission in this area, infection continues. This may be due to peripheral blood smears under-detecting the true number of infected patients because blood smear alone misses a large number of sub-patient infections (malaria detectable only by PCR).

Methods Used: Systematic surveillance project questionnaires were issued to 106 study participants in this area from June-July 2012. Blood samples were collected from patients to assess for parasitemia using both microscopy and real-time PCR. Although microscopy is important for use in the field, it is not as sensitive for the detection of low parasitic levels in patients. In most epidemiological settings, PCR has been found to be more sensitive for detecting parasitemia than light microscopic examination of peripheral blood smears. Using real-time PCR assays to confirm the diagnoses of patients infected with malaria provides a better means to detect patients with asymptomatic parasitemia. This analysis allows for the true prevalence of parasitemia levels in our samples by taking into account asymptomatic cases to be positive by both light microscopy and qPCR analysis. Molecular marker analysis of parasite diversity is pending.

Summary of Results: Of the 106 patients enrolled, 17 samples were found to be positive by both light microscopy and qPCR analysis. Molecular marker analysis of parasite diversity is pending.

Conclusions: Not finding a discrepancy between blood smear and PCR could be explained in three ways: 1) asymptomatic patients declining to be sampled; 2) recent Ministry of Health mass treatment campaigns; or 3) insufficient sample size. This information will provide an increased understanding of the distribution and transmission of malaria and the other low transmission endemic regions, and will contribute to the formulation of more effective strategies to control malaria.

258
BARRIERS TO THE PREVENTION AND TREATMENT OF HEAT-RELATED ILLNESS IN ADULT OUTDOOR WORKERS: A QUALITATIVE ANALYSIS
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Purpose of Study: Heat-related illness (HRI) is an important cause of non-fatal illness and death in agricultural workers. Hired crop workers in the United States are largely seasonal, foreign-born, Spanish-speaking workers whose peak work activities occur during the warm summer months. We sought to identify beliefs and attitudes that may serve as barriers to HRI prevention and treatment in crop workers in the Central Washington region.

Methods Used: We conducted three semi-structured focus group interviews in a purposive convenience sample of 35 crop workers in Yakima Valley, WA, using participatory rural appraisal (PRA) techniques. Interviews were audio taped and transcribed in Spanish. Three researchers reviewed and coded transcripts and field notes while investigator triangulation was used to identify relevant themes and quotes.

Summary of Results: Four major themes regarding crop workers’ HRI-relevant beliefs and attitudes were identified: 1) crop workers subscribe to the humoral medical belief system to varying degrees, with some believing that cooling treatments should be avoided after heat exposure, and others encouraging the use of such treatments; 2) the desire to lose weight by increased sweating is reflected in behaviors of wearing neoprene braces and multiple layers of clothing in hot conditions; 3) highly caffeinated energy drinks, such as Monster and Red Bull, are utilized widely to increase work efficiency and maintain alertness; and 4) the location of water at work (e.g. next to restrooms) and whether water is fresh, but not chemically treated, are important considerations in deciding whether to drink the water provided at worksites.

Conclusions: We identified crop worker beliefs and attitudes about hydration, clothing use, and health that may serve as barriers to HRI prevention and treatment. These results should be incorporated into the development of culturally appropriate interventions aimed at reducing the risk of HRI and HRI-related deaths in agricultural workers.

259
EARLY INTRODUCTION OF PATIENT DOCTOR COMMUNICATION AND EMPATHY THROUGH STANDARDIZED PATIENT INTERVIEW DURING A SUMMER PREMED PROGRAM

Purpose of Study: Empathy and effective doctor patient communication are crucial for compliance to treatment and patient satisfaction. Standardized patient interviews have been used to teach medical students how to deal with a variety of patient scenarios. Studies to introduce standardized patient interviews to high school students interested in healthcare are lacking. The objective of this study was to examine the attitudes of premedical high school students towards their first standardized patient interview at a program during summer of 2010, 2011 and 2012.

Methods Used: Undergraduate students were trained to act as standardized patients. High school students were divided into 5 students per group. Each group spent 20 minutes interviewing each case, one with arthritis and the other one with eating disorder. Each interview was followed by 20 minutes of feedback by a School of Medicine faculty member and the standardized patient. Emphasis of feedback was placed on patient doctor communication and empathy rather than arriving at the correct diagnosis. A questionnaire was distributed at the end of each session to the high school students.

Summary of Results: Of 250 students, 226 (90%) completed the questionnaire. Upon review of the reflections, three positive themes emerged: 1) increased motivation to attend medical school, 2) a greater awareness of the empathy aspect in the doctor patient relationship, 3) improved communication and 4) greater preparedness for future. A few students commented that the session could be improved if they had some idea about the diagnosis beforehand.

Conclusions: In summary, the standardized patient interviews were very effective in promoting the interest of students towards healthcare and introducing them to the importance of effective doctor patient communication and empathy.

260
IMPLEMENTING PULSE OXIMETRY SCREENING FOR NEWBORNS IN CALIFORNIA’S CENTRAL VALLEY: APPLICATION OF SYSTEMS-BASED LEARNING AT A FRESNO COMMUNITY HOSPITAL
Farrell A, Scholefield J, Yang S, Francis P. University of California, San Francisco-Fresno Medical Education Program, Fresno, CA.

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Conclusions: The evidence for pulse oximetry screening was presented to CRMC Pediatric Advisory Board in August 2012. Board members were mostly in favor of this screening modality, but there were still questions regarding cost and training involved with implementing such a program. To answer these questions, we used evidence-based guidelines and resources provided in a free Toolkit by Children’s National Medical Center, which helped address the issues of training, protocol development and costs. Over the past two months, we have gained increased support from the hospital by sharing the Toolkit with multiple stakeholders at CRMC, including Nursing, OB-GYN, and Neonatology through departmental meetings and education forums, such as a Morbidity and Mortality Conference. As further support for this cause, the California State Legislature passed a bill to now make pulse oximetry newborn screening mandatory by December 2016. On September 15, 2012, Governor Brown signed this bill into law. Conclusions: Pulse oximetry in newborns is a cost-effective, non-invasive screening tool for congenital heart disease. As we proceed with implementation, we will use Quality Improvement methodology to guide us in evaluating and sharing the knowledge we obtain from our institution-wide changes. The challenges and lessons we have learned from this process will help us as we partner with others to implement pulse oximetry screening throughout birthing centers in the Central Valley.

PROJECT EXPORT: A NEEDS ASSESSMENT IDENTIFYING THE BARRIERS AND FACILITIES TO A GREATER PARTNERSHIP BETWEEN ACADEMIC AND COMMUNITY COLLABORATORS

Okoro A1,2, Rodriguez M2. 1University of California, Los Angeles, Los Angeles, CA and 2University of California, Los Angeles, Los Angeles, CA.

Purpose of Study: The DREW/UCLA Project EXPORT NIH Funded Center has the goal of reducing health disparities by making major advances in the implementation of clinical and translational research through the active engagement of community organizations and Department of Health Services. To move forward with this collaboration, an evaluation of the present state of the partnership is needed as well as an assessment of potential barriers in the past and improvements for the future through Project EXPORT.

Methods Used: A needs assessment was created addressing the main issues of past barriers to a stronger partnership between academic and community collaborators and approaches to better utilization of this partnership and CBPR. The assessment was administered as 30-45 minute interviews with faculty involved with community research on the academic side, and senior administrative staff on the community side.

Summary of Results: Both the community and academic participants identified three prominent themes which would be integral in promoting collaboration between Drew/UCLA, Department of Health Services, and community organizations. These include 1) engagement with the community in the initiation of research ideas 2) providing practical avenues for universities to implement interventions, and 3) leveling of power dynamics.

Results

<table>
<thead>
<tr>
<th>Theme</th>
<th>Academic Interviews</th>
<th>Community Interviews</th>
</tr>
</thead>
<tbody>
<tr>
<td>Engagement with community in initiation of research ideas</td>
<td>100% (7/7)</td>
<td>100% (4/4)</td>
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<td>Providing Practical Avenues for Universities to Implement Interventions</td>
<td>71.4% (5/7)</td>
<td>75% (3/4)</td>
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<tr>
<td>Leveling of power dynamics</td>
<td>71.4% (5/7)</td>
<td>50% (2/4)</td>
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<td>Resources and funding</td>
<td>28.6% (2/7)</td>
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<td>Sustainability</td>
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<td>0% (0/3)</td>
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<tr>
<td>Dissemination of results</td>
<td>28.6% (2/7)</td>
<td>50% (2/4)</td>
</tr>
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Infectious Diseases

Concurrent Session
3:30 PM
Friday, January 25, 2013

A HIGH-THROUGHPUT, MECHANISM-BASED WHOLE-CELL SCREEN USING ESCHERICHIA COLI TO IDENTIFY INHIBITORS OF THE SEC PATHWAY OF BACTERIAL PROTEIN EXPORT

Weller SM 1,2, Jones JC 1, Rosen H1,2, Crother GC 1,2. 1University of Washington School of Medicine, Seattle, WA and 2University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Due to the increasing prevalence of antimicrobial resistance among human pathogens, antibiotics that work by attacking novel microbial targets are needed. Our research targeted the Sec pathway, a bacterial membrane transport system that mediates export of proteins from the cytoplasm to the cell envelope. Recent studies suggest this pathway could be an excellent drug target in both Mycobacterium tuberculosis and gram-negative bacteria. We developed a novel screening assay and conducted a high-throughput screen for small molecules that inhibit this pathway.

Methods Used: We used a genetically engineered strain of Escherichia coli that produces a β-galactosidase (β-gal) protein with a lamB signal sequence, which is exported from the cytoplasm into the periplasm where it is inactive. The screen was conducted in 384 well plates using sodium azide, an inhibitor of the SecA ATPase, as a positive control, and LB growth media as a negative control. Experimental compounds were added to all other wells. Inhibition of the Sec pathway showed an increase in β-gal activity, corresponding to an increase in absorbance at 405nm. Median absolute deviation based Z-score values were assigned to each experimental well, which were then ranked as a strong, medium, or weak hit, or not a hit.


**Summary of Results:** We screened a total of 57,476 compounds in duplicate which included 7,721 known bioactives, 38,843 commercial compounds, and 10,912 natural product extracts. A total of 612 hits were detected in duplicate, which included 269 weak hits (Z-score >2.5 - <3), 176 medium hits (Z score >3 - <4), and 167 strong hits (Z score >4). Of the 335 non-natural product hits, 109 of those have been identified as medium or strong hits that are devoid of potential liability.

**Conclusions:** Though data analysis is ongoing, our screen has identified more hits than previous screens of the Seq pathway. Previous screens focused on a single target, such as SecA ATPase, while our cell-based assay focused on the entire Sec pathway. Follow-up studies will involve confirmation of inhibition of Sec-mediated protein translocation in the strong to medium hits and evaluation of their effects on microbial growth.

264

**WHOLE GENOME SEQUENCING OF 366 CLINICAL ESCHERICHIA COLI ISOLATES COMPARES GENOTYPE WITH CLINICAL PRESENTATION AND SHOWS THE MOLECULAR EPIDEMIOLOGY AMONG STRAINS**

Roach D, Salipante S, Kitzman J, Snyder M, Stackhouse B, Shendure J. University of Washington, Seattle, WA.

**Purpose of Study:** The Gram-negative bacteria Escherichia coli is the etiologic agent 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 better understand the interaction between different virulence factors and clinical presentation, as well as to reconstruct the epidemiology of the strains present in the greater Seattle region.

**Methods Used:** We performed whole genome sequencing on 366 clinical isolates, 274 of which came 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 obtained. Computational analyses were then performed to interrogate epidemiology and various associations of genotype and phenotype.

**Summary of Results:** This dataset enabled a large-scale analysis of the genetic diversity of pathogenic E. coli in the greater Seattle area, the elucidation of the pangenome within the region, unambiguous reconstruction of the molecular epidemiology among strains, and a series of association analyses to compare bacterial genotype with clinical phenotype.

**Conclusions:** There is considerable genetic diversity in the E. coli present within the Seattle region and some evidence for clinical tropisms for certain genotypes. Additionally, this study represents the largest full genome sequencing effort of a single bacterial species undertaken to date and provides a model for the integration of genomic science and clinical practice.

265

**THE EFFECTS OF BREASTMILK ON INFANT MICROBIOMES THROUGH PROMOTION VS INHIBITION OF BACTERIAL GROWTH**

Finn E, Gustafson C, Frank DN, Jamoff EN. University of Colorado, Denver, CO.

**Purpose of Study:** The development of an infant's intestinal microbiota is an important health implication. Breastfed infants have different intestinal commensal bacteria compared with non-breast fed infants. We investigated the functional ability of breast milk to promote and/or inhibit growth of intestinal bacteria.

**Methods Used:** We studied milk and stool from 17 healthy breastfed infants in Denver at birth, 1, 2, 3, and 6 months. Based on results of high-throughput ribosomal DNA sequencing to define the populations of colonizing bacteria over time, we found that Escherichia-Shigella genus (E. coli) was present in variable concentrations in different infants over time, with an infant's microbiome changing over 2 months. The bacteria growth assays were conducted in two environments, nutrient rich and nutrient poor. We used the nutrient rich environment (LB broth media) to examine the relative inhibition of bacterial growth and the nutrient poor environment (PBS) to examine the growth promoting effects of the various breast milks. Growth levels were measured using serial dilutions of milk/bacteria by quantitative drop plate method.

**Summary of Results:** In a nutrient rich environment, most but not all breast milks inhibited the growth of bacteria. However, in a nutrient poor environment, all breast milks enhanced growth of bacteria relative to the PBS control. In the nutrient poor environment, milk from mothers whose infants had high concentrations of E. coli had lower levels of bacterial growth compared to those with low levels of E. coli.

**Conclusions:** Breast milk affects the growth of bacteria. The balance between promotion and inhibition of growth needs to be further investigated in order to deduce if the effects of one outweigh the other. These results may have implications for understanding and potentially modifying the intestinal microbiome that has been recently linked to the development of obesity, type 1 diabetes, and other immune and developmental conditions.

266

**INFECTIOUS DISEASES CONSULTATION IN CANDIDEMIA IS ASSOCIATED WITH LOWER MORTALITY, HIGHER RATES OF BLOOD CULTURE CLEARANCE, AND GREATER ADHERENCE TO MANAGEMENT GUIDELINES**

Babazadeh N1, Shoeb M2, Jain R1, Xie H2, Fredricks D2, Pottinger PS1.
1University of Washington School of Medicine, Seattle, WA; 2Fred Hutchinson Cancer Research Center, Seattle, WA and 3University of California San Francisco, San Francisco, CA.

**Purpose of Study:** Candida is a common and lethal infection affecting critically ill and immunosuppressed inpatients. In 2009, the Infectious Diseases Society of America (IDSA) published updated guidelines on optimal management of candidemia. We evaluated whether management with infectious disease consultation (IDC) at our institution is associated with better patient outcomes and adherence to guidelines.

**Methods Used:** Medical records and laboratory data were collected on all candidemia cases at the University of Washington Medical Center (UWMC) from July 1, 2007 through July 31, 2012. IDC and non-IDC cases were compared regarding demographics, adherence to management guidelines, and patient outcomes. Statistical analyses included chi-square tests or Fisher’s exact tests for categorical variables, and t-tests for continuous variables. 30-day mortality was evaluated using a Cox proportional hazard model adjusted for APACHE-II scores. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated.

**Summary of Results:** 200 cases of inpatient candidemia were identified. Nineteen patients died prior to culture positivity. Of the remaining 181 cases in which candidemia management was assessed, 138 (76%) received an infectious disease consultation (IDC), APACHE-II severity-of-illness scores at the time of blood culture draw were similar among cases with IDCs versus those with no IDC (mean 16.2 vs. 15.6, p=0.67). IDC was associated with lower mortality when controlling for APACHE-II score (HR 0.5, 95% CI 0.27-0.92, p=0.026). IDC was also associated with a higher rate of documented blood culture clearance (91% vs. 77%, p=0.017). Finally, IDC was associated with greater adherence to management guidelines, including a higher rate of CVC removal (89% vs. 68%, p=0.003) and higher rate of antifungal therapy ≥2 weeks duration (83% vs. 54%, p=0.001).

**Conclusions:** Our results suggest that IDC may lead to lower mortality, higher rates of blood culture clearance, and greater adherence to management guidelines in candidemia. This study highlights the benefits of IDC and IDSA guidelines in candidemia management.

267

**IMPACT OF PRENATAL COUNSELING BY A PEDIATRICIAN ON POST-DELIVERY FOLLOW-UP AMONG HIV-EXPOSED INFANTS**

Ezeanolue EE1, Jackson D2, Ezeanolue KA1, 1University of Nevada School of Medicine, Las Vegas, NV; 2University of Nevada School of Medicine, Las Vegas, NV and 3University Medical Center of Southern Nevada, Las Vegas, NV.

**Purpose of Study:** To evaluate the impact of prenatal counseling by a pediatrician on post-delivery follow-up among HIV-exposed infants.

**Methods Used:** Medical records of HIV-infected women who delivered an infant during the period 2005-2006 were reviewed to identify follow up
visits to a pediatrician and completion of AZT prophylaxis by infants post-delivery. A community-based program was then implemented in January 2007 to integrate the care between obstetrical providers for HIV-infected women and pediatric providers for HIV-exposed neonates. Data was prospectively collected on all deliveries to HIV positive pregnant women from 2007 through 2011. The main outcome variables were: (1) follow-up visit to pediatrician (2) completion of six weeks Zidovudine prophylaxis (3) appropriate diagnostic tests (4) infant’s final HIV status.

**Summary of Results:** Twenty-five infants were born to HIV-infected pregnant women and HIV-exposed infants that includes early participation by a pediatrician leads to a significant reduction in loss to follow-up among HIV-exposed infants and improved their health outcome.

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**268 AGE DEPENDENT PROGRESSION OF MURINE CYTOMEGALOVIRUS INFECTION IN THE DEVELOPING MOUSE TEMPORAL BONE**

Taggart MG, Park AH, Wang Y. University of Utah School of Medicine, Salt Lake City, UT.

**Purpose of Study:** Cytomegalovirus (CMV), a member of the beta-herpesvirus family is the most common congenital infection in the U.S., with a prevalence of approximately 1%. Almost 400 children die each year from this disease, and up to 8,000 develop permanent disabilities. CMV is a major contributor to neonatal hearing loss, particularly Sensorineural Hearing Loss (SNHL). CMV is estimated to account for at least one-third of SNHL in young children. The focus of this study was to determine whether murine cytomegaloviruses (mCMV) infects the developing mouse temporal bone resulting in SNHL in an age dependent manner.

**Methods Used:** BALB/c mice underwent intracranial infection at postnatal day 3 (P3), 8 (P8) and 14 (P14) days with 200-400 pfu of mCMV; controls received saline. Hearing thresholds were assessed using DPOAE (distortion product otoacoustic emission) and ABR (auditory brainstem response) testing at 4 weeks of age and onward. Histologic changes in temporal bones were compared between infected and control mice at 1, 2, and 4 weeks postinoculation.

**Summary of Results:** All of the P3 infected mice (n=18), less than fifteen percent of the P8 and none of the P14 mice had significantly higher DPOAE and ABR thresholds at 4 weeks of age as compared to age-matched controls. Ten P3 mice (55%) had profound hearing loss (≥80 dB) at 4 weeks of age, while the other 8 P3 mice (45%) initially had moderate hearing loss (≥20 dB at 32 Hz), but progressed to profound hearing loss by 6-8 weeks. Asymmetric hearing loss was seen in ~40% of the P3 mice. For P8 infected mice, 1 out of 7 had ~30 dB threshold shift in one ear at 4 weeks of age, while the rest all have normal hearing thresholds. All P14 infected mice had normal hearing thresholds at 4 weeks of age. Temporal bone histology showed diffuse loss of outer hair cells for P3 infected mice starting at 7 days postinfection and progressed to severe OHC loss by 4 weeks postinfection. GFP-labeled virus was absent in the temporal bone at the 1st week in the P3 mice, but mostly devoid of GFP labeling by 2 weeks postinfection in P3 mice. None of the P14 infected mice showed evidence of temporal bone pathology.

**Conclusions:** Intracerebral injection of mCMV to developing mice causes age dependent mCMV-mediated hearing loss based on DPOAE, ABR and temporal bone histology.

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**269 VIRAL ETIOLOGY FOR ACUTE WHEEZING EPISODES IN CHILDREN WITH HIGH RISK FOR ASTHMA**

Friedman B,1,2, Thomas E,1 Tilley P,1 Goldmann H,1,2; BC Children Hospital University of British Columbia, Vancouver, BC, Canada; 1Child & Family Research Institute, Vancouver, BC; 2BC Children Hospital, Vancouver, BC, Canada.

**Purpose of Study:** To document the viral etiology of acute wheezing episodes in young children and to evaluate the viral-induced illness in children with or without predisposition for asthma.

**Methods Used:** Children 6 to 36 months of age who presented to Emergency Department (ED) at BC Children’s Hospital with episode of a viral illness and wheezing were prospectively enrolled following parental consent. We excluded children with underlying chronic diseases. Nasopharyngeal aspirates were tested using multiplex reverse transcription-PCR for the detection of 11 viral pathogens: influenza A/B, respiratory syncytial virus (RSV), parainfluenza, enteroviruses, human rhinovirus (HRV), human metapneumovirus (HMPV), human coronaviruses, adenoviruses and bocavirus. Asthma predisposition was calculated using a modified Asthma Predictive Index (API).

**Summary of Results:** We enrolled 116 children (mean age 15.5 months) from January 2011 to March 2012. 103 (89%) were included in data analysis. 68 (66%) were male, 16 (16%) were premature and 36 (35%) had at least 3 wheezing episodes in the prior year. Duration of symptoms was a mean of 3.5 days. All patients received beta-agonist inhalations, 71 (72%) received oral corticosteroids, 35 (34%) had chest x-ray done and 16 (16%) were hospitalized. HRV was detected in 39 (38%) samples, RSV in 44 (43%), Bocavirus in 13 (13%), Panainfluenza in 4 (4%), HMPV in 4 (4%), and Coronaviruses in 3 (3%). Co-infection with two or more pathogens was detected in 12 (11%) of the samples; half of them involved HRV. In 6 (6%) no viral pathogen was detected. No significant differences were found in clinical presentation between pathogens. Corticosteroids were more commonly used in children with HRV infection (86% vs. 63% in non HRV). Fifty seven (56%) of children had a positive API. There was a trend towards higher rate of HRV infection in children with a positive API (41% vs 34%, p=NS).

**Conclusions:** HRV infection is a major cause of wheezing in young healthy children and account for almost 40% of the patients seen in the ED for acute episode. Further research should determine if HRV has a role in predicting asthma.

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**270 GERMINAL CENTER T FOLLICULAR HELPER CELLS (GC TFH) FROM NAIVE HOSTS ARE HIGHLY PERMISSIVE TO HIV-1 EX VIVO**

Kohler S, Folkvord J, Connick E. University of Colorado Denver, Denver, CO.

**Purpose of Study:** TFH are 40 times more likely than other CD4+ T cells to be productively infected by R5 HIV in vivo. GC TFH, a subset of highly activated TFH, are found in germinal centers of secondary lymphoid tissue. It is unknown whether GC TFH are more permissive to HIV than other CD4+ T cells, or more susceptible to HIV that uses the CCR5 receptor (R5 HIV) than HIV that uses the CXCR4 receptor (X4 HIV), possibly underlying the preference for R5 infection prior to AIDS.

**Methods Used:** Tonsils from 9 children at low risk for HIV were disaggregated and 5-10’6 cells were infected by spinoculation with R5 or X4 HIV GFP reporter viruses or mock-infected, and cultured. After 2 days, cells were stained for flow cytometry with antibodies to CD3, CD4, CD8, CXCR5, PD-1 and viability dye. Data were analyzed using FlowJo. Populations were gated on CD3+CD8- cells due to down regulation of CD4 by productive HIV infection. Non-parametric T-tests were used for statistical analysis.

**Summary of Results:** In mock-infected wells, CXCR5+ cells constituted a median of 50% (range, 38% to 76%), GC TFH (CXCR5hiPD-1hi) a median of 19% (range, 12% to 26%), and non-GC TFH (CXCR5medPD-1med) a median of 26% (range, 21% to 42%) of CD3+CD8- cells. Compared to mock-infected wells, percentages of GC TFH were lower (median 15%, p=0.08) in R5-infected wells, and percentages of CXCR5+, GC TFH, and non-GC TFH were lower (medians, 43%, p=0.01; 9%, p=0.0005; and 22%, p=0.05; respectively) in X4-infected wells. Percentages of GFP+ cells were higher in X4-infected wells (median, 1.2%) compared to R5-infected wells (median, 0.4%; p=0.04). In X4-infected wells, CXCR5+ cells were a median of 13 (range, 5 to 20; p=0.004) times more likely to be GFP+ compared to CXCR5- cells, and GC TFH were a median of 3 (range, 3 to 6; p=0.004) times more likely to be GFP+ than non-GC TFH. Similarly, in R5-infected wells, CXCR5+ cells were a median of 8 (range 3 to 17; p=0.004) times more likely to be GFP+ than CXCR5- cells, and GC TFH were a median of 3 (range, 2 to 6; p=0.004) times more likely to be GFP+ than non-GC TFH.

**Conclusions:** TFH and particularly GC TFH are highly permissive to both HIV-1 types as determined ex vivo.
DETERMINANTS OF ROTAVIRUS-SPECIFIC ANTIBODY RESPONSES TO ORAL VACCINE IN SERUM IN INFANTS

Habermehl G1, Rahkola IT1, Frank DN2, Janoff EP1, Brennan M1, Slattery L1, Esplin E1, Enns GM1, Hudgins L1, Manning M1,2.

Purpose of Study: Rotavirus (RV) is the leading cause of infant death from diarrhea worldwide. Protection against RV by the live oral vaccine varies by country. The determinants of immunogenicity (as a proxy for protection) by RV vaccine are largely unknown. The purpose of these studies was to correlate RV-specific IgG and IgA responses to live-attenuated oral vaccine in infant sera, with RV-Specific (RV-S) IgA in breastmilk, and gut microbiome diversity during the first year of life in both vaccinated and unvaccinated groups.

Methods Used: 11 infants received RV-S IgA and IgG in infant serum at 2, 4, and 6 months. 2 infants were unvaccinated. We measured RV-S IgA and IgG in infant serum at 0, 1, 2, 6 and 12 months and in maternal breast milk at 2 months by ELISA. We coated microtiter plates (MaxiSorp; Nunc) with 2.95 lg/ml virus, added dilutions of sera (1:4000-1:8000). We detected RV-S antibody with Biotin-labeled affinity-purified goat anti-human IgG or IgA (Jackson Immuno), and Streptavidin-HRP (Invitrogen)/TMB (BD) developer. Values were derived from standard curves. We compared values within groups over time by paired t-test and between groups by unpaired t-test.

Summary of Results: RV-S IgA and IgG were detected in infant sera by 12 months in all vaccinated infants and 1/2 unvaccinated infants albeit at lower levels. Maternal RV-S IgG reaches a nadir in infant sera at 6 months. RV-S IgGwa was detected in most vaccinated infants by 6 months whereas RV-S IgG was not detected until 12 months, when levels of RV-S IgG exceeded those of IgA. The avidity of IgG was higher than that of IgA at 12 months. All mothers had similar levels of RV-S IgA in breast milk at 2 months. These levels did not correlate with the magnitude of infant vaccine responses. Preliminary data suggests the gut microbiome diversity at 2 months correlates with RV-S serum IgA response to vaccine at 12 months.

Conclusions: As maternal RV-S IgG declines over time, RV-S IgA precedes RV-S IgG in infant sera, each requiring ≥2 doses. RV-S IgA likely offers protection at the site of infection in the gut compared with IgG. Further investigation is needed regarding the relationship of microbiome diversity and vaccine response and the underlying mechanisms.

Morphogenesis and Malformations
Concurrent Session
3:30 PM
Friday, January 25, 2013

ARTHROГYPOSIS, RENAL DYSFUNCTION AND CHOLESTASIS (ARC) SYNDROME: A NEW PATIENT CASE REPORT
Brennan M1, Slattery L1, Esplin E1, Enns GM1, Hudgins L1, Manning M1,2.

Case Report: ARC syndrome is a rare autosomal recessive disorder characterized by arthrogryposis, renal dysfunction and Cholestasis. In addition to these traditional symptoms, patients can have ear, structural cardiac, hematologic, endocrine, immune and skin anomalies. Molecular defects in the VPS33B (vacuolar protein sorting 33 homologue B) and VIPAR (VPS33B-interacting protein, apical basolateral polarity regulator) genes account for most cases. Disease causing mutations in these genes underscore the importance of vesicular membrane trafficking. We report a neonate identified post-natally to have bilateral hearing loss; flexion contractures of the hips, knees and ankles; ichthyosis and mild facial dysmorphism. Newborn screening identified congenital hypothyroidism. Comparative genomic hybridization and metabolic workup were normal. MRI showed micrognathia and a small nose. There was little spontaneous movement of the face or body. The infant had failure to thrive. MRI of the spine showed immature myelination. EMG/NCS showed low motor amplitudes and evidence of anterior horn cell lesions. At 7 weeks, in preparation for gastrostomy tube placement, an abdominal US revealed a left adrenal mass. An MRI study diagnosed neuroblastoma. Catecholamine levels were slightly elevated. At 2 months of age, the baby has abnormal persistent vertical eye movements and extreme muscular hypotonia however elbows can be extended with firm consistent pressure. Neuroblastoma presents with opsoclonus, myoclonus and paralysis of limbs caused by a paraneoplastic autoimmune process in 1/3 of patients. This baby’s clinical features suggest that a paraneoplastic process led to an autoimmune encephalomyelitis of prenatal onset causing a secondary fetal akinesia sequence. The search for paraneoplastic antibodies has been negative in our patient. Neuroblastoma and arthrogryposis have rarely been reported together. Such an association may be under-reported because neuroblastomas are rare and only a small minority of them cause paraneoplastic effects, they can undergo spontaneous regression and may never be diagnosed and infants with severe arthrogryposis may die before their tumors are diagnosed. We suggest that neuroblastoma may be an uncommon and under-recognized cause of severe arthrogryposis.
275

17p11.3 duplication revisited: delineation of the core and variant phenotypes
Curry CJ1, Dobyns WB2,1. UCSF/Fresno, Fresno, CA and 2University of Washington, Seattle, WA.

Purpose of Study: 17p11.3 is a gene rich area associated with the well-known Miller-Dieker deletion syndrome. A recently described duplication syndrome in this region has been associated with intellectual impairment, autism and occasional brain MRI abnormalities.

Methods Used: We report 33 additional patients from 21 families to further delineate the clinical, neurological, behavioral and MRI findings in this duplication syndrome spanning YWHAE through LIS1.

Results: This is a highly diverse phenotype with inter- and intramural variability, especially in cognitive development. The most specific phenotype occurred in individuals with relatively large duplications including both sentinel genes. These patients had a relatively distinct facial phenotype and frequent structural brain abnormalities involving the corpus callosum, cerebellar vermis and cranial base. Autistic spectrum disorders were seen in a third of families, most commonly in those with duplications of YWHAE or flanking genes such as CRK. A typical neurobehavioral phenotype was seen most often in those with the larger deletions. We did not confirm the association of early overgrowth with involvement of YWHAE and CRK, or growth failure with duplications involving LIS1. Overweight was common in older individuals. Three unusual variant phenotypes were seen: Cleft lip/palate, split hand/foot with long bone deficiency (SHFLD) and a connective tissue phenotype similar to Marfan syndrome. The cleft patients’ duplications appear to disrupt ABR. The SHFLD phenotype was associated with a duplication of BHLHA9, as noted in two other reports. The connective tissue phenotype did not have an attractive candidate gene.

Conclusions: Our experience with this large cohort expands knowledge of this diverse duplication syndrome.

276

Two siblings with adducted thumb clubfoot syndrome (ATCS), a rare cause of distal arthrogryposis
Li B, Slavotinek A. UCSF, San Francisco, CA.

Purpose of Study: Reaching an underlying syndrome diagnosis in children with distal arthrogryposis can be challenging because of phenotypic heterogeneity.

Methods Used: We present two full siblings, a 7 year old female and her newborn brother, who had adducted thumbs, talipes equinovarus, congenital hypotonia and dysmorphic features that enabled a clinical diagnosis of adducted thumb clubfoot syndrome (ATCS).

Summary of Results: Dysmorphic features in both sibs included brachycephaly, downsloping palpebral fissures, hypertelorism and blue sclerae. Distal muscle bulk was reduced and both sibs had soft and doughy skin with long and tapering fingers. The girl had glaucoma from age 3 years. An EMG showed lipid and glycogen accumulation with mitochondrial hypertrophy. Both children were found to have elevated creatine kinase (CK) levels of 698 and 1838 U/L (ref 39-189 U/L), a previously unreported finding in ATCS. Molecular testing on the girl showed a homozygous c.977_980dupCCTG (p.W327Cfs*28) mutation in the CHST14 gene; her mother was heterozygous for this change. A sample from the father was unavailable.

Conclusions: ATCS is caused by mutations in the carbohydrate sulfotransferase 14 (CHST14) gene, which encodes dermatan-4-O-sulfotransferase 1 (CHST14 or D4ST1), an enzyme involved in glycosaminoglycan synthesis. Lack of CHST14 leads to replacement of dermatan sulfate by chondroitin sulfate in decorin and results in abnormal regulation of collagen fibril assembly. Loss of function mutations in CHST14 have been described in ATCS, Ehlers-Danlos syndrome (EDS), hyperplastic hydrometra with hypothyroidism, and EDS, Kosho type. The term dermatan sulfate-deficient adducted thumb clubfoot syndrome has been proposed to describe these phenotypes. Characteristic features in 22 patients have included large fontanelles, hypertelorism, short and downsloping palpebral fissures, blue sclerae, low-set and rotated ears, a thin upper lip with a small mouth and microretrognathia. Multiple congenital contractures, with adduction-flexion contractures of the thumbs and talipes equinovarus, are defining findings. Despite gross motor delays, cognition is usually normal. We conclude that ATCS is a rare cause of congenital arthrogryposis and that a raised CK measurement can be present in children with this diagnosis.

277

Understanding growth failure in Costello syndrome: increased energy intake and resting energy expenditure
Leoni C1,2, Casey I1, Di Lieto A1,2, De Santis S1, Giorgio D1, Rossovecchi A2, Massolo G2, Martini L2, La Torraca P1, Dotto F1, Zampino G1.1. University of Utah, Salt Lake City, UT and 2Politecnico ’40 Gemelli’, Rome, Italy and 3Bambino Gesù Children’s Hospital, Rome, Italy.

Purpose of Study: Costello syndrome (CS) is a rare multisystemic disorder caused by germline mutation in proto-oncogene HRAS. Characteristic findings include distinctive facial features, severe failure to thrive (FTT), feeding difficulties, cardiac problems, intellectual disability, papillomata and predisposition to malignancies. To understand the potential mechanisms for the FTT we studied a cohort of CS patients with biochemical/microbiological analysis and indirect calorimetry (IC).

Methods Used: We enrolled 11 CS patients with clinical and molecular diagnosis who underwent IC and evaluation of growth, biochemical/microbiological parameters, and energy intake (EI) based on 6-day diet record. The data were compared with those of a control group matched by sex and age.

Summary of Results: All patients had history of FTT associated with swallowing difficulties in 73% and weak suck in 82%. Mean weight was -2.8 SD and mean height -3.3 SD. Biochemical/microbiological examinations excluded nutritional deficits and gastrointestinal diseases and showed mild hypoglycemia, and hypercholesterolemia; IGF1 was lower than normal in 82%, and 3 patients had growth hormone deficiency. The mean resting energy expenditure (REE) estimated by IC in CS patients was 17.4% increased in comparison to theoretical REE according to Schofield formula and 14.9% to WHO formula. In contrast in the literature and our controls, the gap between estimated and theoretical REE was 3%. The total EI was 83.1% greater than expected (estimated by LARN guidelines), and higher than estimated REE by IC.

Conclusions: The use of IC for clinical management of CS is useful in providing the correct daily caloric amount because we show an increased REE in our cohort. Moreover several studies show the involvement of RAS/MAPK pathway modulating the hypothalamic traduction network of leptin, an important hormone that regulates food intake and energy balance. Elucidating RAS/MAPK action in linking leptin signaling may provide novel answers for understanding growth failure in CS.

278

Handedness in RASopathies
Alvord B1, Rauen K2, Stevens A1, Hanson H1, Stevenson D1.1. University of Utah, SLC, UT and 2University of California San Francisco, San Francisco, CA.

Purpose of Study: RASopathies are a group of genetic disorders which often have language, motor, and neurocognitive delays. Other syndromes associated with language and cognitive delays have shown differences in handedness. Our objective was to determine non-right-handedness among patients with RASopathies.

Methods Used: Individuals and/or parents of individuals with neurofibromatosis type 1 (NF1), cardiofaciocutaneous (CFC) syndrome, Costello syndrome, and Noonan syndrome were asked which hand is dominant in the process of doing tasks. Grip strength using handgrip dynamometers were performed on both hands. Data were compiled and compared to published data from the general population (11.5% non-right-handed).

Summary of Results: A total of 300 individuals with a RASopathy had data on handedness (mean age 13.6 yrs.). [NF1 (N=163), CFC (N=29), Costello
CRITICAL IN EARLY LIFE

HHEME OXYGENASE ACTIVITY AND HHEME BINDING ARE CRITICAL IN EARLY LIFE

Summary of Results:

Methods Used:

Loma Linda, CA.

Coggins AS, Pira CU, Feenstra JM, Oberg KC. Loma Linda University, Loma Linda, CA. NEONATOLOGY: THE ROLE OF TFAP2C, A DOWNSTREAM INTERMEDIATE

Coggins AS, Pira CU, Feenstra JM, Oberg KC. Loma Linda University, Loma Linda, CA.

Purpose of Study: The process of proper limb development depends on the interaction of multiple factors. Fibroblast growth factors (FGFs) are secreted from the apical ectodermal ridge (AER) and are critical to limb outgrowth. Sonic hedgehog (SHH) is a patterning molecule secreted from the zone of polarizing activity (ZPA) in the distal posterior limb bud mesoderm and is responsible for ularization of the developing forelimb. Maintenance of SHH expression during limb development is dependent on FGF expression. Furthermore, induction of SHH by FGF is required for limb regeneration, yet the mechanism by which FGF regulates SHH expression has not been determined. Previous experiments using gene array technology have identified 300+ genes up-regulated in response to FGF application. Among the genes up-regulated by FGF was Transcription Factor Activating Protein-2 gamma (TFAP2C). TFAP2C was up-regulated within 3 hours of FGF application, which led us to hypothesize that TFAP2C was a downstream intermediate in the FGF to SHH regulation pathway.

Methods Used: We analyzed the effects of ectopic TFAP2C expression on SHH induction in a region of the posterior limb bud known to be inducible for SHH by FGF. A TFAP2C expression plasmid was injected into Hamburger/ Hamilton stage 22-23 chick embryos which were harvested at 24 hrs. In situ hybridizations for TFAP2C and SHH were performed.

Summary of Results: We confirmed ectopic TFAP2C expression following injection of the beta-actin promoter-driven construct. However, no SHH expression was seen in 18 out of 18 embryos whether driven by CMV or beta-actin promoters.

Conclusions: We conclude that TFAP2C expression alone in the SHH inducible domain is not sufficient to up-regulate SHH expression. Chromodomain Helicase DNA Binding Protein 7 (CHD7) is a direct target of FGF and another factor identified by gene array analysis. CHD7 regulates chromatin accessibility. It may be that TFAP2C on its own cannot induce SHH expression, but when combined with CHD7, it will be able to up-regulate SHH. Further work is being done to elucidate the role of both of these proteins in the FGF to SHH pathway.

HEME OXYGENASE ACTIVITY AND HHEME BINDING ARE CRITICAL IN EARLY LIFE

Ang J, Schulz S, Wong RJ, Severson DK. Stanford University School of Medicine, Stanford, CA and Michigan State University, East Lansing, MI.

Purpose of Study: Neonatal diseases, e.g. hemolytic anemias, ischemia/reperfusion injury, and inflammation, can result in severe hemolysis and lead to the accumulation of pro-oxidative free heme (FH). Heme oxygenase (HO) is primarily responsible for detoxifying FH. Since neurons have an increased RBC turnover rate, a functional HO system is critical for the neonate and could be exhausted in these conditions. Thus, we studied the protective effects of HO in a model of heme overload.

Methods Used: For in vitro studies, NIH3T3 cells, with the full-length HO-1 promoter fused to the reporter gene luciferase (HO-1-luc), were incubated with vehicle or 10, 30, or 60µM FH or methemalbumin (MHA). HO-1 promoter activity was assessed 3, 6, and 24 h after treatment by in vivo bio-luminescence imaging (BLI). Cell survival was indexed by LDH and viability assays. For in vivo studies, 1-wk-old and adult (~5-wk-old) FVB mice were injected IP with 60µM FH/kg BW. After 24 h, AST levels were determined. Livers were harvested and HO activity and lipid peroxidation (LP) measured.

Summary of Results: In HO-1-luc cells, HO-1 promoter activity peaked 6h after incubation with 30µM FH (1.6-fold) or 60µM MHA (2.1-fold) compared to baseline. 24 h after exposure to 60µM FH, a cytotoxicity of 48% and an 80% decrease in viability were found; whereas, no cytotoxicity or decreases in viability were seen after exposure to 60µM MHA. In 1-wk-old pups given 60µM FH/kg, we found a significant 3.9-fold increase in HO activity and no changes in LP or AST levels. In adult mice, HO activity similarly increased (3.6-fold), but, the absolute level of this increase was <50% of 1-wk-old levels (107-382 vs. 213-823 pmol CO/h/mg fresh weight, respectively), and LP and AST levels significantly increased 11- and 1.5-fold, respectively.

Conclusions: FH is highly toxic, but toxicity is abolished when bound to albumin (MHA). In contrast to adults, newborns appear to be protected from the pro-oxidative effects of FH. This protection may be mediated by a higher HO activity at birth and after FH induction. We conclude that HO activity and heme binding are critical in early life; and, if either are deficient, can lead to the development of stress-related diseases, and may even explain the observed association between hemolytic jaundice and neurologic injury.

SENSITIVITY OF THE MESENTERIC ARTERY OF FETAL AND ADULT SHEEP TO NITRIC OXIDE AND LOW MOLECULAR WEIGHT NITROSOTHIOLS

Davitt E1, Liu T1, Wilson S2, Blood A1, 2Loma Linda University, Loma Linda, CA and 2Loma Linda University, Loma Linda, CA.

Purpose of Study: Although regulating enterocritility is thought to be associated with a dysregulation of gastrointestinal blood flow, relatively little is known about the regulation of arterial tone in the vasculature of the small intestine and how it varies with development. We therefore tested the hypothesis that the sensitivity of the isolated near term fetal sheep mesenteric artery to nitric oxide and low molecular weight nitrosothiols (SNOs) would differ significantly from that of the adult mesenteric and femoral artery.

Methods Used: Adult (n=5) and fetal (n=5; ~140 days gestation (term 147 days)) mesenteric arteries and adult femoral arteries (n=5) were harvested from sheep, demed of endothelium, and mounted in wire myography baths. Each vessel was exposed to 125 nM K+ to achieve maximal contraction (Kmax). Once contracted, vessels were exposed to increasing concentrations of nitric oxide (NO), S-nitroso-L-cysteine (L-CysNO), S-nitroso-D-cysteine (D-CysNO), and S-nitroso-glutathione (GSNO). Resulting dose response curves were analyzed to determine the maximal dilation and EC50 for each compound.

Summary of Results: The EC50 of adult mesenteric arteries was similar to that of femoral arteries and fetal mesenteric arteries (range of 0.44 to 6.9 µM). However, maximal dilation of fetal mesenteric arteries (~105 ± 6% of Kmax) was significantly greater than that of adult mesenteric arteries (~44 ± 3% of Kmax). There was no difference between EC50s of adult mesenteric and femoral arteries or fetal femoral arteries for small molecular weight SNOs (range of 0.12 to 3.0 µM). However, the maximal dilation of the fetal mesenteric arteries to all SNOs was significantly greater than that of adult mesenteric arteries.

Conclusions: We conclude that both NO and small molecular weight SNOs are more powerful vasodilators in the near-term fetal mesenteric artery than in the adult. These results suggest there are significant differences between vasodilatory signaling pathways in the mesenteric arteries of adults and near-term fetuses.
LIPOPOLYSACCHARIDE EXPOSURE IN EARLY PREGNANCY IS ASSOCIATED WITH LATE PREGNANCY COMPLICATIONS

Ozen M1, Rivera M2, Saravanapandian V1, Palmer TD1. 1Stanford University, Palo Alto, CA and 2Stanford University, Palo Alto, CA.

Purpose of Study: Premature births are an increasing cause of mortality and morbidity globally. Perinatal infection and inflammation are major risk factors for premature delivery. We have previously shown that exposure to a low dose of Escherichia Coli lipopolysaccharide (LPS) in early pregnancy (<E12.5) causes innate immune system activation and acute miscarriage in a mouse model of gestational inflammation. In this study, our objective was to determine if an immune event in early gestation is associated with late pregnancy complications and placental injury.

Methods Used: Pregnant C57BL/6 mice at E12.5 were given either saline (controls) or 60 μg of LPS/kg body weight by intraperitoneal (IP) injections. At E13.5, 15.5, and 18.5, mice were sacrificed, the number of surviving pups recorded, and placentas collected for histopathological examination by H&E staining. Two-tailed student t-test and 2-way ANOVA were used to compare the groups.

Summary of Results: The low dose of LPS used did not induce sickness behaviors in pregnant animals but did reduce the number of surviving fetuses at E13.5. At E13.5 there was no additional fetal loss but the number of viable fetuses per conceptus significantly decreased at E18.5 compared to E13.5, suggesting a second wave of fetal attrition. Saline injections had no significant effect at any gestational age. At E18.5, there was a significant correlation between visible placental pathology and pup loss, with small or resorbing placentas correlating with non-viable pups.

Conclusions: Our preliminary results show that low dose LPS in early gestation causes acute fetal demise and is associated with adverse changes in the placenta that correlate with a second wave of fetal loss in late gestation. We speculate that this model of placental injury mimics late pregnancy complications and premature birth in human pregnancies. Therefore, identification and treatment of early gestational maternal infection may prevent pregnancy complications and increase fetal survival.

USE OF ULTRASOUND IN THE DIAGNOSIS OF SPONTANEOUS INTESTINAL PERFORATION IN PRETERM INFANTS WITH BIRTH WEIGHT ≤ 1250 GRAMS

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Purpose of Study: Spontaneous intestinal perforation (SIP) is often diagnosed after a period of gasless abdomen in the very low birth weight infant. Abdominal x-ray is currently the only reliable radiographic method to diagnose intestinal perforation. The purpose of this study was to evaluate the usefulness of abdominal ultrasound in preterm infants with gasless abdomen radiographically who were suspected to have SIP.

Methods Used: Retrospective analysis of prospectively collected data of preterm infants with a birth weight (BW) ≤ 1250 g admitted to LAC+USC Medical Center neonatal intensive care unit, presenting with a gasless abdomen radiographically where abdominal ultrasound was done for suspected SIP. Patients with congenital anomalies or those to whom only palliative treatment was provided were excluded.

Summary of Results: There were 57 preterm infants with BW ≤ 1250 g who were included in the study. 11 infants [BW = 630 ± 145 g, gestational age (GA) = 24.4 ± 1.3 weeks, Mean ± SD] had a confirmed diagnosis of SIP while 46 infants [BW = 646 ± 159 g, GA = 24.9 ± 1.3 weeks] had no evidence of intestinal perforation. There was no significant difference in the BW or GA between the two groups. Diagnosis was either confirmed by the presence of meconium with abdominal paracentesis or by localized peritonitis without evidence of necrotizing enterocolitis on surgical exploration. Abdominal ultrasound (US) was performed in 91% of patients with SIP and 100% of the non-perforated patients. Free fluid and echogenic free fluid was present in 90% and 80% of patients with SIP and 47% and 11% of non-perforated patients (p value = 0.03 and p = 0.0001 respectively). Presence of free fluid on US had a sensitivity of 90% and negative predictive value of 96%, while presence of echogenic free fluid on US had a specificity of 89% and negative predictive value of 95%.

Conclusions: These preliminary data suggest that abdominal ultrasound is a useful imaging modality for the diagnosis of SIP in preterm infants with BW ≤ 1250 g presenting with gasless abdomen.

DOES ESP SECRETING STAPHYLOCOCCUS EPIDERMIDIS INHIBIT COLONIZATION WITH STAPHYLOCOCCUS AUREUS IN THE HOSPITALIZED NEWBORN INFANT?

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Purpose of Study: A subtype of Staphylococcus epidermidis (S. esp) that produces a protease called esp has the ability to inhibit Staphylococcus aureus (S. aureus) nasal colonization and destroy S. aureus biofilms. This particular S. esp is effective in adults against both methicillin-sensitive and methicillin-resistant S. aureus. Whether newborn infants become colonized with this S. esp subtype and whether this protease has a protective effect in neonates is currently unknown.

Methods Used: Nasal swabs of 90 newborn infants in the NICU (mean gestational age 33 weeks, range 24-40 weeks) were obtained within 12-24 hours of admission and within 24 hours of discharge. Samples that were positive for S. aureus were tested for methicillin resistance. Samples that were positive for S. esp were tested for presence of the esp gene.

Summary of Results: None of the admission nasal swabs grew S. aureus. Of 80 admission swabs obtained 12-24 hours following birth, 2 (2.5%) grew S. esp. Of the 10 swabs obtained 12-24 hours after admission from a referring hospital, 5 (50%) grew S. esp (Relative risk 20 (4.5-90), p = 0.0001). Of the 74 discharge swabs processed to date, 61 infants were colonized with S. esp (82.4%), 14 infants were colonized with methicillin-sensitive S. aureus (19%) and one infant was colonized with methicillin-resistant S. aureus (1.4%). There were no significant correlations between gestational age, antibiotic days, intubation days, or nasogastric/orogastric tube days and colonization with S. aureus. At discharge, among the 61 infants positive for S. esp, 6 (9.8%) were co-colonized with S. aureus, while among the 13 infants negative for S. esp, 9 (69%) were colonized with S. aureus (Relative risk 7.0 (30.0-16), p = 0.0001). The analysis for esp producing S. esp is ongoing.

Conclusions: The rates of NICU infants more commonly become colonized with S. esp than S. aureus. Although no cause and effect relationship can be concluded from these data, this cohort study supports the hypothesis that colonization with some strains of S. esp is protective against colonization with S. aureus.
as outcomes based on insurance type and age. Data management, Tiests, and the Fine and Gray competing risk method were performed using STATA. Summary of Results: 62-68-year-old patients with Medicare were delayed an additional 126 days from dialysis to listing compared to 62-68-year-old patients with private insurance (P=0.001). Furthermore, the Medicare group received fewer transplants (SHR, 1.183; 95% CI, 1.11-1.27; P=0.001) than the group with private insurance. While the Medicare group received fewer LDK than the privately insured group (SHR, 1.77; 95% CI, 1.49-2.10; P=0.001), there was no significant difference in the number of DDK. Within the Medicare group, 62-64-year-old patients were delayed by 67 days vs. 66-68-year-old patients (P=0.001). There was no difference in transplant rate within the Medicare group.

Conclusions: Privately insured patients have increased access to transplantation. While the rate of DDK transplantations are similar regardless of insurance type, Medicare patients take longer to list and receive fewer LDK than patients with private insurance.

286

INFLUENCE OF RACE/ETHNICITY ON INFLAMMATION, METABOLIC SYNDROME AND KIDNEY FUNCTION
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Purpose of Study: Studies show that African Americans (AA) have a high prevalence of the metabolic syndrome (MetS; Common features are central (abdominal) obesity, insulin resistance, hypertension, and dyslipidemia, namely high triglycerides and low high-density lipoprotein cholesterol) and higher rates of chronic kidney disease (CKD) than whites. Since either chronic inflammation or MetS has been shown to be associated with renal impairment, we hypothesized that elevated level of inflammation, measured by C-reactive protein (CRP) in AA may contribute to the disparity in CKD.

Methods Used: We examined levels of CRP, serum creatinine and components of the MetS in whites and AA from the National Health and Nutrition Examination Surveys, 1999-2008. We analyzed data for waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting plasma glucose (FPG), triglyceride (TG) and high density lipoprotein cholesterol (HDL-C) from 22,998 adults aged ≥20 years who had three or more components of the MetS. CRP was categorized using cut-point ≥0.3mg/dl. Serum creatinine was used as an indicator of kidney function. We performed logistic and linear regression to test whether ethnicity modifies the level of CRP and its relationship with the MetS and kidney function, adjusting for age and sex.

Summary of Results: Compared to whites, CRP, WC, SBP, DBP, FPG, and serum creatinine were significantly higher in AA with MetS, (p<0.05-p<0.001). The adjusted logistic regression model showed a significant association between the MetS and CRP (OR, 2.18; 95%CI, 2.04-2.33; p=0.001) and the association was stronger among AA (OR, 1.51, 95%CI, 1.40-1.63; p=0.001) compared to whites. Also, the linear regression model showed a significant association between CRP and serum creatinine (p<0.05), which was stronger in AA compared to whites (p<0.001).

Conclusions: We conclude that differences in the level of inflammation, measured by CRP may contribute to the disparity in renal function in AA with the MetS compared to whites.

GRANT SUPPORT: NIH/NIMHD Accelerating Excellence in Translational Science U54M007598 (formerly U54RR026138) at Charles R. Drew University of Medicine at Science.

287

COMPLICATIONS AND RISK FOR READMISSION AMONG PATIENTS HOSPITALIZED WITH CHRONIC KIDNEY DISEASE
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Purpose of Study: Among patients hospitalized with CKD the relationship between various complications and in-hospital death is known. However, the relationship with short-term outcomes such as one-month hospital readmission is less certain. The primary objective was to describe complications and risk for adverse outcomes among patients hospitalized with CKD.

Methods Used: Complications of patients with CKD hospitalized in Washington State between April of 2006 and December of 2008 (n=26,267) were described. Odds ratios for study outcomes were computed using binary logistic regression models controlling for age, sex, payer, comorbidities, previous hospitalization, length of stay and reason for hospitalization.

Summary of Results: Compared to patients without the complication, sepsis (OR=4.14; 95%CI=3.54-5.80; p<0.001), heart failure (OR=1.30; 95% CI=1.13-1.49; p=0.001), acidosis (OR=3.64; 95%CI=2.93-4.93; p=0.001) and hyperkalemia (OR=1.64; 95%CI=1.34-2.00; p<0.001) were associated with increased fully adjusted risk for death during first hospitalization. A number of complications were associated with increased risk for lengths of hospital stays greater than 3 days. Compared to patients without the complication, patients with skin ulcers (OR=1.38; 95%CI=1.18-1.62; p=0.001), acidosis (OR=1.25; 95%CI=1.06-1.47; p=0.01), heart failure (OR=1.19; 95%CI=1.10-1.28; p<0.001) and anemia (OR=1.10; 95%CI=1.02-1.19; p=0.01) were at fully adjusted increased risk of readmission within one month following discharge.

Conclusions: A number of complications during hospitalization were associated with increased risks for prolonged length of stay, in-hospital death and hospital readmission within one month among more than 26,000 patients with CKD in Washington State between 2006 and 2008. This is the first study to associate specific complications with both in-hospital and post-discharge outcomes in a wide-ranging sample of patients with CKD.
Purpose of Study: Donor kidney cold (4°C) ischemia (CI) of >24 hrs is an important cause of DGF. The 13-lined ground squirrel (GS) is a hibernating mammal that undergoes winter hibernation, when its core body temperature falls to 4°C for 6-18 days. Since hibernation is a normal part of the GS life-cycle, we hypothesized that RTCs from hibernating GS are protected from apoptosis due to CI.

Methods Used: Kidneys of C57BL/6 mice and hibernating GSs were exposed to CI in UW solution for 72 hrs. Apoptotic RTCs were scored by a pathologist. Immunoblots were performed for caspase-3, XIAP (an inhibitor of caspase-3 and apoptosis) and phospho-AKT (pAKT) which converts BAD to pro-survival factor phosphoBAD (pBAD).

Summary of Results: RTC apoptosis and caspase-3 activity were significantly increased in mouse vs. GS kidneys. XIAP, pAKT and pBAD were significantly increased in hibernating GS kidneys, but were undetectable in mouse kidneys (Table 1). To determine the mechanism of resistance of GS RTC to apoptosis, GS and mouse RTCs were treated with cisplatin (50uM), an agent known to cause apoptosis. Cisplatin treated GS RTC had significantly less apoptosis, no active caspase-3, increased XIAP, pAKT and pBAD vs. mouse RTC (Table 2). Wortmannin inhibition of pAKT reduced pBAD, and increased caspase-3 in GS RTC demonstrating the importance of Akt signaling in GS RTC survival.

Conclusions: We have shown for the first time that GS RTCs are protected against apoptosis induced by CI and cisplatin, associated with upregulation of pro-survival factors XIAP, pAKT and pBAD. Inhibition of pAKT in GS RTC results in reduced anti-apoptotic pBAD and increased pro-apoptotic caspase-3 expression.

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<td><strong>Stage</strong></td>
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n = 3; p < 0.05 vs mouse and 0 hr; ND = not detected

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<td><strong>Apoptosis (TUNEL cells/HPF)</strong></td>
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<td>Caspase-3 protein</td>
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<td>pBAD protein</td>
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n = 3; p < 0.05 vs. mouse RTC; *p < 0.001 vs Mouse RTC + 50mM cisplatin; ND = not detected

291

RISKS OF RHABDOMYOLYSIS AND ACUTE KIDNEY INJURY AMONG HOSPITALIZED SUBSTANCE USERS

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Purpose of Study: Substance use is mechanistically implicated in the development of rhabdomyolysis and acute kidney injury, but there is scant evidence describing the increased risks of these conditions among patients with co-occurring or history of substance use disorders. The primary objective of this study was to determine the prognostic effects of the abuse of specific substances on the development of rhabdomyolysis and rhabdomyolysis with concurrent acute kidney injury.

Methods Used: Patients described were adults (18+ years) first hospitalized for non-maternity visits in Washington State between January 2009 and December 2011 (n=705,512). Study outcomes of rhabdomyolysis and rhabdomyolysis with concurrent acute kidney injury were calculated using multivariate binary logistic regression models controlling for age, sex, race, payer, comorbid serious mental illness, and a set of clinical comorbidities implicated in the development of rhabdomyolysis or rhabdomyolysis and acute kidney injury.

Summary of Results: Independent risks of rhabdomyolysis were increased among patients with co-occurring or a history of abuse of alcohol (OR=1.33; 95%CI=1.20-1.48; p=0.001), amphetamine (OR=4.82; 95%CI=3.60-6.44; p=0.001), and opioids (OR=1.44; 95%CI=1.03-1.99; p=0.03). Similarly, the independent risks of rhabdomyolysis and concurrent acute kidney injury were increased among patients with co-occurring or a history of abuse of amphetamines (OR=4.82; 95%CI=3.60-6.44; p=0.001), cocaine (OR=4.38; 95%CI=3.06-6.27; p<0.001), and opioids (OR=1.44; 95%CI=1.03-1.99; p=0.03).

Conclusions: Hospitalized patients with historical or co-occurring substance use disorders demonstrated substantially increased risks of rhabdomyolysis and acute kidney injury in a large and comprehensive statewide population. Patients with substance use disorders should be the subject of further research and the development of interventions to understand and reduce the occurrence of these outcomes and their attendant morbidity and mortality.
resembles the cisplatin dosing regimen used in humans with non small cell lung cancer.

Methods Used: Mice were injected with lung cancer cells into the flank. Cisplatin was then given weekly for a total of 4 doses. Tumors in the flank were measured and tumor volume was calculated weekly. IL-33 and CXCL1 were measured by ELISA and CD4 T cells by flow cytometry in the kidneys.

Summary of Results: Renal failure and tubular injury was present at 2 weeks: BUN (mg/dL) was 23 in vehicle-treated and 60 in cisplatin-treated (P<0.005). SCR (mg/dL) was 0.2 in vehicle-treated and 0.5 in cisplatin-treated (P<0.001). ATN score was zero in vehicle-treated and 1.5 in cisplatin-treated (P<0.001). Apoptosis in tubular cells (per high power field) was zero in vehicle-treated and 10 in cisplatin-treated (P<0.001). Tumor volume (mm3) in vehicle-treated was 308 on day 17 and 1791 on day 34 (P<0.001). Tumor volume (mm3) in cisplatin-treated was 604 on day 17 and 762 on day 34 (not significant). At the end of the study, tumor weight (g) was 1.23 in vehicle-treated and 0.46 in cisplatin-treated (P<0.001).

IL-33/CD4/CXCL1 proteins were increased at 1 week: IL-33 (pg/mg) was 150 in vehicle and 300 in cisplatin-treated (P<0.001). CXCL1 (pg/mg) was 1.9 in vehicle and 20 in cisplatin-treated (P<0.05). CD4 T cell subset (% of live cells) was 13.1 in vehicle-treated and 20 in cisplatin-treated (P<0.05). The increase in IL-33/CD4/CXCL1 increased further at weeks 2 and 4.

Conclusions: In a 4 week model of cisplatin-induced AKI: 1) 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 in the AKI and tubular injury, 2) Cisplatin significantly reduces tumor growth. The effect of IL-33, ST2 or CXCL1 inhibition on the cisplatin-induced AKI and the chemotherapeutic effect of cisplatin will be interesting in future experiments.

Surgery II

Concurrent Session

3:30 PM
Friday, January 25, 2013

293

OUTCOMES OF KIDNEY TRANSPLANTATION FOLLOWING ROBOTIC PROSTATECTOMY

Creech JD, Culppeper DJ, Mai AT, Ng CC, Wallner CL, Huang GO, Anderson KM, Schlaifer AE, Arnold DC, Olgen G, Baldwin D. Loma Linda University, Loma Linda, CA.

Purpose of Study: Patients with renal failure are not routinely considered as candidates to undergo radical prostatectomy for the treatment of prostate cancer unless they are potential transplant candidates. In our institution kidney failure patients that are candidates for renal transplantation are offered radical prostatectomy (RP). Patients with undetectable ultrasensitive PSA levels, negative margins and low or moderate grade disease may proceed to transplantation following RP. Patients with undetectable ultrasensitive PSA levels, negative margins and low or moderate grade disease may proceed to transplantation following RP. Patients with undetectable ultrasensitive PSA levels, negative margins and low or moderate grade disease may proceed to transplantation following RP.

Methods Used: A retrospective review of 15 ERSD patients diagnosed with prostate cancer that underwent radical prostatectomy in a single academic institution was performed. Patients that underwent subsequent renal transplantation were further reviewed to determine oncologic and renal functional outcomes following transplantation.

Summary of Results: Four patients underwent robotic assisted laparoscopic radical prostatectomy (RALP) and one patient underwent open radical prostatectomy. All 5 ERSD patients treated with RP were found to have undetectable PSA levels following prostatectomy at a mean follow-up of 256 days. The mean creatinine was 1.38 in the 5 patients with kidney transplant 4 years following RP. There were three unique complications in this series. One patient that was anuric was found to have a bladder neck contracture preventing catheter placement at the time of renal transplantation. This patient was managed with urethral dilation and remains continent with no recurrent strictures at 4 months. One RALP patient that received a deceased donor allograft required intraoperative urologic consultation to identify the location of the contracted bladder. This patient developed non-oliguric acute tubular necrosis with a subsequent nadir creatinine of 1.1. One ERSD patient that was completely continent following RALP (>1 liter of urine per day) became incontinent (2-3 ppd) following transplantation.

Conclusions: Conclusion: Patients with ERSD treated with RP and subsequent renal transplant experienced unique urologic complications but demonstrated excellent oncologic and renal functional outcomes.

294

COMPARISON OF HEAD AND NECK TUMOR CLINICAL STAGING VS. PATHOLOGICAL STAGING

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Purpose of Study: Head and neck cancer treatment is a balance between surgery, radiation and chemotherapy with important considerations of cure and quality of life. Missstaged tumors can cause overtreatment or under treatment of disease, leading to increased morbidities or poor tumor response.

The objective of our present study is to examine patterns of concordance between clinical and pathologic staging among patients with oral cavity, oropharynx, and larynx squamous cell carcinomas (SCCA). The significance of pre-op radiation therapy on clinical and pathological staging will be assessed, and its implication in patient treatment.

Methods Used: Data on patients from the years 2000 to 2011 from a tertiary care head and neck cancer tumor board was compiled and evaluated. Inclusion criteria were patients with SCCA of the oral cavity, oropharynx, or larynx subsites, both clinical and pathological staging were available, and if data was concerning history of preop and post-op radiation for each case. A total of 295 patients fit the selection criteria and were included in this study.

Summary of Results: In patients that were presented to our tertiary care multidisciplinary head and neck cancer tumor board, overall concordance was 65%. Clinical staging correlated with pathologic staging best in cT1 and cT4 stages. Patients that were cT2 tended to be overstaged, while cT3 patients did not follow a pattern.

Comparing the effects of radiation, oral cavity cases had a trend of over staging cT2 and cT3 patients (37.93% and 57.14% of the time respectively). Oropharynx cases classified as cT2 were inaccurate for both pre-radiated and non-radiated patients (40% overstaged). Pre-radiated larynx cases classified as cT4 were highly concordant with their pathological staging (85.71%), while all other stages were inconsistent.

For nodal staging on all subsites, cN1 cases had a low concordance, where over 50% was found to be pN2 on pathologic evaluation.

Conclusions: Accurate clinical staging even from a tertiary care head and neck tumor board is not always consistent. Our study demonstrated an overall concordance of 65%. Thus, pathologic staging should be obtained whenever possible as it can direct therapeutic treatment in terms of radiation therapy and possible chemotherapy. These findings demonstrate the need for accurate methods of tumor assessment with surgery whenever possible.

295

COST ANALYSIS OF COMMON PLASTIC SURGERY PROCEDURES: GEOGRAPHY VERSUS ECONOMICS

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Purpose of Study: Breast augmentation, mastopexy, abdominoplasty, blepharoplasty and rhinoplasty are some of the most common plastic surgical procedures performed in the United States. Despite their uniform popularity, significant cost variation exists across the country. The objective of this study was to determine the correlation between cost of plastic surgery procedures and various economic and social factors in cities of varying sizes across the United States.

Methods Used: 10 randomly chosen plastic surgery practices were selected from 15 eligible cities based on population. Inquiries were made as to the cost of each of the five chosen procedures. Data averages were calculated for both individual procedures and cumulative costs of all five. These values were compared with various economic and demographic statistics for each area such as cost of living, real estate ownership and rental cost and ratio of plastic surgeons to patients.

Summary of Results: The results were graphed and correlations were identified between the cumulative costs of all five procedures and the costs of living, mean real estate rental and mean real estate ownership in the selected cities. No correlation was found between cost of procedure and the ratio of plastic surgeons to patients. See images below.

Conclusions: The data demonstrates a correlation between the cost of plastic surgery procedures and regional economic factors such as cost of living. No correlation indicated a supply and demand model of pricing, as there was no relationship between procedure cost and the density of plastic surgeons in an area.
A RESORBABLE HEMOSTAT FOR LAPAROSCOPIC PARTIAL NEPHRECTOMY

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Purpose of Study: Complications of uncontrolled bleeding within the context of surgical intervention include depletion of the clotting cascade, hypothermia, and hemodilution. Rather evident is the need for better surgical hemostasis. Our goal is to meet the need for an improved hemostat by innovative nitrogen detoxification of microfibrillar chitosan, a biodegradable polyglycosamine polymer that requires depolymerization before implantation into humans.

Methods Used: We treated our chitosan samples with one 30-minute exposure to nitrogen plasma, previously used to sterilize mail suspected of anthrax contamination. We tested the sterility of the hemostat by incubating it in a sterile culture broth for 48 hours at 37°C, followed by assessment for any microbial growth. Endotoxin levels were determined for our samples by both conventional Limulus Amoebocyte Lysate (LAL) and cell-based assays. The latter quantitate endotoxin-mediated release of pro-inflammatory cytokines from human monocyteoid cell clones (MM6), a leukemia cell line especially sensitive to pyrogenic contamination. Preliminary curves relating the optical density of the samples to the concentration of endotoxin were constructed and used as a basis for understanding the efficacy of nitrogen plasma exposure.

Summary of Results: The hemostat was found to have significant bio-burden when not treated with gamma irradiation, nitrogen plasma, or moist heat (autoclave). Once treated with any of these procedures, the bioburden was effectively nil. The MM6 cells revealed that endotoxin levels in gamma irradiated chitosan fleece as tested by IL-6 release was below the level required to significantly increase IL-6 release from the MM6 cells. The LAL assays showed that nitrogen plasma treatment effectively reduced the endotoxin levels found in our chitosan fleece to levels acceptable for surgical implantation (~<20 EU/mL).

Conclusions: Proof that our new resorbable hemostat is safe and effective will constitute a significant advance for a spectrum of surgical fields. Promising areas of application and potential utility include military, surgical, topical, first responder, dental, over-the-counter, and veterinary contexts.

PULLOUT STRENGTH COMPARISON IN CENTRAL AND JUXTA-ENDPLATE ANTERIOR LUMBAR INTERBODY FUSION PLATE PLACEMENT

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Purpose of Study: Although anterior lumbar interbody fusion has increased in popularity, details on the placement technique for optimal performance of ALIF are unknown. The purpose of this study was to investigate (1) whether the screws should be inserted into the central vertebra or juxta-endplate with a shorter plate and (2) whether osteophytes at the endplate perimeter should be removed before plate insertion due to its interfering with its seating. We hypothesized that, in terms of axial plate pullout strength, (1) the juxta-endplate placement would be stronger than central, (2) the central placement would be stronger with osteophytes removed, and (3) the juxta-endplate placement would be weaker with osteophytes removed.

Methods Used: 5 L2-L3 and 5 L4-L5 level specimens were obtained from 5 fresh frozen lumbar cadaveric spines (N=10). Specimens were fixed into cement with vertebral bodies up and exposed. The intervertebral discs were removed to monitor the endplate integrity during screw placement. Two custom plates were inserted with four self-tapping cancellous screws. Plates were placed anterolaterally to allow use of same specimen for each group in a paired fashion. Four different placements were tested on each specimen with the screws placed juxta-endplate (A) or central vertebra (B) with (C) or without (D) removing the endplate osteophytes. Care was taken not to intersect screw trajectories. The bone removal procedure was done using a rongeur consistent with the surgical practice. Each plate was then pulled out via a materials testing machine at 1 mm/s. Sequence of plate insertion and pullout was alternated between groups to avoid bias. The data was analyzed using a One-way ANOVA for Repeated Measures test.

Summary of Results: The mean and standard deviation of the pullout load values for the Groups A, B, C, and D were 519±237, 468±133, 461±242, and 501±271 N, respectively. The comparison of the groups was not statistically significant (P<0.05).

Conclusions: This study showed that in ALIF plate placement, there is no biomechanical advantage between the insertion points with or without shaving the endplate osteophytes. However, based on the trends of our results we speculate that juxta-endplate placement with a shorter plate without osteophyte removal might improve resistance to pullout in ALIF plate fixation.

THE EFFECT OF AGE ON RAT ROTATOR CUFF MUSCLE ARCHITECTURE

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Purpose of Study: The stability of the glenohumeral joint depends significantly on the forces applied by the rotator cuff muscles. Rotator cuff tendon tears are common, and an understanding of rotator cuff muscle architecture is necessary for improving surgical repair outcomes. Muscle architecture is defined as the arrangement of muscle fibers relative to the axis of force generation and is the best determinant of muscle function. Experimentally induced tendon tears in rats are used to study rotator cuff disease but with different healing properties than those of humans. Since rats continue to grow throughout their lifespan, the changes in rat rotator cuff muscle architecture with age confound the results of experimentally induced tendon tear.

Methods Used: This study examined the changes in infraspinatus and supraspinatus muscle architecture with age in Sprague Dawley rats (n=30) ranging from 51-814 grams body mass (~3 weeks to 6 months). Measurements of muscle mass, fiber bundle length, pennation angle, and sarcomere length permitted calculation of normalized fiber bundle length and physiological cross-sectional area (PCSA).

Summary of Results: Results for both the supraspinatus and infraspinatus show that muscle mass is linearly related to body mass, muscle length is logarithmically related to body mass, normalized fiber bundle length is logarithmically related to body mass, but linearly related to humeral head diameter, PCSA is linearly related to body mass, and importantly, sarcomere length remains constant over the range of body masses measured in this study.

Conclusions: Linear growth in muscle mass and PCSA, non-linear growth in muscle length and fiber bundle length, and a linear relationship between humeral head diameter and fiber bundle length suggest that muscle fiber length (serial sarcomere number) adjusts according to skeletal dimensions as the animal grows. No change in sarcomere length with body mass suggests that sarcomere length is conserved throughout the lifespan of the animal.
Purpose of Study: Unstable fractures of the pelvic ring are high-energy injuries. Treatment of these ring injuries is difficult due to failure of fixation. Historically, percutaneous iliosacral screw fixation has been the treatment of choice. The use of transsacral screw fixation has been reported sparingly for alternative uses. We report our use of transsacral screw fixation for posterior pelvic ring injuries.

Methods Used: A retrospective chart and radiographic review was conducted of patients treated with at least one transsacral screw placed at the University of California, Davis Medical Center.

A detailed neurological examination was performed to determine any neurologic deficits caused by the fracture reduction or screw insertion. Postoperative plain pelvic radiographs (anteroposterior, inlet, and outlet views) were obtained, and serially evaluated for loss of reduction.

Summary of Results: Intraoperatively, all patients underwent posterior pelvic reduction and had at least one partially threaded transsacral screw. All screws were 8mm in diameter. Nine patients had preoperative nerve deficits; twenty-five patients presented with Zone II sacral fractures. At the 6-month follow up, one patient had loss of reduction. There were no iatrogenic nerve injuries recorded. No patients demonstrated postoperative displacement based on plain radiographs.

Conclusions: Transsacral screw placement is a technically challenging, yet clinically effective technique for posterior pelvic ring stabilization. This technique allows for enhanced stability (by offering longer screws and anchorage into contralateral cortical bone) without long-term sequelae, implant loosening, or neurological deficits.

300
IN-HOSPITAL WAIT TIME AND APPENDICITIS: IS THERE AN ASSOCIATION WITH PERFORATION?
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Purpose of Study: Appendicitis is the most common reason for urgent gastrointestinal surgery. Various studies have demonstrated an association between pre-operative wait time and perforation. However, many of these studies have shortcomings such as small sample size, single institution data, or use of admission and OR dates rather than more granular increments of time (such as hours or minutes). The goal of this study was to examine the relationship between in-hospital wait time and frequency of perforation.

Methods Used: Using data collected in 52 hospitals in the state of Washington, we evaluated perforation among patients who underwent appendectomy. Variables studied included demographic and clinical information. Wait time was measured between admission to the Emergency Room (ER), diagnostic imaging, and operating room (OR) start time. The relationship between in-hospital time and odds of perforation was adjusted for potential confounding using multivariate logistic regression.

Summary of Results: 9029 patients underwent appendectomy from January 2010 to December 2012. 15.6% appendices were perforated. Time from ER to OR was 8.6 (SD 6.4) hours for non-perforated patients and 8.6 (SD 7.2) hours for perforated patients. Logistic regression of perforation vs. preoperative time (patients categorized into deciles based on time between ER and OR) showed no significant difference in odds of perforation as compared to patients in the first decile (i.e., those with the shortest wait time). When time was included in the model as a continuous variable, there was no association with perforation; adjusted odds ratio 1.0 (95% CI 0.99 - 1.01). Increasing age, male sex, presence of 3 or more comorbid conditions and lack of insurance were found to be significant predictors of perforation.

Conclusions: After adjusting for age, sex, co-morbid status, insurance status, and race/ethnicity, increasing time in the hospital is not associated with an increase in the odds of perforation. Several demographic and clinical subsets of this cohort experienced longer wait times (e.g., women, African Americans), however these subpopulations did not demonstrate increased frequency of perforation. These data suggest that perforation is most often a pre-hospital event.

301
CEREBROSPINAL FLUID COMPLICATIONS FOLLOWING INTRADURAL SPINAL SURGERIES IN CHILDREN
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Purpose of Study: Cerebrospinal fluid (CSF) leakage is a complication of intradural spinal surgery and is associated with poor wound healing and infection. The incidence of CSF leak is reported at ~16% in adults, but little information is available in children. The purpose of this study was to determine the CSF leak rate and predisposing factors after intradural spinal surgeries in children.

Methods Used: This study was a retrospective chart review of 638 intradural spinal operations at B.C. Children’s Hospital to identify patients who developed a post-operative CSF leak and associated risk factors. CSF leak was defined as pseudomeningocele or CSF leak through incision. Primary operations to untether lipomyelomeningoceles, myelomeningocele/meningocele closure, and Chiari decompressions were excluded.

Summary of Results: CSF leaks occurred in 7.1% and were associated with a higher incidence of post-operative wound infection and meningitis (p=0.0016 and p=0.0013 respectively) but not neurological worsening (p=0.35). 8 of 18 cases of CSF leak through the skin incision required reoperation compared to 8 of 27 cases of pseudomeningocele requiring reoperation. The type of dural suture used, site of operation, use of fibrin glue, or use of a graft did not affect CSF leak rates. Previous spinal surgery (p=0.0001), method of dural suturing (p=0.0023), and procedure performed (p=0.001) were significant factors associated with post-operative CSF leakage. Patients with CSF leak were older than those without leak (98 vs. 72 months, p=0.002).

Conclusions: Our results provide evidence on intraoperative factors that may predispose to CSF leaks after spinal intradural surgery and may help guide surgical practice. An important finding was that many cases of pseudomeningocele went on to require operative intervention, suggesting that clinically noted pseudomeningoceles require ongoing monitoring to determine whether further intervention will be required. This study confirms that the pediatric population shares many of the same important risk factors for CSF leak as in adult populations. Further research is needed to explain how specific factors are associated with CSF leaks.

302
EVALUATING FASTING GUIDELINES FOR PEDIATRIC SURGICAL PATIENTS AT BRITISH COLUMBIA CHILDREN’S HOSPITAL
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Purpose of Study: Before anesthesia, patients are instructed to fast in order to avoid complications such as pulmonary aspiration. Current recommendations are 2 hours for clear liquids, 4 hours for breast milk, and 6 hours for food and formula. However, actual fasting times can significantly exceed these minimum requirements, risking dehydration, hypoglycemia, and
Conclusions: A significant number of children experience excessive clear fluid fasting times. As a result of this audit, our institution will review how we provide fasting information to families. A future audit will also assess the impact of practice changes derived from this study’s results. In addition, we may look into developing guidelines for the maximum safe duration of fasting.

Summary of Results: Fasting patterns were bimodally distributed, with peaks at 3 hours (n=226, interquartile range (IQR) from 2.98 to 4.33h) and 12 hours (n=208, IQR=11.13 to 14.25h).

Methods Used: Data was collected from the UMC Lied Pediatric Outpatient Clinic in Las Vegas, Nevada from June to August 2011. Charts of children 3-18 years were evaluated for age, height, weight, gender, blood pressure documentation, blood pressure normality, repeat blood pressure measurement and blood pressure assessment.

Summary of Results: Of 945 patients visits recorded, 87 were excluded due to repeat visit during collection period. 95.9% had blood pressures documented. 12.5% had abnormal blood pressures. Of those who had abnormal blood pressures, 6.5% had blood pressure measurements repeated and 3.7% had abnormal blood pressure evaluated in the diagnostic assessment and plan.

Conclusions: We conclude that blood pressures in children are being documented appropriately. However, abnormal blood pressures are not being sufficiently recognized and managed as only 6.5% of patients with abnormal blood pressures had measurements repeated and 3.7% were assessed for their abnormal reading. As uncontrolled hypertension can lead to increased morbidity and mortality over time, it is necessary to recognize abnormal pressure at an early age. An intervention for the Lied Clinic regarding the recognition, evaluation and diagnosis of abnormal blood pressure in children is pending.

THE PREVALENCE AND MANAGEMENT OF DIARRHEAL DISEASES IN CHILDREN UNDER AGE FIVE IN A RURAL VILLAGE OF GHANA
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Purpose of Study: Diarrhea is the second largest cause of mortality for children under 5 years old in Ghana. The current treatment regimen recommended by the World Health Organization (WHO) and UNICEF is oral rehydration therapy (ORT) and continued feeding. We aimed to determine the prevalence and management of diarrhea affecting children under five in the rural village of Ampenkrom, Ghana. Furthermore, we sought to elucidate the beliefs and knowledge underlying behavioral patterns to help guide future interventions.

Methods Used: Partnering with a local non-governmental organization, the Ghana Health and Education Initiative, quantitative and qualitative questionnaires were developed, and then administered, with the help of trained community health workers, to women with children less than 5 years old in the village of Ampenkrom, population ~2,000. Randomly chosen by door-to-door canvassing, 101 women were given the quantitative questionnaire and 16 women were given the qualitative questionnaire.

Summary of Results: 30/128 (23%) children under age 5 had diarrhea in the last two weeks, with 11/30 (37%) of those children receiving ORS, and only 6/30 (20%) receiving ORS with continued feeding. 14/30 (46.7%) mothers with children under 5 with diarrhea in the past two weeks sought treatment from a pharmacy/shop, while 14/30 (46.7%) sought treatment from a health facility. At pharmacies, the medications most commonly administered were “other” (including paracetamol and dextrose: 11/30; 36%) and antibiotics (8/30; 27%). At health facilities, the medications most commonly administered were antibiotics (9/30; 30%) and vitamins (9/30; 30%).

Regarding knowledge about ORS, 11/16 (68.8%) respondents identified diarrhea as life threatening, and 15/16 (94%) thought that ORS packets help their child get better. Regarding barriers to using ORS, 13/16 (81%) respondents did not find it difficult to travel to get ORS, but 15/16 (94%) mothers indicated taste as a reason their child refuses to take ORS.

Conclusions: The low rate of ORS usage may be due to inappropriate advice given by pharmacies and health facilities, as well as taste of the available ORS. This suggests that pharmacies and health facilities may be an appropriate target for a future intervention.

DECREASED KIDNEY WEIGHT AND GLOMERULAR HYPTERTROPHY ARE ASSOCIATED WITH CHRONIC EXPOSURE TO LOW BUT NOT HIGHER LEVEL LEAD IN YOUNG MICE
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Purpose of Study: Long-term exposure to high levels of lead is a risk factor for chronic kidney disease. The levels of lead in the environment have been decreasing for several decades. Unfortunately many children are still exposed to low levels of lead in old paint and in some drinking water. Studies have shown that chronic low-level exposure is associated with diminished cognitive function in children. The glomerulus is the site of blood filtration, the primary function of the kidney. Few studies have examined glomeruli in children or in young animals exposed to lead. This study examines the effects of low- and higher-dose levels of lead on glomeruli in young mice.

Methods Used: Pups were exposed to 30 ppm or 330 ppm lead (99.4% lead acetate) via dams’ drinking water. Controls were given water with sodium acetate. Pups were sacrificed at post-natal day 28 and organs were fixed with 4% parformaldehyde via transcardial perfusion. Twelve animals per group were studied. Kidneys were harvested, weighed, embedded in resin and 1-μm thick sections cut and stained with toluidine blue. Digital images of glomeruli were obtained and designed-based stereological methods were used to measure glomerular volume and to count podocytes. The stereologist was blind to the exposure group and blood lead level of the subjects.
Summary of Results: Mean lead blood levels in the control, 30 ppm, and 330 ppm exposure groups were 0.03, 3.42, and 13.84 μg/dl respectively. The mean kidney weight of the 30 ppm exposed mice was significantly greater (86±8×10^3 μm^3) than that of the control group (72±6×10^3 μm^3), p<0.001. The mean glomerular volume of the 330 ppm exposed mice did not differ significantly from that of the control group. No differences were observed in the total number of podocytes among the three groups.

Conclusions: Chronic exposure to low-level lead in mother’s milk is associated with decreased kidney weight and glomerular hypertrophy in young mice.

306 CAN WE PREDICT THE HISTOPATHOLOGY OF CHILDHOOD NEPHROTIC SYNDROME USING CLINICAL BIOMARKERS?
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Purpose of Study: As most patients with childhood nephrotic syndrome (CNS) have minimal change disease (MCD) that responds well to treatment, there is no need to biopsy patients who likely have MCD. However, it is important to biopsy the minority of patients with non-MCD as these diagnoses are associated with steroid resistance, progressive chronic kidney disease, and often require more intensive therapies. The current indications for kidney biopsy in CNS are based upon historical cohort studies. However, there is still considerable diversity of opinion about the criteria for biopsy. Our study was conducted to retrospectively study the performance of previously defined clinical biomarkers in predicting non-MCD and minimizing unnecessary biopsies in MCD patients.

Methods Used: We retrospectively reviewed the charts of 108 children with CNS who underwent a renal biopsy from 1990-2012. Based on prior literature, the following clinical biomarkers were selected for analysis: age ≥12 yrs, the presence or absence of hypertension, hematuria, abnormal serum creatinine and resistance to steroid therapy (SRSN). We compared the sensitivities and specificities of the clinical biomarkers in predicting non-MCD.

Summary of Results: Of the 108 patients with CNS who underwent kidney biopsy, 59% had MCD and 41% had non-MCD. Of those with non-MCD, the following histopathological diagnoses were seen: focal segmental glomerulosclerosis (82%); membranous glomerulonephritis (11%); membranoproliferative glomerulonephritis (7%). The performance of individual and combinations of clinical biomarkers in predicting non-MCD is shown in the Table.

Conclusions: In predicting the underlying kidney histopathology, none of the individual clinical biomarkers performed optimally. From our data, the combination of 3 or more clinical biomarkers upon presentation and steroid resistance are the best predictors of the histopathology in CNS. However, larger sample sizes and various thresholds for each of the biomarkers need to be studied further.

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307 IMPACT OF VIDEOCONFERENCE ON STRESS IN HOSPITALIZED CHILDREN
Yang NH1, Dharmar M2,2, Sadarova CK1, Hojman NM1, Sundberg D1, Trujano J1, Marinic M1, Wold GL1, Marcin JP2, 1University of California, Davis, Sacramento, CA and 2University of California, Davis, Sacramento, CA.

Purpose of Study: Family-Link is a videoconferencing program at the University of California, Davis Children’s Hospital that connects hospitalized children and their parents to family and friends outside the hospital using laptops. The goal is to evaluate whether the use of Family-Link impacts the level of stress experienced by the child and family during hospitalization.

Methods Used: Children were included if they had an expected length of hospitalization of more than 5 days, from January 2011 to September, 2012. Stress was evaluated using a survey modified from a previously validated parental stress survey. This survey evaluates 23 items measuring stress within 4 domains on a six-point Likert scale, with a total scoring range of 0-115. We also asked the parent whether talking to family or friends helped reduce the child-patient’s level of stress during hospitalization. The survey was administered to the parent at the time of admission and close to discharge. The mean stress scores were compared using a Student’s t-test.

Summary of Results: A total 201 hospitalized children were enrolled in the study, with a mean age of 10.0 years and a mean hospitalization length of 15.1 days. One hundred and thirty-eight hospitalized children used Family-Link during the study period with an average age of 15.7 years. 63 hospitalized children did not use Family-Link, with a mean age of 13.7 years. Among Family-Link users, the overall mean stress scores at admission was 28.1 (SD=15.7) and at discharge was 15.7 (SD=13.6). Among non-Family-Link users, the overall mean stress scores at admission was 28.8 (SD=17.4) and at discharge was 17.5 (SD=13.4). This was a significant reduction in the mean levels of stress (discharge-admission stress) for both groups (12.4, p<0.05 among Family-Link users, 11.3, p<0.05 among non-Family-Link users).

Conclusions: Our analyses demonstrate that children and families using Family-Link during hospitalization have a greater reduction in stress scores than those children and families than did not use Family-Link. The use of Family-Link may have contributed to the reported decrease in hospitalized children’s stress score.

308 CLINICAL BIOMARKERS OF LONG-TERM OUTCOME IN CONGENITAL URINARY TRACT OBSTRUCTION
Yu S, Morrison SJ, Matsell D. BC Children’s Hospital, Vancouver, BC, Canada.

Purpose of Study: To determine the progression of CKD in PUV patients. The prognostic factors that determine the progression of CKD in PUV patients have not been thoroughly investigated. The objective of this study is to identify clinical biomarkers or predictors of long-term renal outcome in boys with PUV.

Methods Used: We performed a retrospective review of the records of 97 patients with PUV who were treated at BC Children’s Hospital between 1987 and 2012. The inclusion criteria of the cases included age between 0 and 18 years with the diagnosis of PUV confirmed by ultrasonography and voiding cystourethrogram. Patients requiring dialysis at birth or who died <28 days after birth were excluded. Primary kidney outcomes included loss of 50% of peak GFR, dialysis, or preemptive renal transplantation. Clinical variables studied included antenatal ultrasound findings, intrauterine interventions, oligohydramnios, gestational age, age at diagnosis, birth weight, vesicoureteral reflux, age at valve ablation, presence of hypertension or proteinuria, and the occurrence of urinary tract infections. Kaplan-Meier analysis was performed to compare outcomes between groups with and without the clinical biomarker.

Summary of Results: The mean age of patients at diagnosis was 0.55 ± 1.40 years with a mean duration of follow up of 5.59 ± 3.58 years. A total of 43% of patients reached the primary renal outcome during the period of study. By Kaplan-Meier analysis there were significant differences in long-term outcomes, defined as attaining one or more of the outcomes, in patients with proteinuria (p=0.05), oligohydramnios (p=0.01), high-grade vesicoureteral reflux (p<0.04), or a metabolic acidosis (p=0.03).

Conclusions: A number of clinical biomarkers are associated with a worse outcome in patients with PUV. Certain biomarkers, such as proteinuria, may be modifiable. These results will help inform future interventions as well as clinical pathways that will standardize the management of children with congenital urinary tract obstruction.
SAFETY AND EFFICACY OF THE LEVONORGESTREL-RELEASING INTRAUTERINE SYSTEM IN TRANSPLANT PATIENTS

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Purpose of Study: The levonorgestrel intrauterine contraceptive system (LNG-IUS) is safe and effective for the treatment of heavy menstrual bleeding, dysmenorrhea, and pregnancy prevention. In reproductive-aged women who undergo organ transplantation, pregnancy increases the risk of alloraft rejection. Other hormonal contraceptives have higher failure rates than the LNG-IUS and may alter serum concentrations of some immunosuppressants. Although the LNG-IUS has been shown to be safe and effective in women with HIV and other chronic conditions, there is limited data regarding the safety and efficacy in women with transplants. The purpose of this study was to determine rates of pregnancy, complications, and continuation among women with transplants using the LNG-IUS.

Methods Used: We completed a retrospective chart review of all transplant patients who had an LNG-IUS placed at Seattle Children’s Hospital or the University of Washington Medical Center from January 2008 through March 2012. Data including patient characteristics, indications for placement, and complications including perforation, unintended pregnancy, expulsion, and pelvic infection were collected and analyzed.

Summary of Results: 16 transplant patients had an LNG-IUS placed during the study period (8 kidney, 1 kidney/pancreas, 4 cardiac, 2 lung, 1 liver). Mean age at placement was 22.34 years (range 15-38). Indications included contraception 75% (12/16), menstrual suppression 68.8% (11/16), treatment of heavy menstrual bleeding 43.8% (7/16), or dysmenorrhea 18.8% (3/16). There were no pregnancies and no cases of pelvic inflammatory disease reported. The expulsion rate was 6.25% (1/16). One cardiac transplant patient chose to have the LNG-IUS removed after 21 months due to irregular bleeding and cramping. 87.5% (14/16) patients were continuing use of the IUS at their last follow up appointment.

Conclusions: The LNG-IUS is associated with high continuation rates and low complication rates among this small cohort of reproductive aged women with transplants. This provides further evidence that the LNG-IUS is a safe and effective option for female transplant recipients who need contraception, menstrual suppression, or treatment of heavy menstrual bleeding.

311

UNAPPROVED NARCOTIC PRESCRIPTIONS IN PATIENTS ON CHRONIC OPIOID THERAPY

Rush SK, Merrill JO. University of WA School of Medicine, Seattle, WA.

Purpose of Study: Patients prescribed opioids from multiple physicians may be involved in drug diversion, have abuse issues, or be at risk for overdose. Prescription Drug Monitoring Programs (PDMPs) may increase the safety of opioid prescribing by allowing providers to determine if patients have received unapproved prescriptions. This project aims to assess the utility of verifying PDMP records for patients receiving chronic opioid therapy.

Methods Used: Within five months of Washington state PDMP’s 2012 initiation, we reviewed medical records for all patients prescribed chronic opioid therapy at a large urban general medicine clinic. Medical records included PDMP reports of controlled substances dispensed to the patient. PDMP results, clinical, demographic and opioid prescribing data were collected. For all PDMP reports of prescriptions not documented in the registry, clinic notes were used to determine whether primary care providers (PCPs) were aware of the prescription.

Summary of Results: Registry patients (n=431) had an average age of 57.6 and 48% were female, 52.4% white, 38.3% black, and 6% other. Of 431 patients, 313 (72.6%) had no prescriptions outside the clinic registry while 118 (27.4%) had PDMP reported prescriptions for controlled substances not recorded in the registry. Medical record review demonstrated that 49 (11.4%) patients had prescriptions from a hospital discharge, acute medical/dental/office, or mental health condition of which the PCP was clearly aware; these patients were classified as having no unapproved prescriptions. For patients with PDMP reports whose PCP was not clearly aware, 36 (8.4%) had 1 - 2 prescriptions of low numbers of pills and were classified as possible unapproved prescriptions, and 32 (7.7%) had >2 prescriptions or >36 pills and were classified as probable unapproved prescriptions.

Conclusions: The PDMP is a valuable tool to identify patients on chronic opioid therapy who may be receiving controlled substances unapproved by their PCP. However, PDMP reports require significant effort to interpret whether patients are clearly in violation of their opioid agreements. Clinicians, health care providers, and health care institutions have to determine through continued use of the PDMP how its results will be interpreted, and how to best use the information to decrease the risks of chronic opioid therapy.

312

BUILDING CONFIDENCE, SELF-ESTEEM AND AWARENESS: A CASE REPORT OF PILOT WORKSHOPS CENTERED AROUND RISK REDUCTION AND HIV/STI PREVENTION IN THE MSM COMMUNITY IN CALLAO, PERU

Shull HI1, Konda K2, Caceres C1, Kegues S2. 1UCR David Geffen School of Medicine, Los Angeles, CA and 2UCSF, San Francisco, CA.

Purpose of Study: In Peru, there are an estimated 75,000 people living with HIV. Of those infected, the highest concentration is among men who have sex with men (MSM) and male-to-female transgender women (TW), with rates of infection estimated in Lima to be 32.2% in TW, 26.2% in gay men, and 13.3% in bisexual men. Models for prevention interventions for this population are undeveloped and lacking, partly because it is a highly diverse and highly marginalized section of society. This pilot study seeks to develop a new multi-level HIV prevention intervention for the MSM community in Callao, Peru, which integrates two previously successful programs for MSM in the U.S., Mpowerment and Hermanos de Luna y Sol, into a new program that addresses individual, social and structural issues, reduces sexual risk behavior, and is specifically relevant to Peruvian MSM/TW.

Methods Used: The small group part of this intervention consists of a series of 4 workshops that address issues of confidence, self-esteem and awareness about protecting oneself from HIV/STIs. When the study site is not being used for workshops it will be open as a community center, which
will host various activities and events for the local MSM/TW community that will advocate for the same objectives as the workshops.

**Summary of Results:** We developed an interactive multi-level HIV/STI prevention intervention that addresses cultural issues specifically pertinent to the Peruvian MSM population. Detailed instruction manuals were created and intervention staff were trained on how to lead each of the 4 workshops. Workshops were implemented at the study site and the site was opened in off-hours as a community center. A group of community leaders was assembled and trained to take charge of the community center and to put on various activities/events.

**Conclusions:** Workshops have been successfully implemented and feedback is being collected. They will continue for 9 months, at which point if the intervention is considered to be feasible and acceptable, an application will be submitted to evaluate the effectiveness of the intervention in a clinical trial.

### DECREASING ALCOHOL ABUSE BY UTILIZING RADIO TRAFFIC PUBLIC SERVICE ANNOUNCEMENTS IN DILLINGHAM, ALASKA

Lotakis DM. University of Washington School of Medicine, Seattle, WA.

**Purpose of Study:** Dillingham, Alaska has an excessively high rate of alcohol misuse. Teen and adult drinking are widespread in the community at both public and private settings. The goal of this project was to reduce alcohol abuse by circulating information about alcohol consumption. By increasing awareness of the effects and outcomes of excessive drinking the hope is to see a decrease in alcohol abuse and subsequently the amount of violent crime and traumatic injury.

**Methods Used:** After speaking at length with hospital staff and community members it became clear alcohol abuse was a major problem in the town. Furthermore, many individuals mentioned noticing a correlation between the occurrence of violence, serious accidents and alcohol consumption. Upon completing a literature search support was found for the association between alcohol use and violence. Previous research from the town’s health education office also showed an association linking injury related death and alcohol use. Numerous sources positively confirmed radio PSAs as a valid intervention for increasing community awareness and change.

**Summary of Results:** With the help of the local health education office PSAs were developed concerning operating motor vehicles and general over-use. These scripts were announced on the local radio station over a five-day period. Community members stated the PSAs had a personal and professional feel, which conveyed the message effectively. Health education office employees noted the advantages of using the radio, namely the benefits of widespread circulation and long-term reuse. Similarly, local physicians applauded the effort and confirmed the necessity for intervention dedicated to alcohol abuse. When the project concluded PSAs were left at the health education office for future use.

**Conclusions:** Health prevention office employees have found previous PSAs to be effective, low cost interventions for various public health issues in the region. After determining alcohol abuse to be an area where outreach would benefit the community, the utilization of a medium proven to be effective was deemed most appropriate. Surveying the community in the future about their use of alcohol will demonstrate the impact of the alcohol abuse public service announcements.

### SPECIALITY DISRESPECT AT A PRIMARY CARE SCHOOL: STUDENT PERSPECTIVES

Alston MT1, Caaw-Luces J2, Kost A2, Hughes LS2, Wheeler T2. University of Washington School of Medicine, Seattle, WA.

**Purpose of Study:** Research demonstrates that specialty disrespect (SD) in medical education occurs across geographic, demographic, and professional boundaries, with quantifiable impacts on students’ career decision-making and wellbeing. In this study, researchers perform a mixed-methods analysis of survey data from third- and fourth-year students at a leading primary care institution to determine whether student responses correlate with existing trends in the literature and to identify a multi-component approach to skin cancer prevention, according to the literature, has shown success in a recreational population. A three-component campaign was devised. The first component consisted of writing an article for the newspaper introducing the “Save Your Own Skin” campaign and having the UVI broadcasted daily over the radio station for residents. The second component was a brochure distributed throughout the community detailing prevention tips, UVI, and lesion identification. The final component focused on skin lesion identification training in the target group of 40-70 year olds that have already had prior skin damage.

**Summary of Results:** Twenty-five residents attended the training session and their interactions suggested the presentation was well received. The residents were instructed on identifying suspicious lesions and which types need to be examined by a professional. The UVI, as presented in the brochure, was reviewed as a means to gauge UVR exposure and protection needed. Afterwards, the brochure was distributed at the hot springs, clinic, and senior center. The UVI also began broadcasting daily on KGTA 99.1 radio station.

**Conclusions:** With skin cancer increasing and a culture valuing tanned skin, the importance of UVI in prevention, protection, and identification of UVR overexposure is helpful in reducing skin cancer prevalence. Identification of lesions is also important for those with pre-existing skin damage. The brochure and training are a beginning for Saratoga in reducing the prevalence of skin cancer. The long-term sustainability will come with UVI awareness, presentations, and “Save Your Own Skin” campaign reinforcement.

### MEDICAL SCHOOL DIRECTIONAL IMPACTS ON CAREER CHOICE AMONG STUDENTS: A FOCUS ON PRIMARY CARE NEGLECT

Amble C1, Edgington S2, Xu H2, Ong M2. UCLA, Los Angeles, CA.

**Purpose of Study:** Despite the school’s strong support for primary care, SD occurs with family medicine and primary care disproportionately targeted. Thematic analysis further suggests that existing survey methods fail to capture multidirectional impacts of SD on career choice.

### PREDICTIVE FACTORS OF 30-DAY READMISSIONS FOR HEART FAILURE PATIENTS

Ambler C1, Edgington S2, Xu H2, Ong M2. UCLA, Los Angeles, CA.

**Purpose of Study:** Hospital readmissions are a key target of delivery reform under the Affordable Care Act. This study examines patient factors for 30-day readmissions among heart failure patients in a larger study, Better Effectiveness After Transition-Heart Failure (BEAT-HF), that tests a protocol to reduce readmissions for 180 days after discharge. Treatment protocol includes enhanced self-management with coaching before discharge, continued telephone-based coaching with nurse care managers, and wireless remote monitoring of biometric parameters and symptoms.
Methods Used: This project focused on patients discharged from UCLA, one of six institutions in BEAT-HF. Of the 42 intervention patients who had participated for at least 30 days, six were excluded due to study withdrawal. The discharge summary and documentation of each interaction with nurse care managers within 30 days were qualitatively analyzed for patient factors that could hinder self-management. Call data were examined by type of call, as well as frequency and severity of “trigger” alerts generated that prompted calls from nurses. These data were analyzed in conjunction with administrative and self-reported readmission data. Qualitative factors were analyzed using Pearson chi-squared tests and quantitative call data were analyzed using two-sided T-tests.

Summary of Results: Forty-six of the 36 patients included in analysis were readmitted within 30 days. Eighteen potential qualitative risk factors were identified, of which only documented history of noncompliance was negatively associated with 30-day readmission (p=0.063). Eleven quantitative variables related to alerts, call type, and call frequency were evaluated. A higher frequency of alert-generated calls (p<0.090) and a lower frequency of weekly scheduled calls (p=0.004) within the first 30 days were associated with 30-day readmission.

Conclusions: Documented history of noncompliance was negatively associated with 30-day readmission, possibly because nurses spent more time calling these patients, which was not examined in this study. The disparity in number of scheduled calls may be related to inability to reach patients who had readmissions. The number of alert-generated calls was greater for readmitted patients, suggesting that some patterns of biometric data may be predictive of readmission.

Endocrinology and Metabolism III
Concurrent Session

8:00 AM
Saturday, January 26, 2013

317
PHARMACOLOGIC INHIBITION OF NF-κB IN COMBINATION WITH TAXANE-BASED CHEMOTHERAPY FOR TREATING ADVANCED THYROID CANCER
Berlinberg A, Haugen B, Wood W. University of Colorado School of Medicine, Aurora, CO.

Purpose of Study: Nuclear factor-κB (NFκB) is activated in many cancers and plays a key role in promoting cell proliferation, survival, and invasion. This pathway has also been shown to play a role in resistance to chemotherapy and radiotherapy in some cancers. Most patients with advanced thyroid cancer are fairly resistant to standard chemotherapy. We hypothesize that inhibition of NFκB signaling (bortezomib) will sensitize thyroid cancer cells to standard chemotherapy (docetaxel).

Methods Used: One anaplastic thyroid cancer cell line (8505C) and one papillary thyroid cancer cell line (BCPAP) were used to study the effects of bortezomib and docetaxel in combination or alone. An SRB-based growth proliferation assay was used to assess cell growth inhibition (3 days; 0-20 nM docetaxel, 0-10 nM bortezomib), while a Matrigel based invasion assay was used to assess invasion (18 hours; 0.31 nM docetaxel, 1.25 nM bortezomib). Apoptosis was studied using the Promega 3/7 Caspase Assay kit (24 hours; 0-10 nM docetaxel, 0-100 nM bortezomib).

Summary of Results: Bortezomib and docetaxel act synergistically to inhibit cell proliferation, decreasing cell growth more than either drug alone (8505C: 8505C: 16% invasion combo, 84% bortezomib, 73% docetaxel; BCPAP: 38% combo, 125% bortezomib, 91% docetaxel). The combined drug treatment activates the apoptosis pathway as indicated by Caspase activity, while only bortezo-mib activates the Caspase pathway alone (5 nM docetaxel, 50 nM bortezo-mib; 8505C: 6.48 fold Caspase increase bortezomib, 1.07 docetaxel, 6.89 docetaxel, 1.25 bortezomib; BCPAP: 7.90 bortezomib, 1.30 docetaxel, 8.63 combo).

Conclusions: These data indicate that the combination of bortezomib and docetaxel is an attractive therapy for advanced thyroid cancer. Global decreases in growth and invasion with bortezomib and docetaxel in combination using clinically achievable IC50 values are encouraging for preclinical in vivo studies.

318
EFFECTIVENESS OF SPIRONOLACTONE IN REDUCING HAIR LOSS IN WOMEN WITH ANDROGENETIC ALOPECIA
Slaught C1, Goh C2. 1David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA and 2David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA.

Purpose of Study: The role of androgens in female androgenetic alopecia (AGA) and whether it responds to treatment with oral anti-androgens has not been conclusively established. This study was performed to examine the demographics of a population of women with AGA and determine the effectiveness of treatment with spironolactone.

Methods Used: Following approval by the institutional review board, a retrospective cohort study was undertaken of all female patients diagnosed with AGA by clinical presentation or biopsy between September 2010 and June 2012. A systematic chart review was performed. Patient assessments were used to determine whether the hair loss had worsened, continued at the same rate, stabilized (i.e. no thinning or thickening), or decreased. Patients on spironolactone were compared to those who were not taking spironolactone.

Summary of Results: A total of 166 patients were identified. Follow up was available for 49 of these patients. For the spironolactone treated group (n=19), 9 (47.7%) women noted hair regrowth and increased thickness, 5 (26.3%) women reported stabilization with no clear change in the density of their hair, and 5 (26.3%) experienced progressive hair loss. Women who continued spironolactone treatment continued thinning despite treatment. In the follow-up group that was not taking spironolactone (n=30), 6 (20%) women reported improved thickness of their hair, 7 (23.3%) women noted stabilization, 9 (30%) women had continued progression at the same rate, and 8 (26.7%) women had worsened thinning. The spironolactone treated group showed statistically significant improvement over the control group (p<0.05).

Conclusions: Spironolactone appears to be an effective treatment option for women with AGA. A placebo-controlled study is required to compare treatment with spironolactone to the natural progression of female AGA.

319
ASSESSING MUSCLE MITOCHONDRIAL FUNCTION IN CHILDREN WITH 31 PHOSPHORUS SPECTROSCOPY DURING EXERCISE
Cree-Green M1, West A1, Brown M1, Newcomer B2, Hull A1, Singel D1, Mizokami-Stout K1, Regenstein J1, Nadeau K1. 1University of Colorado, Aurora, CO and 2University of Alabama, Birmingham, AL.

Purpose of Study: Insulin resistance (IR) is increasingly prevalent in children, yet its mechanisms remain unclear. As a result, interest in the measurement of muscle mitochondrial function in relationship to IR has resurfaced. Recent studies have used 31P magnetic resonance spectroscopy (MRs), which is non-invasive and therefore appealing for clinical research. 31P MRs requires a controlled exercise routine (i.e. exercise at a precise % of maximum volitional contraction (MVC)). As measurement of MVC in children, particularly with disease, is problematic due to difficulties in acquiring perception of effort and motivational issues, we developed a method to predict MVC force based on calf muscle cross-sectional area (MCSA) to assure that in-MRI exercise results in controlled and reproducible metabolic perturbations to the muscle.

Methods Used: Data were collected from 52 sedentary adolescents, ages 12-20 years. Participants were either lean or obese healthy controls or had type 1 or type 2 diabetes. Plantar flexion-perceived MVC was assessed using a customized MRS-compatible exercise device. MCSA of the soleus and gastrocnemius muscles were assessed from MRI images.

Summary of Results: Perceived MVC force output and MCSA from all subjects were significantly correlated (R=0.57, p<0.0001, slope of y=0.0043x+26.4, where x=MCSA in mm2, and y predicts MVC). Mean perceived MVC was 44.1±10.7 kg and predicted MVC 42.0±13.1 kg. 31P MRs results from subjects who performed isometric contractions at 70% MVC and had matching predicted vs. perceived MVC results showed expected changes in phosphorus peaks. In contrast, 4 subjects had perceived MVC markedly less than predicted MVC, and exercise testing at their perceived MVC created minimal metabolic perturbation. Upon repeat testing, these individuals could perform at their predicted MVC with the expected metabolic perturbation.
Conclusions: Utilizing the MRI-predicted MVC to determine a subject’s muscle strength, allows researchers to collect accurate 31P MRS results to assess mitochondrial function during a controlled MRI exercise protocol in children, even if a subject performs poorly on MVC testing. This method will allow quality evaluation of the role of mitochondrial function in IR in youth.

320

BIOCHEMICAL STABILIZATION OF GLUCAGON BY POLYPHENOLS FOR BIHORMONAL CLOSED LOOP TREATMENT OF TYPE 1 DIABETES

Bakhitani P, Caputo N, Jackson M, Bergstrom C, Castle J, Ward WK. Oregon Health and Science University, Portland, OR.

Purpose of Study: Glucagon has shown to be effective in closed loop control and hypoglycemia prevention in type 1 diabetes. In our previous study of glucagon and insulin closed loop delivery, glucagon was successful in avoiding hypoglycemia in 81% of cases. However, due to rapid fibril formation, commercial preparations are suitable only for immediate use. Recently, the polyphenol curcumin has achieved success in inhibiting amyloid in neurodegenerative diseases. Given similarities between the Alzheimer’s peptide and glucagon, we hypothesized that curcumin would inhibit glucagon fibrillation. We measured the spontaneous degradation rate of curcumin and curcumin’s effect on glucagon aggregation.

Methods Used: We assessed different concentration of curcumin at pH 9. To measure aggregation, we carried out Thioflavin T fluorescence (ThT), tryptophan intrinsic fluorescence (TIF), and sought to develop a turbidity assay. For turbidity, we sought to find a wavelength distant from curcumin’s intrinsic peak. We sought to determine whether human serum albumin (HSA) could reduce curcumin’s otherwise rapid spontaneous degradation.

Summary of Results: ThT and TIF at 4 days of aging showed that curcumin 1000 μM + HSA and 10 μM + HSA markedly lowered fibrillation. A turbidity assay was developed by finding a maximum absorbance at 630 nm, far from curcumin’s peak absorbance. The results of this assay corroborated the ThT and TIF results. Studies addressing degradation kinetics of curcumin were consistent with findings of others; HSA markedly slowed spontaneous curcumin degradation.

Conclusions: During a 7 day period of aging at body temperature, low concentrations of curcumin markedly reduce the formation of amyloid fibrils of glucagon at alkaline pH. The addition of albumin to the curcumin further increases the effectiveness of curcumin by reducing spontaneous degradation of glucagon. Prior studies have shown that acid pH is known to favor rapid fibrillation of glucagon, while a pH of 10 nearly eliminates such fibrillation. By adding the polyphenol curcumin and reducing the pH to 9, both problems (fibrillation and degradation) are greatly minimized, suggesting that this formulation may be suitable for bihormonal closed loop treatment of persons with type 1 diabetes.

321

PERCEPTIONAL DISPARITIES AFFECT TYPE 2 DIABETES CARE AMONG ZUNI INDIANS

Sulahria AJ, Carroll C, Mals R, Burge MR. University of New Mexico Health Sciences Center, Albuquerque, NM.

Purpose of Study: The Zuni Pueblo is an endogamous group of Native Americans with a population of 11,000, and a high prevalence of T2D. We recruited 59 subjects with previously diagnosed T2D from the Zuni Health Initiative (ZHI). A 110 question survey exploring at-will allow quality evaluation of the role of mitochondrial function in IR

322

RELATIONSHIP BETWEEN TESTOSTERONE AND LIPOIDS BY DIABETES STATUS AMONG MEN IN A LARGE HOSPITAL DATABASE

Murray-Krezan C, Davis H, Burge MR. University of NM HSC, Albuquerque, NM.

Purpose of Study: Male testosterone concentrations have been shown to correlate negatively with serum triglyceride (TG) concentrations in some studies, and it is also known that diabetes is associated with alterations in TG and HDL cholesterol metabolism. It is not known whether diabetes (DM) status affects the relationship between serum testosterone and these serum lipid parameters. We hypothesized that testosterone levels have a stronger relationship with TG and HDL in the diabetic and prediabetic states as compared with the nondiabetic state.

Methods Used: We queried the Electronic Medical Record (EMR) of a large University Hospital for all adult men who received an A1c and a total testosterone (TT) determination within 6 months of each other between the years 2007 and 2011, and we also obtained the following covariates: age, diabetes status (nondiabetic, prediabetic, or diabetic), fasting lipids, ethnicity (Hispanic, or other), BMI, and the presence or absence of active androgen therapy. Linear regression models were fit to determine the relationship between TT, TG, HDL, and DM status.

Summary of Results: Our sample consisted of 455 men with A1c and TT within 6 months of each other. Mean age was 55 (SD=12) years, with 41% Hispanic, and 14% on androgen replacement therapy. Mean BMI was 31 (SD=8) kg/m², and 23% were nondiabetic. Univariate analyses indicated that DM status and the log of the TG/HDL ratio were independently associated with TT (A1c: F=3.26, p=0.03; log TG/HDL: t=-5.22, p<0.0001). We employed a multiple regression model for TT as a function of log TG/HDL, DM status, androgen therapy, BMI, ethnicity, age, and all of their two-way interactions (n=282 with no missing data). Only the main effects of log TG/HDL, BMI, and androgen therapy remained after adjusting for all others with the overall trend that TT decreased as log TG/HDL increased [β=-0.042 (95% CI = -0.083,0.0001)]. A further reduction in TT was observed for those on androgen therapy [β=-0.70 (95% CI=1.29,0.11)].

Conclusions: In this dataset derived from the Electronic Medical Record, diabetes status exerted no demonstrable effect on the relationship between total testosterone and the TG/HDL ratio in men after adjusting for age, BMI, ethnicity, and androgen replacement therapy.

323

PREVALENCE OF OBESITY, TOBACCO USE, AND DYSLIPIDEMIA IN VA GERIATRIC PATIENTS STRATIFIED BY AGE GROUP


Purpose of Study: Obesity, tobacco use, and dyslipidemia are well recognized risk factors for cardiovascular disease (CAD) and mortality in the geriatric population. The VA health care focuses on weight loss, smoking analyzed with respect to the following two questions and answers in greater depth: (1) How easy do you find eating the right foods to help you manage your diabetes? (A&B) Very Easy or Fairly Easy vs. (C&D) Difficult or Very Difficult; and (2) What do you find most difficult about your diabetes? (A&B) Healthy Diet or Exercising vs. (C-F) Doing Injections, Testing Glucose Levels, Other, or “I don’t find anything difficult.”

Summary of Results: 40F and 19M subjects participated, with age = 50±12 years, BMI = 33±9 kg/m2, duration T2D = 14±10 years, and A1c = 8±2%. Subjects who found Eating the Right Foods “Easier” had a lower A1c than those who found Eating the Right Foods “More Difficult” (n=25, 7.3±12.0% vs. n=32, 8.5±2.0%, p<0.05). Additionally, fasting triglycerides were reduced among those who found Diet or Exercise to be the “Most Difficult” aspects of diabetes care compared with other aspects (n=27, 155±77 mg/dl vs. n=30, 239±201 mg/dl, p<0.05).

Conclusions: This study demonstrates that disease perceptions may affect important clinical indicators among Zuni Pueblo members with T2D.

202

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cessation and other CAD risks reduction. However, prevalence of obesity, tobacco use, dyslipidemia, and their association with life span in the VA geriatric patients have not been fully studied. We seek to determine the prevalence of these risk factors in different age groups of VA patients.

Methods Used: A retrospective chart review was conducted on patients aged 65 to 90. We set 5 age groups with increments of 5 years. The mean value of BMI, total cholesterol (TC), LDL, HDL, triglyceride (TG), and the ratio of TC/HDL and TG/HDL were compared among groups by ANOVA. The percentage of smokers in each group was analyzed by the Chi-square test.

Summary of Results: A previous cohort study of population with ages of 50 to 71 found lower mortality rate in people with bmi of 25, compared to those with either higher or lower BMI. Higher mortality with lower BMI is due to non CAD related comorbidity. Our results indicated that patients with near normal BMI, non smoking status, lower values of TC, LDL, TG, and higher value of HDL tended to have longer life span. Similarly, the ratio of TC/HDL and TG/HDL had an inverse relationship with age. This suggests the mortality benefit of weight control, non smoking, and lipid management. study is limited by cross section design and male majority.

Table 1: Comparison of Clinical Risk Factors among Different Age Groups

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<thead>
<tr>
<th>Age Range</th>
<th>Number of Patients</th>
<th>BMI</th>
<th>TC</th>
<th>LDL</th>
<th>HDL</th>
<th>TG</th>
<th>TC/HDL</th>
<th>TG/HDL</th>
<th>Smoker %</th>
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</thead>
<tbody>
<tr>
<td>51-55</td>
<td>150</td>
<td>25</td>
<td>180</td>
<td>100</td>
<td>60</td>
<td>120</td>
<td>1.5</td>
<td>0.5</td>
<td>10%</td>
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<tr>
<td>56-60</td>
<td>180</td>
<td>26</td>
<td>200</td>
<td>120</td>
<td>70</td>
<td>150</td>
<td>1.4</td>
<td>0.4</td>
<td>15%</td>
</tr>
<tr>
<td>61-65</td>
<td>210</td>
<td>28</td>
<td>220</td>
<td>140</td>
<td>80</td>
<td>180</td>
<td>1.3</td>
<td>0.3</td>
<td>20%</td>
</tr>
<tr>
<td>66-70</td>
<td>240</td>
<td>30</td>
<td>240</td>
<td>160</td>
<td>90</td>
<td>200</td>
<td>1.2</td>
<td>0.2</td>
<td>25%</td>
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<tr>
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<td>270</td>
<td>35</td>
<td>260</td>
<td>180</td>
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<td>220</td>
<td>1.1</td>
<td>0.1</td>
<td>30%</td>
</tr>
</tbody>
</table>

Conclusions: The results showed that the prevalence of obesity, tobacco use, dyslipidemia, and their association with life span in the VA geriatric patients have not been fully studied. We seek to determine the prevalence of these risk factors in different age groups of VA patients.

RISK FACTORS FOR PERSISTENT DIABETIC MACULAR EDEMA

Diep T1, Tsui I2,1. David Geffen School of Medicine at UCLA, Los Angeles, CA.

Purpose of Study: Diabetic macular edema (DME) is a major microvascular complication of diabetes mellitus and the leading cause of visual impairment in the diabetic population. Its multifactorial pathogenesis, including metabolic abnormalities such as chronic hyperglycemia, hypertension, and other systemic and ocular risk factors, is believed to damage the blood-retinal barrier, thereby leading to increased fluid extravasation and accumulation within the macula. Inflammation and vascular dysfunction compromises the state of retinal neurons, thus causing loss of visual acuity. The purpose of this study was to comprehensively and systematically review the literature for the clinical risk factors in persistent DME.

Methods Used: A literature search was performed using PubMed to look for risk factors and treatment response in persistent DME. Selected relevant studies were identified and classified according to pathophysiology or clinical relevance for inclusion in this review. Priority was given to larger, randomized studies; single case reports, editorials, and non-English articles were excluded.

Summary of Results: A total of 65 studies and articles were included in this review. Systemic factors found to increase the incidence and risk of DME were: race and ethnicity, glycemic control (including duration of diabetes, Hba1c level, pregnancy, and insulin treatment), hypertension, dyslipidemia, nephropathy and proteinuria, anemia, sleep apnea, and the use of glatiramer acetate. Other factors found to increase the risk of DME were: age, duration of diabetes, hypertension, hyperlipidemia, obesity, smoking, and the use of certain medications. The results showed that the prevalence of obesity, tobacco use, dyslipidemia, and their association with life span in the VA geriatric patients have not been fully studied. We seek to determine the prevalence of these risk factors in different age groups of VA patients.

Conclusions: The results showed that the prevalence of obesity, tobacco use, dyslipidemia, and their association with life span in the VA geriatric patients have not been fully studied. We seek to determine the prevalence of these risk factors in different age groups of VA patients.

ASSOCIATION BETWEEN HIGHER FASTING SERUM GLUCOSE LEVELS AND THE PATTERN OF LOWER REGIONAL GRAY MATTER VOLUMES IN COGNITIVELY NORMAL ADULTS

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Purpose of Study: In Alzheimer’s Disease (AD) patients, characteristic findings are seen with structural magnetic resonance imaging (MRI) including global atrophy as well as regional reductions in gray matter volume (GMV) in prefrontal, temporoparietal, and orbitofrontal cortices. Additionally, negative correlations between peripheral insulin levels and regional GMV are seen in insulin resistant subjects in the middle temporal gyrus, an area associated with verbal fluency and declarative memory. The current study investigated whether elevated fasting glucose (FGS) levels were associated with lower GMV in brain areas that have been preferentially affected by AD. This association was further quantitatively characterized between carrier and non-carrier groups of the apolipoprotein E (APOE) ε4 allele.

Methods Used: SPM, an automated brain mapping computer package, was used to spatially normalize individual brains to a standard brain template to obtain GMV maps from MRI and to examine correlations between higher FGS levels and lower structural MRI GMV measurements in 118 cognitively normal, non-diabetic individuals 64:16 years of age, including 59 APOE ε4 non-carriers and 59 carriers.

Summary of Results: As predicted, significant correlations were seen between higher levels of FSG and lower GMV in AD-affected regions such as left parietal and occipital lobes and left and right frontal and temporal lobes. Negative correlations between FSG and regional GMV in the middle temporal gyrifound significant findings seen in insulin resistant subjects. These associations are also seen in AD-related areas in both carriers and non-carriers.

Conclusions: Higher FGS levels in cognitively normal, non-diabetic older adults are associated with lower GMV in AD-related brain areas, confirming elevated FSG may be associated with AD risk. Demonstration of this association in both APOE ε4 subgroups suggests the risk associated with FSG may be independent of APOE ε4 status. Lastly, this study encourages the consideration of elevated FSG and other indicators of glucose control as targets for AD prevention trials, complementing the findings previously established with fluorodeoxyglucose positron emission tomography neuroimaging.

UTILITY OF FDG-PET IN THE EVALUATION OF LARGE-JOINT OSTEOARTHRITIS

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Purpose of Study: To evaluate 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) imaging as a modality for the diagnosis and classification of osteoarthritis (OA) of large joints and specifically the shoulder, hip, and knee joints. We also aim to assess the value of semiquantitative PET in predicting OA using SUV as a marker for the evaluation of osteoarthritic joint degeneration.

Methods Used: Patients undergoing whole body FDG-PET imaging for other primary disease were consented per Institutional Review Board. Patients were excluded if they had a history of primary bone tumors or diseases, osseous metastases, hyperparathyroidism, collagen disorders, or other inflammatory joint conditions. Included patients were given a questionnaire evaluating pain, stiffness, and physical function of their shoulders, hips, and knees. Each response was given a score based on a five-point Likert scale. Radiographic OA grading was performed using CT scout views of the studied joints and scored on a modified Kellgren Lawrence scale. PET OA grading was performed through visual and SUV assessment of FDG uptake in axial images by two evaluators.
Summary of Results: 60 patients have consented for the study, with 16 excluded per exclusion criteria. 110 joints have been evaluated to date. The average age of the evaluated patients was 61 years old (range 42-76) and the male to female ratio was 2:3. PET imaging interobserver correlation was found to be 0.74 (p < 0.0001) and PET visual scale to SUV correlation 0.89 (p < 0.0001). PET appears to better correlate with the self-reported symptoms than radiographic scoring (Total score r = 0.33 - 0.34 versus 0.2 - 0.28) although both are significant (p < 0.05). Visual PET scoring correlates with all subcategories of self-reported symptoms (p < 0.05) and PET correlates better with pain, stiffness, and physical dysfunction scores than radiographic scoring (r = 0.21 - 0.36 versus 0.09 - 0.31).

Conclusions: Increased FDG uptake assessed using visual and semiquantitative approaches significantly correlates with both self-reported symptoms and radiographic findings of OA. FDG-PET may provide a novel methodology for the diagnosis and evaluation of joint degeneration in large joint OA.

TARGETED DATA INDEPENDENT ACQUISITION FOR MASS SPECTROSCOPY PROTEOMICS

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Purpose of Study: Mass spectroscopy proteomics has made large strides towards reproducible measurement of large suites of proteins for biomarker assays. In Data Independent Acquisition (DIA), protease-digested samples are analyzed by liquid chromatography-coupled tandem mass spectrometers (LC-MS/MS). Unfragmented peptide ions (precursors) are detected (MS1), isolated, and then fragmented to yield characteristic spectra (MS2). Precursors are isolated and fragmented in consecutive, regularly-sized mass-to-charge (m/z) windows. Proteins are identified by detecting characteristic peptides through MS2 comparison to spectral libraries. Larger isolation windows can cover more precursors but increase noise and lower detection success. Peptides have poorly understood “detectability” characteristics. Spectral libraries such as Bibliospec offer peptide “replicate scores” as untested proxies for DIA detectability.

We propose a Targeted Data Independent Acquisition (TDIA) method. In TDIA, the positions and sizes of isolation windows are optimized by computer algorithm to maximize desired precursor coverage and minimize noise. We create a first generation TDIA program and investigate the relationship between protein abundance, Bibliospec score, and peptide “detectability.”

Methods Used: S. cerevisiae lysate was analyzed by LC-MS/MS using DIA (450-700 m/z range, 10 m/z window width) and TDIA (25 windows, avg 9.1 m/z width). In TDIA, 667 precursor peptides uniquely representative of 50 proteins were chosen. TDIA optimized 10 m/z windows for highest detected precursor coverage density, mandated >2 peptides per protein, and resized windows to lower noise.

Summary of Results: Of the 50 chosen proteins TDIA detected 35 (68% detection of covered peptides) and DIA detected 27 (52%). Both indicate “detectability” highly correlated to abundance. Detectability at 9 and 10 m/z windows drops precipitously for Bibliospec scores < 3.

Conclusions: TDIA is a viable method for measuring large suites of proteins. Shrinking precursor isolation windows from 10 to 9 m/z may offer significant benefits. Further research must be done to model the relationship between abundance, Bibliospec score, and detectability in terms of the maximum isolation window size. This model can then be incorporated into the algorithm to optimize window position and size for a given set of targeted proteins.

DIAGNOSTIC STAGING OF LIMBAL STEM CELL DEFICIENCY OF THE CORNEA

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Purpose of Study: Limbal stem cell deficiency (LSCD) is a clinically diagnosed blinding disorder that is caused by the incapability of normal corneal epithelium regeneration by limbal stem cells. Our objective is to elucidate the changes in corneal cytology and epithelial marker expression in varying stages of LSCD to establish a more quantifiable diagnosis of LSCD.

Methods Used: A total of 16 eyes diagnosed clinically with LSCD were selected for impression cytology and in vivo confocal microscopy (ICM) examination. 10 eyes with normal presentation on slit lamp examination were selected for ICM examination. Volume depth scans of the central cornea as well as the superior, nasal, inferior, and temporal limbus were collected with the Heidelberg Retina Tomograph III Rostock Corneal Module (Heidelberg Engineering GmbH, Dosenheim, Germany). Epithelial layer thickness, basal cell density, and basal cell diameter were measured in images demonstrating clear epithelial cell morphology. Previously collected LSCD impression cytology specimens were stained of PAP staining and then incubated with rabbit anti-K12 (corneal marker), mouse anti-K13 (conjunctival marker) antibodies (Santa Cruz Biotechnology, Santa Cruz, CA), and appropriate secondary antibodies thereafter.

Summary of Results: Cytokeratin (K) 13 negative staining was demonstrated in 2 eyes initially clinically diagnosed as LSCD at the time of impression cytology and ICM but resolved to alternate pathology at a later date.

Conclusions: Presence of K13 may be vital in ruling out true LSCD despite positive clinical presentation. Our preliminary data show that ICM offers an accurate method of identifying and quantitatively measuring significant changes in the corneal epithelium in LSCD eyes.

INCREASING PRESCRIPTION MEDICATION ADHERENCE AMONG VULNERABLE SENIORS

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Purpose of Study: Non-adherence with prescription medication regimens is a documented problem among seniors in the United States. This problem may be magnified in King County, WA, as it is home to one of the most diverse zip codes in the nation. Seniors in this racially, ethnically and linguistically diverse population are faced with additional challenges to receiving good healthcare. The purpose of this project was to increase adherence with prescription medication treatment plans among vulnerable seniors through patient education and by empowering seniors to be peer educators.

Methods Used: Patients, providers and pharmacists were consulted and interactions among patients and providers were observed. Relevant literature was reviewed to determine the most effective way of reaching seniors and as a resource in designing educational materials. Staff persons at several non-profit organizations that work with vulnerable seniors were consulted. Incentive was high enough to attract staff and an organization was chosen to host a pilot activity. The activity, conducted in Spanish, included lecture, discussion, and group exercises. A handout, consisting of a true/false quiz, talking points to be used with peers, and a take-home message, was developed and printed in Spanish and distributed to participants.

Summary of Results: The pilot educational activity was well-received and quickly expanded into an animated discussion among over forty participants about medication adherence. Participants relished the opportunity to practice using the peer talking points with each other and stated that they will use the talking points in the future. The organization’s group leader requested that the activity be duplicated at other locations throughout King County.

Conclusions: The interest in this activity among many of the non-profit organizations that work with vulnerable seniors as well as the enthusiasm exhibited by the participants confirms that there is need and potential to expand this project. One way of doing so is to establish a service-learning group for UW Health Sciences students that would use the comprehensive work laid by this project to reach an extensive number of seniors throughout King County. To this end, the process of forming an interprofessional Registered Student Organization has been initiated.

PROMOTING UNDERSTANDING OF DEPRESSION AMONG OLDER ADULTS IN SANDBOINT, IDAHO

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Purpose of Study: Compared to members of other age groups, older adults with depression are less likely to receive treatment. Failure to treat depression among older adults has been linked to poorer health outcomes and increased...
healthcare costs. In Sandpoint, Idaho, citizens over age 65 compose 16.7% of the population (vs. 12.4% statewide and 13.3% nationally). Thus, issues affecting seniors are particularly pertinent. The purpose of this project was to promote understanding of depression among older adults to ensure that individuals affected by depression seek appropriate treatment.

Methods Used: Discussions with local clinicians led to the identification of older adults with depression as an appropriate target population. A literature review revealed two key barriers that discourage older adults from seeking care: 1) The misguided belief that depression is a normal part of aging, and 2) The stigma associated with depression. An educational campaign was undertaken to address these two barriers. An educational handout was developed. The handout included the two questions from the Patient Health Questionnaire 2, a tool shown to be highly sensitive for identifying major depression in adults over age 65. The handout was distributed and its contents were discussed at a breakfast event at the Sandpoint Senior Center. Summary of Results: Approximately 20 seniors attended the event. The handouts were distributed, and individual or small-group discussions about depression were held. Many were surprised to learn that depression is not a normal part of aging. The director of the Senior Center volunteered to continue the campaign into the future, ensuring continuity. She posted a copy of the handout in a prominent location and promised to call attention to the topic at upcoming events. She was also given copies of the handout to distribute.

Conclusions: The perception that depression is a normal part of aging and the stigma that older adults associate with depression represent two major barriers to care. Both of these barriers can be addressed with minimal investments of time and money through community-based educational interventions. Effective, sustained educational campaigns will help more seniors to seek appropriate care, ultimately reducing the community’s healthcare costs and improving health outcomes.

### Neonatology – Developmental Biology

Concurrent Session

8:00 AM Saturday, January 26, 2013

#### 331

**GRADED OXYGEN SATURATION TARGETS FOR PREMATURE INFANTS IN RELATION TO OUTCOMES**

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**Purpose of Study:** In recently concluded randomized controlled trials, use of low oxygen saturation targets from birth to 36 weeks postmenstrual age (PMA) in preterm infants < 28 weeks gestation was shown to decrease retinopathy of prematurity (ROP), but, with an increase in mortality as compared to high oxygen saturation targets (91-95%). Retinal metabolism and role of growth factors are different during vasoo proliferative and vasoproliferative phases of ROP. Prior to 2002, we used 89-94% as the oxygen saturation target in preterm infants < 1000 grams. We implemented graded oxygen saturation targets in 2002 (83-89% until 33 weeks PMA, 90-94% between 33-36 weeks PMA and >94% after 36 weeks PMA) while breathing oxygen. We report the results after implementation of graded oxygen saturation targets.

**Methods Used:** Maternal and neonatal data on infants born < 28 weeks from our prospectively entered database were collected as 2 cohorts - Group 1, before graded oxygen saturation targets and Group 2, after implementing graded oxygen saturation targets. The two cohorts were matched for birth weight.

**Summary of Results:** There were 190 patients in Group 1 and 182 in Group 2. The mean BW was 814±162 and 813±235 grams respectively and mean gestational age was 26 weeks in both groups. ROP and laser surgery rates significantly decreased between the two cohorts. There was no significant difference in mortality rate between the two groups (8.4 vs. 7.1%, p=0.32).

**Conclusions:** A significant decrease in ROP and laser surgery rates without any increase in mortality was observed with the use of graded oxygen saturation targets based on PMA, rather than just either low or high saturation target during the 2 distinct phases of ROP may be a better approach. Further studies are needed to test this hypothesis.
334

MATERNAL TOBACCO SMOKE EXPOSURE DIFFERENTIALLY ALTERS CANNABINOID RECEPTOR EXPRESSION IN OFFSPRING RAT ADIPOSE TISSUE
Treviranus I, Chengshe J, Wang Y, Fitzhugh M, Albertine K, Lane RH, Joss-Moore L. University of Utah, Salt Lake City, UT.

Purpose of Study: Fetal exposure to tobacco smoke causes obesity in adult humans and rodents. Obesity development depends in part on signaling through the endocannabinoid system (ECS). The ECS consists of types 1 and 2 cannabinoid receptors (CB1 and CB2), fatty acid anandamide hydrolase (FAAH) and the circulating endocannabinoids (anandamide and 2-AG). CB1 and CB2 likely contribute differently to the programming of obesity. We hypothesized that maternal tobacco smoke (MTS) exposure during pregnancy would alter the expression of CB1, CB2 and FAAH in the adipose tissue of female and male rats offspring at weaning.

Methods Used: Pregnant Sprague Dawley rats were exposed to tobacco smoke daily from embryonic day 11 to term. Pups were cross-fostered to a control dam. At weaning, female and male offspring subcutaneous (SAT) and visceral (VAT) adipose tissue samples were collected for quantification of CB1, CB2 and FAAH mRNA levels by real time RT-PCR and protein abundance by western blot.

Summary of Results: All results are relative to gender and age-matched controls. MTS decreased CB1 mRNA levels in SAT of female rats (90%*) with no effect on male rats. CB2 was unchanged in SAT of both genders. However, MTS decreased CB1 protein abundance in both male and female SAT and VAT (40-85%*). MTS did not alter Cnr1 in SAT of both genders (85%) and male (95%*) rats. Conversely, MTS increased CB2 protein abundance in both genders and depotss (3-5 fold*). MTS decreased Faah (FAAH gene) mRNA levels in VAT of females (80%*) with no changes in males, while MTS decreased Faah in SAT of both genders (60%). MTS also decreased the FAAH protein abundance in both male (50%*) and female VAT and SAT.

Conclusions: MTS differentially alters ECS components in the offspring. Interestingly, changes in the adipose tissue ECS arise before the onset of obesity in MTS offspring and may be an important mechanism involved in programming of obesity. MTS decreased CB1 protein abundance in both adipose depots of the offspring. Similarly, obese subjects have decreased CB1 content in the adipose tissue and high serum levels of endocannabinoids. Thus, we speculate that serum endocannabinoids in MTS offspring may be increased inducing CB1 down regulation.

335

EFFECTS OF ERYTHROPOIETIN AND DARBEPOETIN ON HUMAN FETAL NEUROGENESIS
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Purpose of Study: Erythropoietin (Epo) and darbepoetin (Darbe) are currently being evaluated for their potential as neuroprotective agents for premature infants. Animal studies have shown positive effects of Epo and Darbe on fetal neurogenesis and on decreased neuronal apoptosis. A minimal number of studies have evaluated the effects of Epo and Darbe on developing human neural tissue. We evaluated the ability of Epo and Darbe to stimulate neurogenesis in developing human fetal brain, and related changes in genetic expression and histology.

Methods Used: Fetal brain tissue samples from 10 to 17 weeks gestation were isolated in single cell suspensions and plated at 5 x 10⁴ cells/mL. Cells were grown in basic growth medium with 10% fetal calf serum and 1% antimicrobials for 10 days with 0, 0.1, 1, or 10 U/mL Epo, or in 10, 100, or 1,000 ng/mL Darbe. Cells were removed with Trypsin and counted. Treatments were administered once daily from embryonic day 6 until postnatal day 21 (PND 21). The pups were sacrificed at term and were breast fed ad libitum. At PND21 the pups were sacrificed and BMDMSCs isolated. Cell surface marker analysis (immunostaining and flow-cytometry), PAFR binding (ligand binding assay), and protein expression (Western blotting) were performed at passage 3. Prostaglycanin metabolites such as 8-keto-PGF1α, TxA2 and the LTES were measured with specific ELISAs. All data were analyzed by t test with p < 0.05.

Summary of Results: Perinatal nicotine exposure up-regulated PAFR protein expression by 36% in agreement with increased PAFR binding in nicotine exposed cells. Nicotine exposure also resulted in COX1 protein down-regulation of suppressors of inflammation by BMDMSCs following perinatal nicotine exposure at least partially explain increased cardiorespiratory morbidity in perinatally smoke exposed offspring.

336

IN UTERO NICOTINE EXPOSURE MODULATES EXPRESSION OF INFLAMMATORY PROTEINS BY BONE MARROW DERIVED MESENCHYAL STEM CELLS: RELEVANCE TO THE INFLAMMATORY RESPONSE
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Purpose of Study: Perinatal exposure to maternal smoking is associated with adverse outcome in offspring, including increased predisposition to chronic lung disease, asthma, endotoxemia and cardiovascular disease. However, the underlying mechanisms remain poorly understood. It is well established that bone-marrow derived mesenchymal stem cells (BMDMScs) are important modulators of disease processes, including chronic lung and heart diseases. Smoke exposure is known to modulate a variety of stem cell responses including increased platelet activating factor (PAFr) receptor expression which is an important modulator of cell proliferation, inflammation and pulmonary contractile responses. However, whether PAFR expression is affected, and whether this modulates in utero smoke exposure-induced increased morbidity is not known.

Methods Used: Pregnant rats were divided into 4 groups: Control (placebo); Nic 1mg/kg; sc; Nic 1 mg/kg; sc+RGZ 3mg/kg,i.p, or RGZ 3mg/kg,i.p. Treatments were administered once daily from embryonic day 6 until postnatal day21(PND 21). The pups were sacrificed at term and were breast fed ad libitum. At PND21 the pups were sacrificed and BMDMScs isolated. Cell surface marker analysis (immunostaining and flow-cytometry), PAFR binding (ligand binding assay), and protein expression (Western blotting) were performed at passage 3. Prostaglycanin metabolites such as 6-keto-PGF1α, TxA2 and the LTES were measured with specific ELISAs. All data were analyzed by t test with p < 0.05.

Summary of Results: Perinatal nicotine exposure up-regulated PAFR protein expression by 36% in agreement with increased PAFR binding in nicotine exposed cells. Nicotine exposure also resulted in COX1 protein down-regulation by 55%, and an increased pro-inflammatory prostacyclin profile.

Conclusions: Up-regulation of inflammatory proteins and down regulation of suppressors of inflammation by BMDMScs following perinatal nicotine exposure at least partially explain increased cardiorespiratory morbidity in perinatally smoke exposed offspring.

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and inflammatory chemokine biomarkers. We also wanted to evaluate risk factors for BOS and RAS.

**Methods Used:** Bilateral lung and heart/lung transplant recipients were included in this retrospective, observational cohort study. CLAD was diagnosed using standard spirometric criteria. CLAD subjects were divided into obstructive (BOS phenotype) and nonobstructive. Nonobstructed CLAD patients were further divided into restrictive (RAS phenotype) or indeterminate groups. We examined CT scans for key findings. Bronchoalveolar lavage fluid CXCR3 chemokine concentrations were determined by a bead immunoassay and compared between groups. We determined the impact of CLAD phenotypes on survival with Kaplan-Meier plots and used Cox Proportional Hazard models to assess risk factors.

**Summary of Results:** LB, severe PGD, Pseudomonas, and Aspergillus all appear to be unique risk factors for BOS, but not RAS. Air trapping (78%) and bronchiectasis were the most common CT findings for BOS, while pleural fibrosis (35%) and parenchymal fibrosis (75%) were more commonly seen for RAS. Both BOS and RAS were associated with a worse post-transplant survival compared to no CLAD. After diagnosis, the RAS phenotype had a more rapid progression to death compared to no CLAD. CLAD was diagnosed by changes in CT findings for BOS, while pleural fibrosis (35%) and parenchymal fibrosis (75%) were more commonly seen for RAS. Both BOS and RAS were associated with a worse post-transplant survival compared to no CLAD. After diagnosis, the RAS phenotype had a more rapid progression to death compared to no CLAD. After diagnosis, the RAS phenotype had a more rapid progression to death compared to no CLAD. After diagnosis, the RAS phenotype had a more rapid progression to death compared to no CLAD. After diagnosis, the RAS phenotype had a more rapid progression to death compared to no CLAD. After diagnosis, the RAS phenotype had a more rapid progression to death compared to no CLAD. After diagnosis, the RAS phenotype had a more rapid progression to death compared to no CLAD.

**Conclusions:** While BOS is the most common form of CLAD, a separate "restrictive" phenotype can be distinguished by spirometry. RAS appears to be associated with a more inflammatory chemokine milieu and a more rapid progression to death after diagnosis. Limitations of the study include a low sample size in the RAS group, however with an enlarged sample size, we hope to further investigate if inflammatory chemokines can be used to predict survival.

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**INTERLEUKIN-33 PLAYS AN IMPORTANT ROLE IN ANTIGEN-DEPENDENT AND ANTIGEN-INDEPENDENT ASTHMA-LIKE PHENOTYPE**

Li J, Magat J, Thomas J, Dmouchel J, Bighey T. UCSF, La Jolla, CA.

**Purpose of Study:** Interleukin-33 (IL-33) is a cytokine associated with allergic inflammation and is constitutively expressed in structural cells such as bronchial and alveolar epithelial cells. Recent GWAS studies showed IL-33 and its receptor, ST2, polymorphisms are strongly associated with asthma. Here we address the role of IL-33 in the induction of asthma-like phenotype in antigen-dependent and antigen-independent model.

**Methods Used:** C57BL/6, IL-33 -/-, ST2 -/-, and MyD88 -/- male mice were studied. In the antigen-dependent model, mice were given intraperitoneal ovalbumin (OVA) with alum on days 0 and 7. Intratracheally OVA was administered on days 17-20. In the antigen-independent model, mice were administered 500 ng of intratracheal IL-33 per day for 4 days. Airway resistance was measured and methacholine dose-response curves were performed, followed by bronchoalveolar lavage (BAL), cytokine measurements, lung histology, and immunohistochemistry.

**Summary of Results:** IL-33 induced airway hyperresponsiveness and eosinophilic airway inflammation similar to OVA model. In BAL, GM-CSF, IL-5, and IL-13 levels were greater in the IL-33 group compared with OVA group. In the IL-33 group, IL-33 amplifies its own protein expression in airway epithelium in an autocrine or paracrine manner. IL-33 and ST2 were increased in mRNA and protein levels in lung tissues in both IL-33 and OVA groups. In IL-33 -/- mice, ST2 mRNA expression levels in the lung tissue increased after pulmonary challenge with IL-33, but not OVA. Airway hyperresponsiveness was partially induced in IL-33 -/- mice after IL-33, but not OVA. In ST2 -/- and MyD88 -/- mice, pulmonary challenge with IL-33 or OVA did not induce airway hyperresponsiveness or eosinophilic inflammation.

**Conclusions:** IL-33 is sufficient to induce airway hyperresponsiveness and eosinophilic inflammation independent of antigen. The IL-33 induced asthma-like phenotype is similar to the OVA induced antigen dependent phenotype in a mouse model. IL-33 is necessary for OVA induced allergic asthma-like model. Our data suggest that IL-33/ST2 pathway plays an important role in regulation of both antigen independent and antigen dependent asthma-like phenotype. ST2 and MyD88 are both necessary to mediate the IL-33 signal. IL-33/ST2 pathway may be a rational therapeutic target in asthma.
The presence of CYP3A4*22 was associated with improved asthma control scores by 2.1 points (95% CI: 0.5-3.8).

Conclusions: The presence of CYP3A4*22, which is associated with decreased hepatic CYP3A activity in vivo, was accompanied by improved asthma control among FP treated children. Decreased CYP3A4 activity may improve asthma control with inhaled FP.

ROLE OF IGF-1 IN FIBROBLAST COLLAGEN GEL CONTRACTION

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Purpose of Study: The insulin-like growth factor (IGF)-1 pathway is an important determinant of survival and proliferation in many cells. We previously demonstrated that blockade of the IGF-1 pathway in a murine model of lung fibrosis improved outcome and hastened resolution of fibrosis. We also showed that blockade of the IGF-1 pathway decreased the number of lung myofibroblasts, the cell type responsible for fibrotic lesions. Our preliminary data showed that mouse lung fibroblasts (MLFs) treated with IGF-1 in vitro increased expression of α-smooth muscle actin (SMA) contractile fibers, a hallmark of myofibroblasts. Therefore, we hypothesized that IGF-1 activates fibroblasts to myofibroblasts in the lung and leads to increased contractility.

Methods Used: We used a collagen type-I gel contraction assay to study fibroblast contractility. Mouse embryonic fibroblast cell line (3T3) or primary MLFs were suspended in a collagen type-I solution and loaded into capillary tubes under six conditions: (i) serum free, no cells (negative control); (ii) serum free, cells (baseline control); (iii) serum free, cells + IGF-1; (iv) serum free, cells + transforming growth factor (TGF)B1; (v) serum free, cells + IGF-1 + TGFB1; and (vi) 10% serum, with cells (positive control). Gel lengths were measured at 0 and 48h time points. Contractility was defined as the ratio of capillary gel length at 48-hours to initial length.

Summary of Results: We did not find a significant difference in mean contractility of IGF-1-treated 3T3 cells compared to baseline control (92±2.1 vs. 97±1.9, n=4). There was no significant synergistic effect of IGF-1 and pro-fibrotic cytokine TGFβ1 compared to TGFβ1 alone (93±2.3 vs. 94±3.1, n=7, p=0.0002; n=4). Similar results were found in experimentation using MLFs in place of 3T3 cells.

Conclusions: Despite an increase in contractile α-SMA fibers, IGF-1 did not enhance fibroblast contractility in vitro. IGF-1 may have other effects on fibroblast activation, including pro-survival signals, proliferation, or extracellular matrix production. Other cytokines present in vivo may be necessary to enhance the effect of IGF-1 on fibroblasts.

COST SAVINGS OF AN ALGORITHM FOR ALLOCATION OF ENDOCRINE SURGERY PATIENTS TO THE APPROPRIATE MEDICAL FACILITY BASED ON PERI-OPERATIVE RISK STRATIFICATION

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Purpose of Study: There has been a recent trend in surgery to shift more patients to the outpatient setting whenever safe and possible in order to optimize resource utilization. We describe the influence on costs of an algorithm developed by the UCLA Section of Endocrine Surgery for the allocation of endocrine surgery patients to the appropriate medical facility based on peri-operative risk stratification.

Methods Used: The algorithm uses case risk factors to determine the appropriate medical facility for each patient. High complexity patients are allocated to a tertiary care inpatient facility for high complexity cases, intermediate complexity cases to a community inpatient facility, and low complexity cases to an outpatient facility. The mean costs per case in the community inpatient and outpatient facilities were compared relative to the cost per case in the tertiary care center.

Summary of Results: For all cases combined, there was a 14% cost savings in the community inpatient facility and a 58% cost savings in the outpatient facility (p < 0.0001). For thyroid lobectomies, there was an 18% cost savings in the community inpatient facility and a 53% cost savings in the outpatient facility (p < 0.0001). For parathyroidectomies, there was a 29% cost savings in the community inpatient facility and a 56% cost savings in the outpatient facility (p < 0.0001).

Conclusions: An algorithm for the allocation of surgery patients to the appropriate medical facility based on peri-operative stratification can result in substantial cost savings.

INFLAMMATORY MARKER MCP-1 ELEVATED IN RAT BRAIN FOLLOWING TRAUMA HEMORRHAGIC SHOCK

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Purpose of Study: This study was undertaken to delineate the inflammatory response induced in the rat brain by traumatic brain injury (TBI). Inflammation in the brain is important in the pathophysiology of TBI. MCP-1 is a known inflammatory marker of the brain. We investigated the role of MCP-1 in the evolution of TBI by determining whether the expression of MCP-1 is altered in the brain following TBI.

Methods Used: Male Sprague-Dawley rats were subjected to traumatic brain injury by controlled compression (n=7). Rats were divided into two groups: control (n=7) and TBI (n=7). The rats were sacrificed at 24 hours post-injury, and brain tissue was collected for further analysis. The expression of MCP-1 was determined by Western blot analysis.

Summary of Results: The expression of MCP-1 was significantly increased in the TBI group compared to the control group (p < 0.05). This increase was observed in the peri-injury region of the brain, specifically in the regions that showed evidence of tissue damage.

Conclusions: These findings suggest that MCP-1 is an important inflammatory marker in the brain following TBI, and its expression can be used to monitor the severity and progression of brain injury.
Purpose of Study: Systemic inflammatory response syndrome (SIRS) following severe trauma with hemorrhagic shock (T/HS) contributes to increased morbidity and mortality in resuscitated patients. Though T/HS and SIRS have been studied extensively in liver, lung and kidneys, the inflammatory status of the brain following T/HS remains largely undefined. Elevated concentration of monocyte chemotactic protein-1 (MCP-1), as seen after systemic infection-induced inflammation, has been established as a reliable marker of neuroinflammation. We hypothesized that MCP-1 concentration in the brain would increase in rats subjected to trauma and hemorrhagic shock.

Methods Used: Rats were subjected to T/HS (laparotomy, hypovolemic shock to MAP of 30 mmHg for 45 minutes) and resuscitated with shed blood. Brains were dissected and homogenized in their entirety. Plasma fraction of whole blood was collected from each animal. MCP-1 concentration was determined by ELISA and normalized to total protein concentration in the sample. Significance was tested using Student’s t-Test.

Summary of Results: MCP-1 concentration significantly increased in plasma (p=0.04) and whole brain homogenate (p=0.009) in the T/HS group when compared to controls.

Conclusions: Animals in the T/HS group sustained sufficient injury to cause systemic inflammation as evidenced by elevated plasma MCP-1 concentration. Furthermore, elevated whole brain homogenate MCP-1 concentration in the T/HS group suggests the presence of neuroinflammation as early as three hours post shock. Additional study is required to determine the neuroinflammatory peak following T/HS and should include other markers as well as multiple time points for comparison.

PHOTOPLETHYSMOGRAPHY AS A RELIABLE TOOL IN THE MEASUREMENT OF HEMODYNAMICS IN TISSUE

Ramirez MD. *UCSD School of Medicine, La Jolla, CA and UCSD Medical Center, San Diego, CA.

Purpose of Study: There are few noninvasive tools useful for the measurement of hemodynamics of tissue required to diagnose chronic compartment syndromes (CCS). Photoplethysmography (PPG) has been gaining increasing attention as being a useful tool for measurement. This study attempts to provide evidence for PPG’s utility with two protocols exposing legs to varying pressure. We hypothesize that as changes in external pressure impede blood flow in microvasculature, PPG will record measurements significantly different from baseline measurements.

Methods Used: In an exercise protocol, subject’s leg was placed in a pressure chamber that applied increasing external pressure to the leg up to 40 mmHg, consistent with IP in CCS patients, while the subject performed repetitive dorsiflexion. The opposite control leg was held under constant 0 mmHg pressure and underwent the same regimen. Measurements of volumetric changes in blood (PPG) and oxygenation (NIRS) were recorded 2 min and 5 min post exercise. In the tourniquet protocol, a tourniquet was placed over the subject’s anterior compartment, and the pressure was increased in 20-sec intervals. Measurements were recorded at each interval under tourniquet. ANOVA and Tukeys HSD analyzed significant differences between exposed and nonexposed groups (p<0.05).

Summary of Results: In exercise protocol, PPG AC amplitude of group exposed to pressure was significantly different from control 2 min (p<0.05) and 5 min (p<0.01) post exercise. The AC amplitude significantly increased in experimental compared to control groups. In tourniquet protocol, a significant difference in PPG AC signal and NIRS oxygenation were observed at pressures 70 mmHg to 150 mmHg (p<0.001). The measurements were significantly decreased from baseline.

Conclusions: PPG was capable of detecting changes in blood perfusion of underlying microvasculature due to increasing levels of pressure. The increase in AC amplitude in the exercise protocol may be due to increased distensibility of vessels compensating for impeded flow. The decrease in PPG/NIRS measurements is likely due to impedance of vessels beyond compensation resulting in decreased perfusion. The ability of PPG to detect hemodynamic changes in muscle and skin provides strong evidence for PPG’s utility in measuring blood flow and diagnosing compartment syndromes.
in table below. Mean age was 53 years and total in-hospital survival was 40.4%. Predictors of mortality were female gender (P = 0.03) and ECMO run greater than 8 days (P = 0.01). There were no differences in neurological and renal complications in women compared to men.

Conclusions: As with all cardiac surgery, female gender is associated with higher mortality with ECMO. Longer ECMO run is also associated with poor outcomes. With an overall hospital survival rate greater than 40% our ECMO results show improvement over previous reports. Patients requiring ECMO for cardiac arrest showed higher survival rates that expected, while patients on ECMO for respiratory failure showed low survival.

348

MIDTERM OUTCOMES FOLLOWING OPEN AND ENDOVASCULAR REPAIR OF RUPTURED ABDOMINAL AORTIC ANEURYSM

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Purpose of Study: Endovascular repair of ruptured abdominal aortic aneurysm (rEVAR) has been shown to improve peri-operative outcomes as compared to open surgical repair. This report characterizes the midterm outcomes for all ruptured abdominal aortic aneurysm (rAAA) patients treated between July 2007 and February 10, 2012 to assess whether the early benefits of rEVAR continue to yield improved outcomes when compared with open surgical repair.

Methods Used: In an IRB approved prospective study, we evaluated all patients with rAAA that survived to hospital discharge. Outcome data such as hospital length of stay, destination at discharge, survival, type of surgical procedure, presence of hypotension, and demographics were evaluated using linear regression and multivariable analysis models. Patient survival was evaluated using Kaplan-Meier analysis and compared to a log-rank test.

Summary of Results: A total of 118 patients were admitted to our facility with the diagnosis of rAAA. 8 patients underwent comfort care and 4 died in the operating room prior to repair. Of the remaining 106 patients, 43 patients received open repair and 63 underwent rEVAR. 72 patients survived to discharge with 48% (21/43) of the open surgical group and 81% of the endovascular group surviving (51/63). Of those that survived to discharge, 51% (37/72) were discharged to home and 49% (35/72) were discharged to a skilled nursing facility. The majority of rEVAR patients were discharged to home at 65% (33/51) versus 19% (4/21) of the open repair group. 24 patients have died since their discharge from the hospital. Overall, the follow up rate was 84% (63/72) with 9 patients lost to follow up and an average length of follow-up of 22.8 months. Multivariable regression analysis showed that only the type of procedure performed is predictive of the discharge destination. Survival at midterm follow up had no appreciable correlation with the type of procedure performed, or the discharge destination.

Conclusions: The introduction of rEVAR has resulted in improvements in hospital survival of patients with rAAA and more patients able to be discharged to home than those who underwent open surgical repair. At midterm follow-up, however, the survival rates of rAAA patients were consistent, regardless of the repair method.

349

A MODEL OF COST EFFECTIVE SURGERY IN A RESOURCE POOR SETTING

Rattray K1,2, Gollogly P2, Tam T1. 1University of Washington, Seattle, WA and 2Children’s Surgical Centre, Phnom Penh, Cambodia.

Purpose of Study: Children’s Surgical Centre (CSC) provides free orthopedic, plastic, ophthalmological and general reconstructive surgical services to disabled people in Cambodia. This type of care is often regarded as too expensive and complex in poor countries and has had decades of neglect. Meanwhile need for surgical intervention, especially due to trauma, has dramatically risen. Our study evaluates the cost-effectiveness of our surgical service and training model that we believe can enable high quality care for patients to improve and prolong life.

Methods Used: Disability Adjust Life Years (DALYs) are the sum of years of life lost (YLL) from premature death due to disability plus the years of life lived with disability (YLD). The goal of treatment is to decrease both premature death and suffering from disability - in effect avert DALYs is the goal of medicine. In this study we calculated DALYs averted for 343 patients treated at CSC in January and March 2012. DALYs are a widely used method that allows us to compare treatment models in similar resource poor surgical settings such as Haiti, Sub-Saharan Africa and Southeast Asia.

Summary of Results: Our data over two months yielded 1785 DALYs averted and operating costs totaling $164,543; resulting in $99 per DALY averted. This was on the low end of the published range of $70-$230 per DALY averted from surgical intervention in low to middle income country hospitals and competitive with other basic public health efforts.

Conclusions: This study demonstrates the cost efficacy of reconstructive surgery in Cambodia. Past efforts to expand surgical services by (1) sending foreign doctors to hospitals for brief medical missions, (2) training foreign graduates in Western facilities or (3) sending floating surgical centers to poor countries have been tried and failed. CSC maintains a team of Cambodian surgical, nursing and physical therapy staff in Phnom Penh. Foreign experts of varied specialties rotate through CSC regularly and repeatedly. This allows for enhanced training and continuity of care while keeping total costs to a minimum. Our model suggests that reconstructive surgery should not be neglected when designing integrated health care services in a resource poor setting.

350

INCREASING LEISURE ACTIVITY PARTICIPATION THROUGH EDUCATION OF ITS BENEFITS FOR SENIOR CITIZENS OF ENNIS, MT

Meng G. University of Washington Medical School, Seattle, WA.

Purpose of Study: The importance of a community’s health, specifically elderly health and quality of life, is intimately tied to an active senior center. Recent research has shown the activities these facilities provide can help delay the effects of dementia and neurodegeneration. Ennis, MT, lacks a senior center although many of its elderly engage in lunches provided by Meals on Wheels at the town hall. The aims of the project was to educate these participants on the importance of keeping their minds active while introducing an after lunch activity center.

Methods Used: Studies show that when working in a rural setting, health programs are most effective when member enthusiasm, attendance, and engagement are high. Therefore, four lunches were attended to announce the project and speak with participants about activities of interest. Based on the seniors’ feedback, a game center was introduced at a lunchtime seminar. Montana trivia initiated the event followed by a presentation on the effectiveness of leisure activities on the aging brain. An optional game card game was also offered at the end.

Summary of Results: The event drew 22 senior citizens as well as activity coordinators from the local nursing facility. The initial signs of the project were encouraging as a higher than average number of people showed up for lunch and a few participants stated they would take the lead and encourage activities on a more regular basis. Additionally, a large calendar was organized to announce future events. The activity center was set up in a convenient location along with a brochure regarding presentation material so that the resources were easily accessible to all.

Conclusions: Even though research into the benefits of leisure activities and their ability to delay the onset of dementia is recent, beginning activities with seniors immediately can have an almost immediate impact on their health. Beyond the benefits regarding dementia, a heightened sense of community can assist with alleviation of loneliness, social isolation, and depression. Although this was only a basic step to strengthen community ties within Ennis, MT, it is important to increase awareness and initiate a broader goal of working towards a more permanent senior center.

351

EDUCATING SENIORS ON FALL PREVENTION IN EASTSOUND, WA

Senecal C. University of Washington, University Place, WA.
Purpose of Study: Eastsound, WA is the largest population center of Orcas Island in the San Juan Island chain. It is the cultural and economic center for the island. Demographically the population consists of 24.8% people over 65 years old. This is nearly twice the average for Washington State. It is estimated that one in three adults in this age group fall each year and falls account for the largest amount of injury related death in this population. In an effort to reduce the number of falls among this demographic a community specific fall prevention education program was developed.

Methods Used: Health professionals on Orcas were interviewed and it was established that falls among the elderly are commonly seen on the island. A literature review was conducted to determine evidence-based strategies for fall prevention. In order to provide the most effective materials seniors in the community were engaged to determine what teaching methods would be most useful in learning about fall prevention. From the literature review and discussions with seniors both a brochure targeted at a 6th grade reading level and presentation were developed and delivered to the community.

Summary of Results: Three main methods of prevention were highlighted in a brochure; exercise, prescription review and home hazard removal. While results of the program have not been assessed, early observations are encouraging. The brochures have been well received and are being offered to people at four locations in Eastsound, WA. They are also being specifically offered to patients that fit the target demographic at the Orcas Island Medical Center. The presentation given at the Orcas Island Senior Center was well attended by approximately 40 people. It consisted of a slideshow, visual demonstrations, question and answer session and an opportunity for feedback, which was overwhelmingly positive.

Conclusions: Fall injuries among adults over 65 are an increasing problem nationally as the population ages and even more prevalent in large senior communities like Eastsound, WA. By raising awareness for the issue and providing evidence based methods for reducing falls we can help reduce the burden of this on the senior community.

FREQUENTLY PRESCRIBED MEDICATIONS IMPLICATION ON BONE MINERAL DENSITY IN A VA POPULATION


Purpose of Study: Regular medication use is adversely associated with bone health. Current screening, preventive and therapeutic strategies for osteoporosis are mainly focused on the female population due to gender difference in susceptibility to bone loss. We sought to determine the association between chronic use of certain commonly prescribed medications and the bone mineral density t-scores in a predominantly male population.

Methods Used: 1,239 patient charts with bone mineral density readings between 2003 and 2008 were reviewed. Chronic medication use meant prescriptions for more than 12 months prior to the first BMD measurement. Pharmacy profiles were reviewed of the frequently prescribed medications, including oral steroids, steroid inhalers, thiazides, loop diuretics, coumadin, opiates, statins, proton pump inhibitors, and selective serotonin receptor inhibitors. Demographic data included age, sex, body mass index, tobacco use, and current alcohol consumption.

Mean femoral BMD t-scores from the initial BMD were used for comparison by ANOVA among groups or t-test between groups. Multivariate linear regression analysis was performed to determine the correlation between BMD scores and demographic parameters and use of medications.

Summary of Results: Mean age of patients was 64 years and mean BMI was 26.6. 84% were males. Use of OS, SI, loop diuretics, and Coumadin alone, and combination of loop diuretics and OS, PPI and SI, and PPI and OS were significantly associated with lower BMD. A Multivariate linear regression model showed significant inverse correlation between BMD scores and use, age, use of SI, loop diuretics and SSRI, while BMI was positively associated with BMD scores.

Conclusions: Our results indicate that chronic use of certain medications may be linked to significant bone loss. The potential adverse effects on bone health should be taken into consideration and measures to prevent bone loss and fractures may be necessary if long-term use is justified among geriatric patients. Our findings suggest the need for prospective population study to further evaluate potential long-term bone effects of widely prescribed medications and to determine the indication to initiate bone density screening among susceptible patients for early detection and intervention of osteoporosis.

COMMUNITY EXERCISE STATIONS TO IMPROVE OBESITY AND PHYSICAL INACTIVITY

Handran C. University of Washington, Seattle, WA.

Purpose of Study: Shelton, the county seat of Mason County, has a population of 13,176 and ranks 16th out of 47 in health behaviors among counties reporting health statistics. Specifically obesity and physical inactivity are the most significant health behavior concerns. The purpose of this project is to incorporate exercise stations throughout the pre-existing walking trail in order to improve the trail and allow the community to start a boot camp that can be motivational and provide variation in exercise.

Methods Used: Community members were asked if improving the trail and starting a boot camp would be helpful. A literature review was done to determine the best approach to raise awareness of the risks associated with obesity, how to motivate and promote individuals to exercise, and show that combined exercise training (aerobic and anaerobic) results in greater reductions of cardiovascular risk than aerobic training alone. Furthermore, 10 signs with different exercise combinations were made with community input and tailored for different fitness levels to incorporate on the walking path. After installing the exercise signs, the community was invited to try the trail with the use of the exercise signs.

Summary of Results: Thirty-five participants completed the trail with the use of the exercise stations and provided excellent feedback. According to the director of the Civic Center, the stations will be widely used by her and her clients along with the hopes of continuing a community-based boot camp. In addition, the physician I worked with is going to write prescriptions for his patients to use the stations and gradually build up their physical tolerance with the goal of reducing obesity, physical inactivity, and associated risk factors.

Conclusions: Through the use of a local physician, the civic center director, and community members a group boot camp may be sustainable. With continual use, reductions in obesity and physical inactivity may result. Furthermore, combined exercise programs (aerobic + anaerobic) have shown to have more significant health risk reductions than aerobic alone. Finally, literature supports utilizing community interventions such as community exercise programs to motivate individuals to exercise. Through this project the community may realize their health issues along with providing a cheap accessible way to work on impacting those health behaviors.

EDUCATION AND SUPPORT FOR HISPANIC WOMEN WITH GESTATIONAL DIABETES IN BREWSTER, WA

Harms MA. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Uncontrolled hyperglycemia in pregnancy is a major source of morbidity and mortality for mother and child, both in utero and later in development. The prevalence of Gestational diabetes mellitus (GDM) varies significantly among racially and ethnically diverse populations. Studies have demonstrated that Hispanic women have 2-4 times the risk of developing GDM as non-Hispanic White women. Brewster WA is a town with a population of 2,300 people, 50% of which self-identify as Hispanic. In order to assist Hispanic women with GDM learn more about diabetes during pregnancy, an evening of education and support was planned.

Methods Used: A literature review was conducted to determine effective and culturally appropriate methods for assisting patients to manage GDM. A nutritionist, diabetic educator, and bilingual health care providers were recruited to help plan the event. Clinics in the area were contacted and encouraged to invite use of those medications as well as their families. Informational handouts in Spanish were gathered for distribution following the event. During the two hour program, a healthy meal was prepared, a nutritionist delivered culturally conscious advice on diet, a diabetic educator distributed culturally appropriate advice on diet, and culturally appropriate methods for assisting patients to manage GDM.
promoted exercise and urged for accountability and support from within the family and between participants. Discussions including adverse outcomes of uncontrolled hyperglycemia, the value of diet and exercise, and “how insulin works” were moderated by providers.

**Summary of Results:** Four women with GDM along with their families attended the evening. The program increased awareness of the need to manage GDM, and empowered participants to do so through culturally sensitive education. Women with GDM were brought into contact with provider resources and other participants so that they could share in the excitement and challenge of making lifestyle changes. The event also brought together providers and sparked interest in starting a healthy cooking class for Brewster.

**Conclusions:** Two participants from the event were separately interviewed the following week during routine care and reported increased confidence in their ability to manage GDM and new appreciation for why it is important to do so. Early intervention to provide patient education for gestational diabetes is an important step in ending the intergenerational cycle of obesity and diabetes fueling the current epidemic.

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**355 SYNTHETIC β-GLUCOGALLIN REDUCES SORBITOL LEVELS IN TRANSGENIC MICE OVEREXRESSING ALDOSRE INHIBITOR RELATIONSHIP TO PHEOCHROMOCYTOMA IN A TRANSGENIC MOUSE STRAIN ENGINEERED TO OVER-EXPRESS HUMAN ALR2**

Snow A, Petrasch J. University of Colorado School of Medicine, Aurora, CO.

**Purpose of Study:** Diabetes mellitus is the leading cause of new blindness in the United States. Thus, advancing research in medical treatments that delays or inhibits the progression of diabetic eye diseases is important. There are currently several theories on the pathogenesis of diabetic eye disease, but the activation of the polyol pathway and its enzyme aldose reductase (ALR2) is of particular interest. We hypothesize that inhibition of ALR2 using ALR2 inhibitors (ARI) may be a good strategy to prevent diabetic eye disease. However, results from clinical trials of the current ARIs have failed due to toxicity or inadequate penetration of ARI in target tissues. In India, the Amla or Indian gooseberry (Emblica officinalis) is commonly used in traditional medicine for its preventive properties against diabetes. Specifically, it has been found that Amla contains 1-O-galloyl-D-glucogallin (β-glucogallin), which is a natural inhibitor of ALR2.

**Methods Used:** In this study, we investigated the effects of synthetic β-glucogallin on ex-ovo organ culture using lenses microdissected from a transgenic mouse strain engineered to over-express human ALR2. Our results demonstrate that synthetic β-glucogallin decreases sorbitol produced from ALR2 in lenses from this transgenic mouse model.

**Summary of Results:** Therefore, this study demonstrates that β-glucogallin is capable of penetrating into the intact lens tissue and effectively blocking ALR2 activity.

**Conclusions:** Our studies indicate that β-glucogallin deserves further study as a clinically effective aldose reductase inhibitor for the delay or prevention of diabetic eye disease.

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**356 MALIGNANT PHEOCHROMOCYTOMA - A DIAGNOSTIC AND treatment dilemma**

Jagha B, Navabi K, Burge M, Bouchonville M, Schade D, Davis M, Kerr K, Kaspner P. 1UMM Health Sciences Center, Albuquerque, NM and 2UMM Health Sciences Center, Albuquerque, NM.

**Case Report:** Malignant pheochromocytoma is a rare disease, curable only with surgery and characterized by a variable course. We report a case of a 43 year old female with hypertension presenting with a 6 month history of right abdominal pain, night sweats and fatigue. A CT scan at the referring institution showed a 16 cm right adrenal versus a renal cystic mass which was pursued by percutaneous biopsy; however, there was inadequate tissue for diagnosis. Upon referral, preoperative staging CT and MRI confirmed a large complex right upper quadrant mass thought to arise from the adrenal gland, an enlarged pericaval lymph node, a right pulmonary nodule and a 9 mm L1 vertebral body lesion. Screening labs showed a plasma normetanephrine 42 times the upper limit of normal, and urine normetanephrine 48 times the upper limit of normal.

The patient had a complicated right adrenalectomy, right nephrectomy, and IVC venotomy repair. No lymph node resection was undertaken due to the precarious intraoperative course. Pathology showed a pheochromocytoma with atypical features, 17 x 23 x 9 cm. Surgical margins were negative for tumor, and no vascular or capsular invasion was seen. The PASS score was less than 4. Following initial surgery, a diagnosis of malignant pheochromocytoma could not be made; however, follow up showed persistent normetanephrine elevation. PET/CT scan and In-111 pentetate tin scan showed an enlarging cluster of lymph nodes consistent with metastatic disease in the aortocaval region, multiple pulmonary nodules consistent with metastatic lesions, and a probable L1 lytic lesion with extension into the spinal canal. She was not felt to be a candidate for additional surgical resection and therefore is proceeding with radiation to her L1 lesion and chemotherapy with cyclophosphamide, vincristine, and dacarbazine (CVD).

The described case of malignant pheochromocytoma poses a treatment dilemma given the progressive disease and surgical unresectability. We will present a review of the literature regarding genetic testing, prognostic indicators and therapeutic interventions currently available as well as potential novel therapies.

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**357 PAPILLARY THYROID CARCINOMA ARISING IN STRUMA OVARI**

Navabi K1, Bouchonville M2, Burge M1, Jagha B1, Spafford M2, Saxon S2, Kaspner P1. 1University of New Mexico Health Sciences Center, Albuquerque, NM and 2University of New Mexico Health Sciences Center, Albuquerque, NM.

**Case Report:** Malignant struma ovarii is a very rare form of teratoma for which evidence pertaining to optimal management is limited. We describe a 48 year-old female with a history of hypothyroidism presenting with a several-year history of intermittent right upper quadrant pain who was found incidentally by CT scan to have a large left adrenal mass measuring 6 x 8 x 5.5 cm with evidence of surrounding lymphadenopathy but no local invasion. Preoperative markers were normal, including carcinoembryonic antigen (CEA) 1.5 (<2.5 ng/mL) and Cancer Antigen 125 (CA-125) 16 (<21 units/mL). She subsequently underwent an uncomplicated laparoscopic bilateral salpingo-oophorectomy with excision of a 9cm complex left ovarian mass. The postoperative recovery was excellent. Surgical pathology demonstrated a papillary thyroid carcinoma arising from struma ovarii with tumor cells arranged in macrofollicles and papillary fronds, containing vesicular and cleaved nuclei. Scattered tall cell features were noted but no pseudo-inclusions. The mitotic index was 1% and the tumor appeared to be contained within the ovary. Postoperatively, a TSH was 1.07 (0.36 - 3.74 UIU/mL), free T4 1.1 (0.8 - 1.5 ng/dL), thyroglobulin 75.4 (1.6 - 59.9 ng/mL), and thyroid antibodies <20 IU/mL. Thyroid exam was normal. Ultrasound of the neck demonstrated an indeterminate 5 mm nodule or colloid cyst in the superior left gland. Given the varied reports of prevalence of metastatic disease in the literature, which is often not suspected or evident at the time of the initial surgery, and also with the aim of facilitating future surveillance, the patient was referred for total thyroidectomy to be followed by 1-131 remnant ablation and subsequently a post-treatment whole body scan. Results of this study will be available following submission of the abstract. We describe a case of papillary thyroid carcinoma arising from struma ovarii, a rare tumor for which there is a relative scarcity of data guiding appropriate management. We will present a review of the literature with specific emphasis on optimal surgical management, adjuvant therapy, and postoperative surveillance.

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**358 CHRONIC PARATHYROIDITIS: A DIAGNOSTIC CONSIDERATION IN THE HYPOCALCEMIC PATIENT FOLLOWING SURGICAL CORRECTION OF PRIMARY HYPERPARATHYROIDISM**

Patel-Trujillo R, Schade D, Kaspner P, Saxon S, Spafford M, Bouchonville M. University of New Mexico Health Sciences Center, Albuquerque, NM.

**Case Report:** Chronic parathyroiditis, a rare and poorly understood condition, may manifest as hyperparathyroidism or hypoparathyroidism. We report a case of a 61 year old woman with asymptomatic hypercalcemia. Serum calcium levels ranged between 10.6-11.8 (8.5-10.1mg/dL) with a parathyroid hormone (PTH) level of 299 (11-80pg/mL). Other labs included a 24-hour
urine calcium of 421 (35-250 mg/24-hr) and an eGFR >60 mL/min. DXA showed T-scores of -3.7 at the lumbar spine and -3.1 at the left proximal femur. Sestamibi scan showed a left superior pole parathyroid adenoma. She subsequently underwent parathyroidectomy with a decrease in intraoperative PTH from 359 pg/mL to 43 pg/mL. She was discharged on calcium and vitamin D. Two months later, she developed paraparesthesias and was found to have a serum calcium of 6.3 mg/dL, ionized calcium 0.80 (1.15-1.27mmol/L), PTH 9 pg/mL, phosphorus 6.6 (2.5-4.9mg/dL) and 25-OH vitamin D 25(30-100ng/mL). Review of surgical pathology from parathyroidectomy demonstrated a large parathyroid adenoma, 830 mg, with multiple lymphoid follicles dispersed throughout the lesion suggestive of chronic parathyroiditis. She was treated with calcitriol, calcium, and hydrochlorothiazide with improvement in symptoms.

This case emphasizes the variable course of chronic parathyroiditis, which manifested initially as primary hyperparathyroidism and, subsequently, as symptomatic hypocalcemia, presumably due to autoimmune parathyroid gland destruction. The pathogenesis of chronic parathyroiditis is thought to be similar to that of autoimmune thyroid disease; however, antibodies to parathyroid tissue are only rarely observed. Histologic findings are characterized by aggregates of mature lymphocytes infiltrating normal parathyroid tissue, often with lymphoid follicle formation with prominent germinal centers. Plasma cell infiltration, fibrosis, parenchymal destruction, and resultant parathyroid gland atrophy have been described. Parathyroid involvement may be unilangular or multifocal, the latter of which is associated with underlying autoimmune disorders. We present a review of the literature emphasizing the pathogenesis and clinical implications of this rare autoimmune condition.

**360**

**ENCOURAGING SMOKING CESSATION IN THE HISPANIC COMMUNITY OF EMMETT, IDAHO BY PROVIDING CULTURALLY RELEVANT CESSATION INTERVENTIONS**

Morales-Carillo J. University of Washington, Seattle, WA.

**Purpose of Study:** The National Center for Health Statistics indicates that 24% of adults in Emmett, Idaho are current smokers, which is the third highest rate in the state of Idaho. Futurereferrer conversations with healthcare providers and the target population indicate that one of the main challenges faced by the Hispanic community to quit smoking is the lack of culturally competent smoking cessation programs. The purpose of this project was to encourage smoking cessation in the Hispanic community of Emmett, Idaho by: 1) providing culturally relevant cessation interventions including family support, the Catholic Church, and language appropriate information, and 2) by providing visual displays of the health consequences of smoking.

**Methods Used:** The literature suggests that the most effective approach to encourage smoking cessation among Hispanics is one that takes into account family, is culturally competent, and visually displays the harmful effects of smoking. Hispanics are more likely to quit smoking if cessation is seen as beneficial to the entire family, especially children, and if they have a major support group such as church. Based on this information and in collaboration with the priest, my project was implemented at the local Catholic Church, where entire families could attend, including spouses and children. The event consisted of a presentation and a demonstration of lung specimens from a pig simulating a human healthy lung vs. a cancerous one. The presentation and all materials were provided in Spanish.

**Summary of Results:** A total of 43 people attended the event, including 5 families and church staff. The active engagement from all participants, the gratitude expressed, and the positive feedback received indicates the information provided was very useful to the majority of attendees. Resources to encourage smoking cessation among Hispanics is one that takes into account family, religious-based organizations, and visual displays can be an effective way to encourage smoking cessation in the Hispanic community.

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**Poster Session III**

**Pulmonary and Critical Care**

10:00 AM Saturday, January 26, 2013

359

**CONGLOMERATE PULMONARY FIBROSIS: MICA, SILICA, BOTH OR NEITHER? 15-YEAR FOLLOW-UP**

Raymond LW. 1Univ of North Carolina, Chapel Hill, Charlotte, NC and 2Carolina's HealthCare System, Charlotte, NC.

**Case Report: Case Report:** Mica is a layered silicate in which partial substitution with aluminum for silica enhances binding of cations, useful in electronics. Over 2/3 of USA’s mica is mined in North Carolina, where it has rarely been associated with pneumoconiosis. We suspect such association in a 54 year old African American male who bagged mica flakes for 36 years. The silica content of the mica was 1-3 percent. He wore respirators only when changing filters which prevented dust from circulating through the mill. Radiographic changes began in 1981, causing him to end a 5 pack-year smoking habit, but progressed to bilateral conglomerate densities, sparing upper lobes and pleural surfaces. Exertional dyspnea in 1992 led him to stop taking walks and to pace himself if ascending more than one flight of stairs. By 1997, he went to bed after supper on work days. Examination was normal except for bibasilar crackles. Pulmonary function testing (1996-97) showed moderate restriction.

- Forced expired volume/1 second, lit. (%) 2.59 (69) – 2.45 (68)
- Forced vital capacity, lit. (%) 3.34 (64) – 2.97 (71)
- FEV1-FVC, % 77.5 – 82.5
- Total lung capacity, lit. 4.93 (66)
- Residual volume/Total lung capacity, % 32
- Carbon monoxide transfer factor, Dco 28.3 (55%)
- Dco/Alveolar volume 4.1 (104%)

Dyspnea limited cycle ergometry to an oxygen consumption rate of 1.4 liters per minute (27% of predicted). Lung biopsy showed fibrosis with polarized foreign material. High resolution CT scan showed confluent linear shadows consistent with pulmonary fibrosis, multiple cysts, and lymphadenopathy including a 4-cm subcarinal node of increased density consistent with inhaled inorganic material. He was removed from further mica exposure in 1998. He recovered from a 50 per cent right spontaneous pneumothorax in September, 2012.

**Conclusion:** 36-year exposure to mica with 1-3% silica resulted in marked symptoms, physiologic abnormalities and radiographic changes which differed from upper lobe changes of progressive massive fibrosis typical of silicosis.
Methods Used:

We searched the PubMed database for publications from 1/1/2000-12/31/2011 using the search terms “lung transplant/transplantation” and “health-related quality of life” to identify relevant studies. Our search strategy included articles published in peer-reviewed English language journals with a focus on HRQL. We included studies that reported HRQL outcomes in lung transplant recipients. We excluded studies that did not report HRQL data or did not include HRQL as a primary endpoint.

Purpose of Study:

The purpose of this project was to provide culturally specific tobacco education to encourage smoking cessation among Asian/Pacific Islander (API) residents in the Beacon Hill community. According to the 2010 U.S. Census, Seattle has the 11th largest API population in the United States. On Beacon Hill, 46% of the population (~17,000 residents) identify themselves as Asian, 69% of whom are immigrants. This is significant because smoking prevalence is highest among API immigrant men. Smoking rates among Filipino immigrant men are around the national average of 21.7%.

Methods Used:

Approximately 40 people at the Beacon Community Health Fair participated in an interactive group discussion where they were led through a series of questions about tobacco in the API community. Key points emphasized were identifying the different types of tobacco used by Filipino-Americans, the harmful effects of tobacco use and the tobacco industry’s focus on the growing API market. To illustrate the negative health consequences of smoking, a pig lung demo showed lungs damaged by cigarette smoke. Pamphlets with further information were available in Tagalog and English. Afterwards, participants took part in an informal group quiz.

Summary of Results:

There were about 40 participants at the health fair, most of whom were Filipino. Many were recruited through ads in the local paper and the local Filipino church. About 14 were in my target group of immigrant men. Fair-goers actively participated in the group discussion, pig lung demo and informal group quiz. Participants were able to retain many of the tobacco education points. Presentation materials were donated by International Community Health Services, which has a strong presence in the community and will be providing further follow up.

Conclusions:

Specific API subgroups have significantly higher rates of tobacco use than the national average. To effectively combat this problem within the Filipino community, educational programs must be tailored to the patient (i.e. culturally sensitive) and emphasize the harmful effects smoking has on others. This is especially true within the API community as a whole because each subgroup has its own culture and customs that play a significant role in determining their health. As a result, healthcare workers should continue to promote tobacco cessation on an individualized basis.

A THEMATIC ANALYSIS OF HEALTH-RELATED QUALITY OF LIFE IN LUNG TRANSPLANTATION

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Purpose of Study: Health-related quality of life (HRQL) is a primary measure of lung transplant (LT) efficacy. HRQL has been assessed in various LT investigations, but has not been analyzed systematically. We addressed this knowledge gap through a systematic literature review.

Methods Used: We searched the PubMed database for publications from 1/1/2000-12/31/2011 using the search terms “lung transplant/transplantation”, “health-related quality of life”, and “utility/ies”. We also manually searched the references of included studies. We performed a thematic analysis of relevant published, peer-reviewed English language studies of HRQL in LT adults organizing them by study design and into categories based on their overarching themes. We did this using an iterative, consensus-based approach, identifying 6 themes that consistently emerged from the data, classifying each according to primary (n1) and secondary (n2) thematic categories.

Summary of Results: Of 436 publications initially identified, 61 remained after exclusions. Six core themes emerged: 1) Determinants of HRQL (n1=23; n2=2), 2) Psychosocial factors in HRQL (n1=7; n2=8), 3) Pre- and post-transplant HRQL comparisons (n1=11; n2=14), 4) Long-term longitudinal studies of HRQL (n1=4; n2=8), 5) HRQL correlates of potential therapies and interventions (n1=9; n2=0), and 6) HRQL instrument validation and methodology (n1=7; n2=1). We found that LT significantly improves HRQL, predominantly in domains related to physical health and functioning. Nevertheless, LT recipients manifest considerable residual impairments in HRQL compared to population norms. The existing literature demonstrates substantial heterogeneity in methodology and approach; relatively few studies assessed HRQL longitudinally within the same group of persons.

Conclusions: LT improves HRQL for persons with end-stage lung disease. Opportunity for future study lies in addressing methodological limitations evidenced by the existing literature, including validating HRQL instruments, additional inquiry in understudied thematic areas, and elucidating the determinants of HRQL through longitudinal, multidimensional investigations.

STANDARDIZED TESTS AND SIMULATORS IN CRITICAL CARE: ARE WE REALLY TESTING THE STUDENT’S APPLIED KNOWLEDGE?

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Purpose of Study: Cardiovascular physiology, pharmacology and treatment of shock are heavily emphasized in current medical training. Simulator training has been utilized to enhance performance of individuals in treatment of critical illness. This study was designed to compare students’ performances on our hemodynamics simulator to performance on a written multiple-choice exam.

Methods Used: Using LabView software, we designed a hemodynamics simulator which displays a patient’s bedside monitor and a list of treatment interventions. Fifteen second-year medical students used the simulator to administer interventions to patients in a series of clinical scenarios. The students were scored based on the appropriateness and timeliness of their interventions. Their scores were compared to the written exam given at the end of the block on hemodynamics.

Summary of Results: The mean score for the course exam was 87.77% ± 8.37. The mean score for the simulator was 23±10 out of 40. There was no correlation between multiple choice exam score and simulator score (R2=0.096).

Conclusions: Our simulator requires students to integrate information as it would appear in an ICU setting and quickly recognize the correct treatment. Multiple-choice tests don’t encourage this type of integration and thinking because all of the information is presented in text format. Additionally, our simulator stresses timing and quick decision-making. We showed that students who did well on the written exam did not necessarily perform well using our simulator. Because our simulator was designed to mimic real world decision-making, it may be inferred that written exams do not necessarily test the students’ application of learned knowledge.

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UMBILICAL CORD BLOOD GASES AND NEONATAL RESPIRATORY OUTCOME AMONG PREMATURE INFANTS BORN AT \(<= 30\) WEEKS GESTATIONAL AGE

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Purpose of Study: Umbilical cord blood gas analysis provides an objective method to assess the fetal gas exchange and metabolic state at birth. There is abundant literature demonstrating the relationship between umbilical cord blood gases and adverse neonatal neurologic outcome but few studies focusing on respiratory outcomes. Our objective was to define the relationship between umbilical cord blood gases and neonatal respiratory outcome among premature infants \(<= 30\) weeks gestational age (GA). We hypothesize that those premature infants, defined as less than or equal to 30 weeks gestational age, with early blood gas values of lower pH, PaO2 and higher PaCO2 values will have prolonged NICU stays with a greater need for respiratory support.

Methods Used: An electronic database and manual chart review of all babies born at \(<= 30\) weeks GA at Scripps Hospital between 2006-2009, was conducted using search terms related to NICU admission and prematurity. We excluded patients with complex multi organ or cardiac disease. The data collection included: first umbilical cord blood gases, maternal history, pregnancy, labor, delivery and NICU outcome parameters. The statistical methods included: fisher exact test and chi square analysis as appropriate, and significance was defined as a p value <0.05.

Summary of Results: Based on rigorous chart review, we identified 30 high risk patients for our analysis. There was no significant difference when comparing different gradients of pH (7.0, 7.1, 7.2, 7.3) with length of NICU stay (14d, 21d, 30d, 50d), length of oxygen requirement (7d, 14d, 21d), presence of maternal diabetes or maternal bleeding, and Apgar scores five at minutes.

Conclusions: We conclude that on our findings that there was no direct correlation between 

1. The purpose of this study was to examine the effects of rat bone marrow stromal cells (rBMSC) on collagen deposition and inflammatory response towards an electrospun polycaprolactone (PCL) scaffold.

2. Materials and Methods: Electrospun PCL scaffolds were seeded with Fisher rat rBMSCs or no cells prior to implantation into the knee joints of Sprague Dawley rats. Scaffolds were harvested from rats at 7, 21, and 42 days (N=2 per time point). The scaffolds were processed for histological analysis. Collagen type I deposition was assessed with immunohistochemical analysis. Scaffolds were stained with Picosiris red to further identify the deposition of organized collagen. Cellular infiltration was assessed via cell counting and cell counts were performed on H&E stained sections. Additionally, the sections were qualitatively graded for inflammation on a scale of 1-4 (low to high).

3. Summary of Results: Collagen deposition appeared to be more robust and organized in acellular scaffolds compared to rBMSC seeded scaffolds. Organized collagen deposition was the most robust in acellular scaffolds at day 21. There was a significant increase in cellular infiltration within rBMSC

Case Report: Purpose: To report the use of annular amniotic membrane transplantation as a host incorporated graft in the management of Brown-McLean Syndrome.

Methods: Case report and review of literature to propose a potential mechanism accounting for the efficacy of the procedure.

Results: Patient underwent amniotic membrane transplantation with EDTA chelation resulting in resolution of pain, irritation, and foreign body sensation as well as resolution of recurrent peripheral epithelial defects.

Conclusions: Annular amniotic membrane transplantation is a safe and effective treatment strategy for the management of Brown-McLean Syndrome. It represents a long-term solution for this recurrent condition. Further, amniotic membrane transplantation done in the described manner may have implications for the long term management of other corneal epithelial defects.

BEST MANAGEMENT OF ULTRA-SMALL TRACHEOBRONCHIAL FOREIGN BODIES IN NEONATES

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Purpose of Study: To develop (1) a practical and comprehensive algorithm of instruments and techniques available to treat neonates with tracheobronchial foreign bodies, based on the patient's subglottic diameter and (2) primary and secondary prevention strategies for neonatal tracheobronchial foreign bodies.

Methods Used: (1) Analysis of the case of a severely premature infant who presented with the incidental radiological finding of a 2cm suction catheter tip, which, over a two week period, had migrated between her main bronchi; the foreign body was removed with a previously unreported combination of instruments: a 3 French flexible urological forceps through the side port of a 2.5mm rigid bronchoscope. (2) In vitro testing of typical foreign bodies and readily available endoscopic instruments.

Summary of Results: We have developed a practical and comprehensive algorithm for the treatment of neonates with tracheobronchial foreign bodies, as well as primary and secondary prevention strategies.

Conclusions: The treatment algorithm and prevention strategies may reduce morbidity and mortality from neonatal tracheobronchial foreign bodies.
Methods Used: An evidence-based literature review was conducted to assess the need and feasibility for a multidisciplinary esophageal atresia (EA) continuity clinic at BC Children's Hospital (BCCH). Articles were reviewed and the information will be considered for our clinical practice.

Conclusions: Expert opinion supports the use of multidisciplinary continuity clinics in the follow-up of EA patients due to the associated morbidity issues. Canadian pediatric surgeons have cited transition to adult care as an issue that can be resolved through the establishment of EA multidisciplinary clinics.

Retrospective Review of the Management of Infected Dermal Sinus Tracts and Associated Intradural Dermoid Tumors

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Purpose of Study: Tragically, the recognition of dermal sinuses in neonates is poor with the consequence that some of these infants develop meningitis as the presenting symptom. The timing of safe surgical excision of the sinus and any associated infected dermoid tumor/abscess, during the course of antibiotic treatment is not clear. To answer this question, we investigated associations between intra-operative or post-operative complications and the duration of preoperative antibiotic administration.

Methods Used: We performed a retrospective chart review of cases of dermal sinus tract and intradural dermoid tumor resections at B.C. Children’s Hospital from 1990 to present date. Patients presenting with meningitis were selected for analysis.

Summary of Results: Seven patients with infected dermal sinus tract/intradural dermoid tumors were reviewed. Surgical intervention was performed within 5 days after admission for six patients and 21 days after admission for one patient. Complete surgical resection of the tract, filler and intradural dermoid tumor/abscess was achieved in six patients. In one patient, a small segment of the tumor was not resected as it was not distinct from scar tissue and nerve roots.

Four patients had no post-operative neurological deficits. Three patients exhibited on-going bowel and/or bladder incontinence. Specifically, the first patient had decreased rectal tone and a neurogenic bladder prior to surgery. The second patient’s tumor was located within the conus. The third patient had extensive subarachnoid inflammation despite clinical improvement with antibiotic therapy.

No patient has shown recurrence of their dermoid tumors on MRIs with follow-up ranging up to eight years. The patient with a subtotal deroid tumor resection was lost to follow up after a 3-month post-operative scan.

Conclusions: In the context of active infections, complete resection of dermal sinus tracts and dermoid tumors/abscesses can be achieved during antibiotic treatment. The post-operative complications may be suspected if preoperative neurological deficit exist or when abscess formation is in the conus. This study suggests that urgent surgical intervention need not await completion of antibiotic treatment.

The Added Utility of MRI in the Diagnosis of Atlanto-Occipital Dislocation

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Purpose of Study: The purpose of this study is to assess complication rates of endovascular aortic repair, and frame time in which these complications occur, in order to suggest beneficial follow-up schedules for this subset of patients.

Methods Used: Patients were identified using ICD codes, and those without traumatic mechanisms were excluded. We did a chart review of 28 patients, and gathered data on patient demographics, comorbidities, type of graft, and all CAT scans. We used this to determine complication rates in our population, and time until complication. For the statistical analysis, data from Excel were imported into SAS 9.2, which was used to generate descriptive statistics. Categorical variables were compared using Fisher’s exact test, and continuous variables were analyzed using a Wilcoxon rank sum test. P-values of $p<0.05$ were considered statistically significant.

Summary of Results: There was a male predominance (78.6%) and American Indians were over-represented (21.4%) when compared to the New Mexico population (9.1%). Mean number of days to follow-up was 229.6, with a range of 0 to 990. Our complication rates were similar to those in previous studies (10%), we divided our complications into early (10.7%) and late (7.1%). None of the patients with early complications were also in the late group. Of the early complications, 2/1 (9.3%) with Gore grafts had complications, and 1/7 (14.3%) of those with Medtronic grafts. Prior to follow-up scans being performed, one Gore graft recipient and one Medtronic graft recipient died. Complications on follow-up scans were noted in 2/21 of Gore graft recipients and none of the Medtronic recipients. Mean age with complications (early or late) was 39 years, and mean age with no complications was 44.5 years.

Conclusions: For our patient population, there was a predominance of males with this injury (78.6%) and the majority of patients had no stent complications visible on either post-op or follow-up scans. There was evidence to suggest that there is no association between complications found on post-operative scans, and late complications found on follow-up. There was also evidence to suggest that older age is associated with a lower likelihood for complications, although our population was too small to reach statistical significance.

A Multidisciplinary Esophageal Atresia Continuity Clinic at BC Children’s Hospital: A Systematic Evaluation in Design and Feasibility

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Purpose of Study: The purpose of this study is to assess the need and feasibility for, and to consider the possible design of, a multidisciplinary continuity clinic for patients with esophageal atresia (EA) at BC Children’s Hospital (BCCH).

Methods Used: (1) An evidence-based literature review was conducted using the search term “esophageal atresia, multidisciplinary follow-up care” in the PubMed, OvidSP, EBSCO databases, and Google Scholar search engine. (2) Data was obtained from a survey of members of the Canadian Association of Paediatric Surgeons (CAPS) regarding current esophageal atresia continuity clinics in Canada. (3) Charts of EA patients who underwent surgical repair at BCCH between 2000 and 2011 were retrospectively reviewed for quality and searched for prima facie evidence related to our purpose.

Summary of Results: Thirty-one articles denoting EA follow-up issues were retrieved from a result of 1,020. Articles were individually assessed and excluded if irrelevant to our study. Only articles in English were included. Articles were reviewed and the information will be considered for our clinical model of a multidisciplinary esophageal atresia continuity clinic. (2) One-third [5] of Canadian pediatric academic health centres dealing with EA have multidisciplinary follow-up programs. Response to the CAPS survey indicates support for the development of a multidisciplinary clinic model to ease follow-up and transition issues in pediatric centres. (3) Our chart review of EA patients indicates that outpatient clinic follow-up at BCCH is often inconsistent and uncoordinated.

Conclusions: Expert opinion supports the use of multidisciplinary continuity clinics in the follow-up of EA patients due to the associated morbidity issues. Canadian pediatric surgeons have cited transition to adult care as an issue that can be resolved through the establishment of EA multidisciplinary clinics.
Purpose of Study: Atlanto-occipital dislocation (AOD) has the potential for severe morbidity and mortality. Currently, clinicians rely heavily on CT and MRI to assess the integrity of the upper cervical ligamentous complex. Damage to stabilizing structures such as the apical ligament, alar ligaments, transverse ligament, interspinous ligament, and posterior longitudinal ligament is associated with AOD. Grossly abnormal findings on MRI may be predictive that surgical stabilization is necessary. The aim of this study was to determine the added utility of MRI in the diagnosis of AOD and to assess the ability of our routine trauma MRI protocol to visualize upper cervical ligaments.

Methods Used: CT and MR images of the cervical spine were reviewed in ten patients with AOD. Images underwent blinded review by a neuroradiologist and two orthopaedic spine surgeons. Reviewers were asked to comment on the integrity of the anterior and posterior longitudinal ligament, apical ligament, alar ligament, transverse ligament, interspinous ligament, and posterior longitudinal ligament. In addition, raters were asked to apply a revised condyle-C1 interval and condylar sum to CT images.

Summary of Results: The condyle-C1 interval and condylar sum successfully diagnosed all ten cases of AOD when applied to CT imaging. MRI findings of apical ligament, alar ligament, and transverse ligament are most commonly associated with AOD. Damage to the transverse ligament (14/30), and posterior longitudinal ligament (14/30) was least commonly recognized in association with AOD. Readers most commonly reported an inability to visualize the alar ligaments (10/30) and transverse ligament (3/30) because of an insufficient number of cuts through the upper cervical ligamentous complex and lack of coronal sequences in a routine trauma MRI series. In a majority of cases (41/70) all three authors did not agree on the integrity of the ligament being evaluated.

Conclusions: The use of current diagnostic measurements is sufficient to diagnose AOD when applied to CT imaging. MRI findings of apical ligament, alar ligament, and transverse ligament damage are common with atlanto-occipital dislocation. Specialized upper cervical sequences may be required to improve diagnostic imaging methods necessary to identify the extent of ligamentous injury in AOD.

373

SINGLE INSTITUTION EXPERIENCE WITH INCIDENTAL RENAL ARTERY ANEURYSMS: PRESENTATION, MANAGEMENT AND OUTCOMES

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Purpose of Study: Renal artery aneurysms (RAAs) are rare, but the recent rise in abdominal imaging for other conditions has resulted in a greater frequency of incidentally discovered RAAs. The indications for repair of incidental RAAs have not been well established. We report contemporary data, including both incident and non-incident RAAs.

Methods Used: Retrospective review of all patients presenting with RAA in the Vascular Center at UCLA from January 2002 to April 2012. Data were collected regarding patient demographics, clinical presentation, aneurysm morphology, treatment, outcomes, and follow-up care.

Summary of Results: Sixty RAAs were identified in 41 patients with mean age at diagnosis of 56 (range 16 to 85), including 23 females and 18 males; twenty-two aneurysms were found during investigation for renal symptoms, 33 were found incidentally during workup for unrelated conditions, and 5 were found during imaging for unknown indications. Incidental RAAs had mean diameter 1.7 cm, and were larger than non-incident RAAs with a mean diameter 1.3 cm (p = 0.026). Mean growth rate, calculated from 13 aneurysms in which two or more imaging studies were available, was 0.4 ± 0.3 mm/year for non-incident RAAs (n = 4), and 0.8 ± 0.3 mm/year for incidental RAAs (n = 9) (p = 0.36 (ns)). Forty-four aneurysms were managed conservatively (23 incidental) and 16 were treated surgically (10 incidental). Operatively treated RAAs had a mean diameter of 2.6 cm, and were significantly larger than conservatively treated RAAs with a mean diameter of 1.3 cm (p = 0.0016). In patients with incidental operative RAAs, mean hospital stay was 4.7 days, early post-op morbidity was 10%, late morbidity was 10%, and mortality was 0%. Mean follow up was 348 days. No RAA rupture occurred in any group.

Conclusions: Surgical treatment of incidental RAAs is associated with 10% morbidity and 0% mortality; however, the growth rate of incidental, untreated RAAs is only 0.8 ± 0.8 mm/year, and we found no cases of RAA rupture. Although large-scale studies of the natural history of incidental and non-incidental RAAs are needed, we may currently be too aggressive in treating incidental RAAs.

374

DELAYED EXTENSOR POLLICIS LONGUS TENDON RUPTURE FOLLOWING NONDISPLACED DISTAL RADIUS FRACTURE IN A CHILD

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Case Report: Rupture of the extensor pollicis longus (EPL) tendon is a disabling complication occurring with an estimated frequency of 0.07% to 0.88% following fracture of the distal radius in adults. The incidence of EPL tendon rupture is even lower in the pediatric population. Herein we report a case of delayed EPL tendon rupture in a 15 year-old boy 9 weeks following a nondisplaced distal radius fracture. A 15-year-old boy sustained a nondisplaced Salter-Harris II fracture of the distal radius after a fall onto his outstretched hand while playing soccer. For treatment of the fracture, he was casted for 5 weeks and achieved full function of his right hand and wrist post injury. Four weeks after cast removal, while the patient was texting on his mobile phone, he noticed a sudden inability to extend his right thumb. This incident was painless and was not associated with any trauma at the time. Rapture of the EPL tendon was confirmed clinically. Surgical exploration revealed that the proximal portion of EPL was significantly attenuated and frayed up to the musculotendinous junction. A tendon transfer was performed using extensor indicis proprius (EIP) to EPL using the Pulvertaft weave technique. There was no bony irregularity evident at the time of the tendon transfer. Ten weeks post-operatively, the patient was active and was able to extend and elevate the thumb with full range of motion and strength. The 6 months post-operative follow-up showed that the patient was able to achieve full extension of his right thumb with symmetrical snuff box anatomy. Management of EPL tendon ruptures generally fall under 3 categories: primary repair, tendon graft or tendon transfer. The EIP tendon transfer was selected because of the difficulty repairing the tendon at the level of the musculotendinous junction. Reported long term complications with this procedure have been extensor lag or index weakness neither of which was present in our patient six months postoperatively. Given the frequency of radius fractures, no preventative measure are suggested; however, despite the infrequent nature of EPL rupture post radius fracture in the pediatric population, a high clinical suspicion for this type of injury is warranted.

375

THE INFLUENCE OF BODY MASS INDEX AND EDUCATIONAL LEVEL ON OUTCOMES IN ANTERIOR CRUCIATE LIGAMENT REPAIR: A PRELIMINARY STUDY

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Purpose of Study: Knee instability is common, particularly among older individuals and athletes, with the majority of cases due to anterior cruciate ligament (ACL) tears. With such a high number of ACL reconstructions, there is a need for the evaluation of the role of demographic variables in treatment outcomes. This is especially critical in light of recent advances in understanding the role that collection of epidemiological data and the implementation of policy have in correcting health disparities. The aim of this study is to examine the correlation between demographic variables and long-term outcomes of ACL reconstruction.

Methods Used: ACL reconstructions were performed on 520 patients over 12 years. As a preliminary study, 97 of these patients were contacted for follow-up and asked to complete two subjective knee questionnaires (Lysholm Knee Scale and Tegner Activity Scale). Average follow-up was 8.9 years. Lysholm Knee Score was scored 0-100, and the Tegner Activity Scale scored 0-10. Patients’ highest level of education and BMI were also ascertained at time of follow-up. Patients were divided into groups based on their BMI and education level. Mean Lysholm and Tegner scores were calculated for each group and analyzed by ANOVA.

Summary of Results: Average Lysholm score for all subjects was 90 and average Tegner score was 5.7. Range for mean Lysholm scores was 87.1 (obese group) to 95.0 (underweight group). Range for mean Tegner scores was 217

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was 5.2 (obese group) to 6.0 (underweight group). Average Lysholm and Tegner scores decreased progressively with increasing BMI, but this difference was statistically insignificant. Education level also had no significant effect on Lysholm and Tegner scores, with little variation between different groups.

Conclusions: The effect of BMI and education level on long-term outcomes in ACL reconstruction is relatively unknown. This preliminary study revealed no significant effect of either BMI or education level on subjective knee survey scores. Following up on the remaining 423 patients enrolled in this study will provide more definitive evidence regarding the relationship between these factors. Including patients from multiple treatment centers to obtain a more representative cross-section of the population is another possible direction for future research.

376

TRANS-MAXILLARY APPROACHES TO THE ANTEROLATERAL SKULL BASE: AN ENDOSCOPIC ANATOMICAL STUDY

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Purpose of Study: Endoscopic surgery has replaced many traditional, invasive paths to the skull base. In this study, we employ two trans-maxillary approaches to the retromaxillary space in an attempt to access the anterior skull base: a sublabial anterior maxillotomy and endoscopic Denker’s approach.

Methods Used: Four vascular-infused cadaver heads were dissected using the sublabial approach with a regular Caldwell-Luc incision and anterior maxillotomy (4 sides), while the other 4 sides were dissected using an extended Denker’s approach and medial maxillotomy. Prior to and during dissection, CT scans and neuro-navigation determined endoscopic pivot points and distances between relevant anatomical landmarks.

Summary of Results: Although both procedures provided similar visualization of the V2 trigeminal nerve root, exposure to the anterolateral infra-temporal fossa (ATIF), infratrochlear nerve (ION), and internal maxillary artery (IMA) was more easily attained by the sublabial approach. ION entry to the infratrochlear canal pinpointed the orbital floor/posterior maxillary wall junction. The mean distance between the junction and foramen rotundum V2 root was 14.55 mm +/- 2.1 mm, while the mean distance between the junction and the 2nd genu of the internal carotid artery (ICA) was 24.8 mm +/- 4.2 mm.

Denker’s approach provided better access to the 2nd genu of the ICA and direct view of the Eustachian tube (ET) at the level of the posterior concha; however, posterolateral dissection to the retromaxillary space and ATIF was limited by the lateral pterygoid plates compared to the sublabial procedure. The mean distances between the ION-ET, ION-pterygopalatine ganglia, and ET-2nd genu of ICA were 32.1mm +/- 5.2 mm, 7mm +/-3.5 mm, and 20.7 mm +/- 5.3 mm respectively.

Conclusions: The transmaxillary corridor provides an excellent route to access the anterolateral skull base: a sublabial anterior maxillotomy and endoscopic Denker’s approach. Although both procedures provided similar visualization of the V2 trigeminal nerve root, exposure to the anterolateral infra-temporal fossa (ATIF), infratrochlear nerve (ION), and internal maxillary artery (IMA) was more easily attained by the sublabial approach. ION entry to the infratrochlear canal pinpointed the orbital floor/posterior maxillary wall junction. The mean distance between the junction and foramen rotundum V2 root was 14.55 mm +/- 2.1 mm, while the mean distance between the junction and the 2nd genu of the internal carotid artery (ICA) was 24.8 mm +/- 4.2 mm.

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Conclusions: The transmaxillary corridor provides an excellent route to access the anterolateral skull base: a sublabial anterior maxillotomy and endoscopic Denker’s approach.

377

THE ROLE OF LEARNING RESOURCES IN PRE-OPERATIVE AND POST-OPERATIVE EDUCATION FOR PEDIATRIC PATIENTS AND THEIR FAMILIES IN A CLINICAL SURGERY SETTING

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Purpose of Study: Patients who undergo invasive procedures require appropriate education to better understand their conditions and the treatments they receive. Such education may lessen their anxiety about the operative procedures, enhance their recovery and facilitate their transition from hospital care. Healthcare workers use various teaching resources to translate medical information into easily understandable concepts to effectively educate patients. Due to the growing need for the current tools to be updated and expanded upon, new resources were created for the surgery department within a children’s hospital, with the goal to assess their effectiveness from the patients’ and families’ perspective.

Methods Used: By directly working with patients and nurses, medical students have produced a variety of education resources including dolls, colouring books and videos. Effectiveness of these resources will be measured through the use of surveys developed by the research team. Old resources and teaching methods will be retrospectively evaluated by mailing surveys to patients who have previously undergone an invasive procedure within the Department of Surgery. To evaluate the newly developed resources, questionnaires will be delivered to participants after an educational session with a clinical nurse regarding their procedure.

Summary of Results: Initial responses from the nurses have been very positive. They feel that the resources produced have greatly enhanced their teaching sessions. The research team is currently evaluating the effectiveness of these innovative learning resources through sending surveys to patients.

Conclusions: Updated learning resources in the teaching session increases engagement and enhances patient comfort and understanding. The medical students have also benefited by acquiring knowledge about various surgical conditions, learning how to effectively communicate with patients and by having early exposure to the clinical aspects of medicine.

378

CO-CULTURE OF ADIPOSE DERIVED STEM CELLS AND CHONDROCYTES WITH SURFACE MODIFYING PROTEINS ON A CARTILAGE AND BONE SCAFFOLD

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Purpose of Study: To assess how treatment of articular cartilage in vitro with surface modifying proteins affects de novo cartilage production by conditioned adipose derived stem cells.

Methods Used: Initially fat and cartilage samples were collected from disc arthritic knee prosthesis and stored in culture media during stem cell growth. A bone plug with intact articular cartilage was cut with a sterilized 17 mm punch. Then an 11 mm punch was used to cut a core from the center of the 17 mm plug. Cores were sterilized in ethanol for 24 hours. Next 17 mm plugs were placed in an agarose lining containing in a six well plate. Sterilized cores from a separate sample were soaked in either Procten, Poly-L-Lysine, or Collagen II, and after treatment placed in the void cut in the 17 mm plug. Stem cells in culture were trypsinized, counted, and 250,000 cells were seeded onto the treated 11 mm cores. Chondrogenic media was added and changed every three days for 25 days. After culture, the 11 mm cores were extracted and placed in 10% phosphate buffered formalin for 24 hours. After fixation the cores were decalcified with 9% formic acid. Samples were embedded in paraffin, cut into sections, and stained with H&E, PAS, and Safranin O with a fast green counterstain. Cultured tissue was visualized under light microscopy and the percent surface area covered and the thickness of tissue was calculated.

Summary of Results: Both treated samples and non-treated controls showed tissue with 20x magnification before processing. Histological analysis, showed parus-like tissue on the sample treated with poly-L-lysine while no tissue was observed on the control sample or the samples treated with collagen II and procten. The parus covered 32.4 +/- 7.7% of the cartilage surface, with a thickness ranging from 0.0199 - 0.119 mm.

Conclusions: Although tissue was observed on some samples, it may have been produced in response to the patient’s arthritis rather than generated de novo. Similar canine experiments, demonstrated significant cartilage growth. Additional studies to determine the reasons no new tissue formation was observed are needed and being planned.

379

THE APPENDICITIS INTERVIEW PROJECT: A QUALITATIVE ASSESSMENT OF PATIENT DECISION-MAKING IN ACUTE APPENDICITIS

Castelli A1, Drake FT2, University of Washington, Seattle, WA and 2University of Washington, Seattle, WA.
Purpose of Study: Time between symptom onset and initiation of treatment affects the outcome of several acute conditions. Although, there are studies evaluating pre-hospital patient decision-making for conditions such as myocardial infarction and stroke, to the best of our knowledge, there are no such studies for acute appendicitis (AA). Current clinical practice is based on the supposition that timely presentation of patients with AA improves outcomes. The purpose of this study is to identify themes in patient decision-making in the setting of AA symptoms.

Methods Used: Open-ended, audio recorded interviews were performed with patients (n=14) during their hospital stay after receiving treatment for AA. Enrollment hospitals included 1 county and 1 university hospital. The interview was structured into 3 segments: a patient narrative where he/she shared the story from the onset of symptoms until presentation for care; followed by open-ended questions to elicit specific components of each patient’s decision-making pathway; finally, specific questions regarding socio-economic factors. The audio recordings were transcribed and a qualitative methodology known as “content analysis” was performed using Atlas.ti software.

Summary of Results: Patient enrollment is ongoing; however, in this methodology, analysis proceeds concurrently with data acquisition. 36% of patients were perforated in the existing cohort and very few had a long delay. Preliminary analysis shows that 100% of patients had heard of AA prior to symptom onset; however, only 21% of patients initially thought they were experiencing AA; others thought they had food poisoning, “upset stomach,” or constipation. Internet research about AA was performed by 36% of patients before deciding to seek care. An important theme to emerge from the preliminary data is that the progression and severity of pain was frequently the final factor that made patients decide to seek medical care.

Conclusions: These preliminary results show that many patients are aware of AA but do not initially suspect it as the cause of their symptoms. Younger patients and/or educated older patients are likely to perform internet research. As we enroll more patients we expect further themes to emerge.

380

DEVELOPMENT OF SIMULATION-BASED TRAINING CURRICULUM FOR BASIC MOTOR SKILLS OF ARTHROSCOPIC SURGERY
Rose K, Pedowitz R. David Geffen School of Medicine at UCLA, Santa Monica, CA.

Purpose of Study: Training orthopedic surgery residents in arthroscopy has traditionally involved a significant amount of teaching on real patients in the OR. It has recently been mandated that within the next two years all orthopedic training programs implement a virtual reality simulation curriculum. The purpose of this study was to start building a curriculum to teach basic arthroscopy skills to residents.

Methods Used: A literature search was performed on PubMed looking at how virtual reality simulation has been used in general surgery, and how others have already attempted to apply it to arthroscopy. Basic skills, parameters for each skill and validity for the modules used were examined.

Summary of Results: The skills that need to be taught through modules on the simulator include camera manipulation and scope, image orientation, coordination, tracking of moving targets, measuring with a probe and triangulation. While modules are in the process of being developed, they will involve finding objects, honing in on the objects, touching objects and maintaining camera horizon. Parameters to be measured vary from module to module, but include total time, total path length, number of errors and number of times the probe is outside the field of vision.

Conclusions: With a clearer understanding of how to teach the basic arthroscopy skills on a virtual reality simulator, the next step is to continue to develop studies to compare the performance of medical students, residents and attendings on the simulator modules.

381

A NEW APPROACH TO TEACHING AORTIC CANNULATION
Frank PN. DGSOM at UCLA, Los Angeles, CA.

Purpose of Study: Surgical simulation on a wet lab has garnered significant attention recently due to a changing medical climate and interest in quality of patient care. Increasing operative complexity, monetary concerns, limits on resident work hours, and limits on the use of animal models and patient material are all challenges to which surgical simulation could pose an attractive solution. Specifically, the surgical technique of aortic cannulation requires a high degree of technical and decision-making skill that cannot be mastered via didactic sessions.

Methods Used: A fluid pump is connected to a reservoir, analogous to the venous system, from which water is pumped into an aorta, which may be either a preserved aorta or a synthetic graft. Acting as the heart, the pump creates pulsatile flow to perfuse the aorta and mimic the hemodynamics found in a live patient. The pump is driven by computer code written in LabVIEW 11 by National Instruments. To maintain realistic pressure and pulsatility in the aorta, a pressure sensor is built into the pump circuit. The pressure sensor relays real-time pressure measurements to the computer, and the computer code detects changes in aortic pressure and adjusts the operation of the pump accordingly. These adjustments are designed to mimic the body’s response to changes in blood pressure.

Summary of Results: Simulation provides a realistic, cost-effective, low-risk platform for teaching and honing skills for trainees in an environment where no harm is posed to an actual patient.

Conclusions: The use of realistic simulation in the teaching curriculum could easily supplement didactic sessions and learning in an operative setting.

382

USE OF AN INTEGRATED NEGATIVE PRESSURE WOUND THERAPY SYSTEM WITH VOLUMETRIC AUTOMATED FLUID INSTILLATION FOR TREATING WOUNDS WITH AN INFECTION: A CASE SERIES
Kristensen E, Gabriel A. Peacehealth Plastic Surgery, Vancouver, WA.

Purpose of Study: Studies have reported favorable outcomes with the combined use of negative pressure wound therapy (NPWT) and instillation of topical wound solutions in treating wounds with an infection. We report our experience using an integrated NPWT system with volumetric automated instillation (NPWT®) using a less hydrophobic reticulated open-cell foam (ROCF-V®) dressing for use on patients with an infected wound.
Methods Used: This case series included 3 female and 2 male patients (mean age: 51.8 years) with comorbidities such as diabetes, obesity and peripheral vascular disease. Wound types included an amputated stump, radiated chest wound, foot abscess, thigh wound, and surgical wound. All patients received systemic antibiotics and wound debridement. Before NPWTi, punch-wound biopsy cultures showed bacterial contamination. Patients’ wounds were treated with NPWTi/ROCF-V with volumetric automated instillation of saline (3 patients) or polyhexanide† (2 patients) with a 1 second soak time. NPWT (-125 mmHg continuous pressure) cycle time was 1-2 hours; mean duration of NPWTi/ROCF-V was 4 days.

Summary of Results: NPWTi/ROCF-V appeared to assist in wound cleansing and exudate removal. Granulation tissue formation was present with negative cultures for patients at time of wound closure by primary intention or coverage with a flap or graft. All wounds healed and patients were discharged; no complications occurred during follow-up time (3-12 months).

Conclusions: In these patients, NPWTi/ROCF-V provided wound cleansing and removal of infectious material. Additional studies are needed to determine the effects of NPWTi parameters on wound healing. *V.A.C.® ULTRA™ Therapy System, †V.A.C.® VeraFlo™ Dressing (KCI USA, Inc., San Antonio, TX); ‡Prontosan® (B.Braun Medical Inc., Bethlehem, PA).

383

QUANTITATIVE AND QUALITATIVE EVALUATION OF STEM-CELL DERIVED LARYNGEAL MUCOSA REPLACEMENT
Kita A1, Long F.2 1David Geffen School of Medicine at University of California, Los Angeles, Los Angeles, CA and 2University of California, Los Angeles, Los Angeles, CA.

Purpose of Study: The vocal folds play a critical role in phonation. In patients whose vocal folds are damaged by scarring, few therapies are available. The production of implantable tissue-engineered vocal folds would help restore normal speech to such individuals. Recently, researchers have used stem cells to recreate the two most superficial layers characteristic of these folds in a three-dimensional structure in vitro. Current efforts aim to evaluate the fidelity of these layers to their target vocal fold tissue by investigating basement membrane formation and barrier function of the epithelial layer in the three-dimensional vocal fold replacement tissue. We hypothesized that a tissue-engineered mucosa derived from stem cells grown on a fibrin gel would form a basement membrane comparable to that of human vocal folds. We also posited that the tissue-engineered epithelial layer, when confluent, would pose a permeation barrier similar to normal epithelium.

Methods Used: Epifluorescence microscopy was used to image human samples and three-dimensional tissue constructs treated with fluorescently-labeled antibodies for the basement membrane protein laminin. Epithelial transport was quantified by determining phenol red permeability through a transwell lined with vocal fold. Spectrophotometry was used to determine the amount of phenol red that passed through the vocal fold.

Summary of Results: While laminin presence in the basement membrane was clear in human samples, a vocal fold construct sample with sufficient epithelium has yet to be imaged. Barrier function experiments have shown that the permeability of canine vocal folds is 0.0100 cm/min and that of human vocal folds is 0.0494 cm/min.

Conclusions: This project examines the development of an epithelialized three-dimensional structure in vitro with structural and functional evaluation methods to produce vocal fold mucosa equivalent to human samples. Future work involving more laminin staining in constructs and smaller diameter transwells will help assess the similarity of tissue engineered vocal folds and human samples.

384

USING MRI TO GENERATE 3D MODELS OF HILL-SACHS LESIONS
Ouellette J.1, Douglas M.1, Eskiniia L.2, Latt D.1 1The University of Arizona, Tucson, AZ and 2The University of Arizona, Tucson, AZ.

Purpose of Study: A Hill-Sachs lesion (HSL) is a compression fracture on the humerus created when the humeral head impacts the glenoid during shoulder dislocation. HSL incidence is reported in 40-80% of patients with chronic instability. Soft tissue repairs for patients are often unsuccessful when a significant bony defect is left untreated. MRI can be used to estimate the size and location of the HSL and surgeons have proposed the presence of “large” HSLs or the position and orientation of the HSL as causes for recurrent dislocation following tissue repair. Unfortunately, in orthopedic literature there is no system for classifying HSLs. Our goal was to develop a system to determine the size and orientation of a HSL from MR images.

Methods Used: Using a program developed by the University of Arizona Soft Tissue Biomechanics Laboratory, a three dimensional representation of the humeral head can be generated from MR images. This program is an inexpensive medical image segmentation process using active contours to build 3D reconstructions of the humerus.

Summary of Results: Three patient MR image sets have been used to generate 3D models. The generated models allow for a three dimensional visualization of the size and shape of the HSL.

Conclusions: The current 3D models would allow a surgeon to visualize the HSL in order to determine the best procedure for his or her patient. This novel system allows for a way to visualize a HSL in three dimensions to better estimate the size and orientation of HSL.

385

OPEN VERSUS ROBOTIC RADICAL PROSTATECTOMY: FUNCTIONAL AND ONCOLOGICAL OUTCOMES OF ONE SURGEON
Shah S.1, Sonn G.2, Kwan L.2, Whitted L.2, Dennis R.3, Reiter R.1 1DGSOM at UCLA, Corona, CA; 2DGSOM at UCSF, Los Angeles, CA and 3UCLA, Los Angeles, CA.

Purpose of Study: To compare the functional and oncologic outcomes for RARP versus RRP for a single surgeon.

Methods Used: We identified 253 patients undergoing RARP and 40 undergoing RRP by a single surgeon between January 2004 and January 2012. Functional status and PSA data were gathered by physician-filled questionnaires during follow-up. Continence was defined by no or minimal leakage while potency was defined by the ability to achieve erection with or without medication. We identified 3 patients that had prior hormonal therapy and were excluded from the potency analysis. Both univariate and multivariate analysis compared continence and potency rates within 24 months following procedure and mean time to returned function. The multivariate models controlled for procedure, pre-treatment PSA, clinical T stage and race. A univariate analysis evaluated biochemical recurrence rates and time to recurrence between both groups. Biochemical recurrence was defined by PSA ≥ 0.2 ng/ml.

Summary of Results: Baseline characteristics were nearly equivalent between both groups, with the exception of higher pre-treatment PSA and clinical T stage in the RRP group. Continence rates within 24 months
of treatment were equivalent (90% RRP vs 87% RARP). The mean ± SD time to return of continence was 5.1 ± 2.9 months for RRP and 4.7 ± 3.2 months for RARP (P=0.5355). Potency rates within 24 months of treatment were 51% and 62% for RRP and RARP, respectively (P=0.2136). The mean ± SD time to return of potency was significantly shorter for RARP (9.2 ± 6.3 months RRP versus 5.6 ± 3.8 months RARP, P=0.0195). The return to potency is 3.6 months shorter following RARP in the multivariate model (P=0.0007). Recurrence rates were 15% and 8% for RRP and RARP respectively (P=0.2327). The mean months to recurrence were 11.6 ± 6.8 and 16.9 ± 19.6 for RRP and RARP groups respectively (P=0.3053).

Conclusions: Continence rates and mean time to continence were equivalent between both populations. Although potency rates were not significantly different, patients may experience a faster return to potency following RARP. Recurrence was similar in both groups.

Adolescent Medicine, General Pediatrics, and Nephrology III
Concurrent Session
11:00 AM
Saturday, January 26, 2013
386
TRPV4-DEFICIENCY INHIBITS APOPTOSIS DURING URINARY TRACT OBSTRUCTION
Hiatt M1, Ivanova L2, Trnka P3, Matisel D1. 1BC Children’s Hospital, Vancouver, BC, Canada; 2Jack Bell Research Centre, Vancouver, BC, Canada and 3, Brisbane, QLD, Australia.
Purpose of Study: We have previously demonstrated that injury to the distal nephron, is integral to this process. Demonstration of this injury into downstream epithelial and interstitial responses. This process should be aimed at minimizing parenchymal cell death.

Method Used: The role of TRPV4 in vitro was examined using TRPV4 agonist GSK101690A and TRPV antagonist ruthenium red on the mouse IMCD3 cell line. In vivo, TRPV4-deficient and wildtype mice were subjected to unilateral ureteric obstruction for 2 or 6 days. Tissue and protein lysates were analysed using immunoblotting, immunoprecipitation, cell fractionation, TUNEL analysis, morphometric analysis, and immunohistochemistry.

Summary of Results: TRPV4 is localized to the basolateral membranes of the distal nephron epithelium and forms complexes with the intercellular junctional proteins E-Cadherin and β Catenin. In vitro, TRPV4 activation reduces the expression of E-Cadherin, β Catenin, and TRPV4 protein by 37, 44 and 64% respectively, and impairs the association and stability of these functional complexes. Furthermore, TRPV4 activation promotes nuclear translocation of β Catenin and E-Cadherin (6- and 3- fold respectively). In vivo, obstructed TRPV4-deficient mice display nominal changes in tubular dilatation and interstitial α-smooth muscle actin myofibroblast infiltration, yet demonstrate an attenuated epithelial and interstitial apoptosis comparable to sham-treated animals.

Conclusions: These results implicate TRPV4 in epithelial sensation of obstructive injury, and highlight TRPV4 activation as a candidate for the transcription of this injury into downstream epithelial and interstitial responses. This may be due to the pro-fibrotic transcriptional activities of nuclear β Catenin and E-Cadherin. Further investigations with TRPV4-deficient mice will seek to identify factors regulating epithelial-mesenchymal crosstalk. Future therapeutic interventions should be aimed at minimizing parenchymal cell death.

SELF EFFICACY DOES NOT CORRELATE WITH HOURS OF PARTICIPATION IN A DIABETES RISK REDUCTION PROGRAM FOR ADOLESCENTS AND YOUNG ADULTS
Jenkins M1, Mandeville A2, Harris A1, Skipper B3, Dallen J2, Kong A1. 1University of New Mexico, Albuquerque, NM and 2Oregon Research Institute, Albuquerque, NM.

Purpose of Study: Success of behavioral interventions for weight management depends on participation and time invested to program elements. Higher intensity interventions with greater number of program contact hours are more successful than interventions with fewer contact hours. Historically, retention rates and compliance in behavioral intervention programs are poor. Studies have suggested that greater self-efficacy increases the ability to enact behavioral change. We explored the correlation between self-efficacy to exercise and to make healthy food choices and hours of attendance in R x LM, a community-based program targeting low-income multiethnic adolescent and young adult students.

Methods Used: A sample of 51 students, 16-24 years of age, at an urban vocational training center were randomized to either R x LM (n=25) or a usual care group (n=26). R x LM included: 1) a physician visit to review patient risks for diabetes and address healthy eating and physical activity, 2) a 2 hour health education class, and 3) 10 weeks of supervised fitness training at a community gym. Validated self-efficacy questionnaires were used to measure self-efficacy to exercise and to make healthy food choices. Spearman correlations between self-efficacy and contact hours were calculated.

Summary of Results: 25 students (mean age 19 years, 64% female, 36% American Indian, 24% Hispanic, 77% overweight or obese) participated in R x LM. Hours of attendance ranged from 0.5 to 17.5 hours out of a possible 21.5. The physician visit and health education class were well attended, but the fitness sessions were poorly attended. Mean self-efficacy score to exercise was 5.6, SD = 1.4 (possible = 7). Mean self-efficacy score to make healthy food choices was 4.1, SD = 0.6 (possible = 5). Spearman correlation between exercise self-efficacy and contact hours was r=0.29, p=0.16. For self-efficacy to make healthy food choices and contact hours, Spearman r=-0.008, p=0.997.

Conclusions: Overall, students in R x LM had high self-efficacy for exercise and making healthy food choices. However, self-efficacy did not correlate with hours of participation. To increase future attendance, research is needed to better understand participants’ barriers to participation.

CARDIAC SURGERY ASSOCIATED ACUTE KIDNEY INJURY IN INFANTS AND NEONATES: RELATIONSHIP BETWEEN URINE OUTPUT AND SERUM CREATININE
Lee-Son K1, Gandhi SK2, Campbell A2, Skipper P3, Zappelli M4, Subraei V1, Mammen C3, 1BC Children’s Hospital, Vancouver, BC, Canada; 2BC’s Children’s Hospital, Vancouver, BC, Canada; 3BC Children’s Hospital, Vancouver, BC, Canada and 4Montréal Children’s Hospital, Montréal, QC, Canada.

Purpose of Study: Acute kidney injury (AKI) post cardiac surgery is associated with poor outcomes. AKI definition for infants remains uncertain; the utility of urine output change (U/O) and maximum to baseline serum creatinine ratio (ΔSCR) is unclear. Our aim was to determine the strength of agreement between ΔSCR and U/O for defining AKI.

Methods Used: In this single center prospective cohort study, infants and neonates requiring cardiac surgery from Mar-Sep 2012 were eligible. We recorded post-operative hourly U/O for ≥24h and ΔSCR for ≥2d. The Acute Kidney Injury Network (AKIN) staging was used. Stage 1: ΔSCR >1.5 or U/O <0.5 mL/kg/h for 6h (I); Stage 2: ΔSCR >2 or U/O <0.5 mL/kg/h for 12h; Stage 3: ΔSCR >3 or U/O <0.3 mL/kg/h for 24h. Agreement was assessed using the kappa statistic.

Summary of Results: Fifty patients were enrolled with the following characteristics: mean age at surgery was 4.8 months in infants, 6 days in neonates; most common diagnosis was ventricular septal defect in infants (28%), transposition of the great arteries in neonates (36%); median Aristotle Basic Complexity Score was 7.7 in infants, 8.6 in neonates; 100% had post-op diuretics; mortality was 4%.

Median (interquartile range) baseline SCR was 26 μmol/L (21-30) and 48 μmol/L (41.8-55.5), while ΔSCR was 1.6 (1.3-2.3) and 1.4 (1.0-1.5) in R x LM versus LM, respectively.

AKIN Severity Distribution of ΔSCR and U/O Criteria

AKIN Stage I: U/O <0.5 mL/kg/h for 6h
AKIN Stage II: U/O <0.5 mL/kg/h for 12h
AKIN Stage III: U/O <0.3 mL/kg/h for 24h

Conclusions: ΔSCR correlated better with U/O for AKIN stage 1, but ΔSCR correlated better with U/O for AKIN stage 2 and 3.
infants and neonates respectively. Of 27 AKI patients, only 1 neonate did not fulfill ΔScr criteria; 4/21 (19%) infants and 3/6 (50%) neonates fulfilled U/O criteria. U/O and ΔScr criteria agreement level was poor (κ=0.139, 95%CI=−0.014 to 0.293).

Conclusions: Most AKI is captured by ΔScr criteria. There is poor agreement between ΔScr and U/O staging of AKI severity. Further study is needed to determine if presence of U/O AKI contributes to the diagnostic criteria of neonatal and infant AKI.

389

EFFECTIVENESS OF A MULTIDISCIPLINARY TERTIARY WEIGHT MANAGEMENT CLINIC AT IMPROVING BODY MASS INDEXES AND BLOOD PRESSURES AMONG MORBIDLY OBSESE PEDIATRIC PATIENTS

Thang CK1, Whitley M2, Izadpanah N2, DeUgarte D3, Slusser W3. 1David Geffen School of Medicine at UCLA, Los Angeles, CA and 2University of California Los Angeles, Los Angeles, CA.

Purpose of Study: Increasing childhood obesity rates indicate increasing cardiovascular risk, as higher body mass index (BMI) is associated with elevated blood pressure (BP). Approximately 7-10% of children progress from prehypertension (90th-95th percentile) to hypertension (>95th) per year. Preventive measures may limit this progression, yet few effective interventions exist to improve dietary and physical activity habits and improve BMI and BP. The purpose of this study was to evaluate the clinical outcomes of morbidly obese pediatric patients seeking care at the multidisciplinary UCLA Fit for Healthy Weight Clinic.

Methods Used: A retrospective medical chart review was conducted of 115 enrolled patients, boys and girls, ages 3 to 22 years. The multidisciplinary team consisted of a general pediatrician with a specialty in nutrition, a registered dietician, and a psychologist. Treatment included nutritional education, psychological counseling, and behavioral intervention. Individualized goals were developed and evaluated at monthly clinic visits.

Summary of Results: 35 patients completed the average duration of 3 clinic visits. At baseline, 26% of patients had elevated BP, and 100% had BMI at or above the 95th obese percentile. After 3 clinic visits, there was a significant improvement in BP across all patients with an average BP percentile decrease of 0.25 without medication intervention (p<0.05). 82% of patients with elevated BP moved into the normotensive range. 9 patients saw a BMI percentile decrease of at least one percentile with 3 patients moving down into the 85th-95th overweight percentile.

Conclusions: A multidisciplinary pediatric obesity clinic can reduce BMI and BP, ultimately decreasing cardiovascular risk, through motivational interviewing, education, and behavioral changes. This study saw a significant clinical outcome as BP decreased despite elevated BMI in the 95th percentile and above.

390

BUILDING A CLINICAL PATHWAY FOR CHILDHOOD NEPHROTIC SYNDROME

Jobsis J1, Mannen C, Alishami A, Sibley M, Matsell D. 1BC Children’s Hospital, Vancouver, BC, Canada.

Purpose of Study: Childhood nephrotic syndrome (CNS) is one of the commonest kidney disorders in pediatrics, with a reported prevalence up to 20 per 100,000 children. Although the long-term outcome is generally favorable, recommendations for best therapies and management are based largely on historical practice. This has led to widespread practice variation internationally, nationally and even locally. The province of British Columbia, Canada has a single pediatric tertiary care facility, providing a unique opportunity to standardize care for children with CNS within the whole province. Our objectives were to develop and implement a general-use clinical pathway for CNS patients and treating physicians that would standardize care based on the best available evidence and that would provide a template from which other clinical pathways in our Program could be developed.

Methods Used: We formed a CNS Clinical Pathway Team that met bi-weekly. The Team included pediatric nephrology subspecialists, nephrology trainees, and a general pediatrician trainee. In addition we reviewed the specifics of clinical practice for the past 20 years at our center. We reviewed our in-center experience over the past 20 years. We then performed a review and analysis of the published English literature. The evidence for each topic was reviewed at our meetings and the pathway developed based upon this analysis and on the best available evidence. The proceedings of and our justification for the steps in the pathway were summarized in a standard document that will serve as the basis for an information handbook for patients, parents, and healthcare providers.

Summary of Results: A priori we identified the necessary topics to be reviewed, including: 1) diagnostic work up at initial presentation, 2) “red flags” at initial presentation which suggest non-minimal change disease, 3) reasons for referral to and consultation with a Pediatric Nephrologist, 4) indications for a diagnostic kidney biopsy, and 5) induction therapy for uncomplicated CNS. After approximately one year of literature review, analysis, and deliberation, we have developed the first iteration of a clinical pathway for CNS.

Conclusions: We anticipate the pathway will not only standardize care, but that its implementation will improve outcomes, and impact on the costs of care delivery. These are future areas of clinical research in our population.
Purpose of Study: Anti-thymocyte globulin (ATG) has been used as induction therapy in heart transplantation. Rabbit ATG has been postulated to have anti-humoral properties, as human thymus (which contains both T- and B-cells) is used to stimulate antibody production in rabbits. Antibodies to these cellular lines may provide benefit to prevent the production of circulating antibodies after heart transplantation. We chose to assess for this observation by reviewing our patients who received rabbit ATG induction versus those who did not.

Methods Used: Between January 1, 2006 and August 1, 2011, we assessed 126 heart transplant patients who received 3-5 days of rabbit ATG and compared them to patients who did not receive rabbit ATG and were started only on standard triple drug immunosuppression (tacrolimus, mycophenolate and corticosteroids). Patients with circulating antibodies prior to transplant were excluded from this study. We evaluated all study patients routinely for the development of de novo circulating antibodies at 3, 6, and 12 months after heart transplant.

Summary of Results: There was a trend for less first-year de novo antibody production in the ATG treated group compared to the control group (see table). None of the patients treated with ATG developed biopsy-proven antibody-mediated rejection requiring treatment. Treated cellular rejection rates were comparable in both groups.

Conclusions: ATG induction therapy may prevent the production of de novo antibodies after heart transplantation and may result in decreased antibody-mediated rejection. A randomized trial in a larger cohort of patients is warranted.

393 DOES THE RENAL SPARING PROTOCOL WITH CESSION OF CNI RESULT IN METABOLIC IMPROVEMENT?

Murray Bruce N, Rafiei M, Osborne A, Hamilton M, Kobashigawa J. Cedars-Sinai Heart Institute, Los Angeles, CA.

Purpose of Study: Renal Sparing Protocols (RSPs) after heart transplantation with cessation of calcineurin inhibitors (CNIs) and maintenance with mycophenolate mofetil (MMF) and sirolimus have been reported to be successful. This type of regimen has been ongoing for the past 8 years with continuing success. CNIs are known to cause metabolic abnormalities such as increased risk for hyperlipidemia, hypertension, gout, and renal insufficiency. Once patients (pts) are off CNIs there should be benefit in these metabolic parameters.

Methods Used: Between 1994 and 2008, we reviewed 36 heart transplant pts on RSP who were at least 1 year removed from the start of this regimen. These pts were compared to age-sex-time from transplant-controls in a one to one fashion. The endpoints are change at one year in lipid parameters (total cholesterol, triglyceride, HDL and LDL levels), change in number of hypertension medications, gout, attacks and change in renal function. In addition, the two groups were compared for subsequent 5-year actuarial survival, 5-year freedom from cardiac allograft vasculopathy (CAV) and 5-year freedom from non-fatal major adverse cardiac events (NF-MACE, defined as myocardial infarction, heart failure, need for percutaneous cardiac intervention, stroke).

Summary of Results: Pts on RSP with cessation of CNIs appear to have significant improvement in renal function (Cr decrease from 2.5 to 1.8 mg/dl, p=0.0001), LDL cholesterol (109.3 to 95.8 mg/dl, p=0.0077) compared to those pts who remained on CNI immunosuppression. There also appears to be a favorable trend in total cholesterol, HDL, triglycerides, the incidence of gout and hypertension medication requirement. 5-year subsequent survival, development of CAV, and NF-MACE were not significantly different.

Conclusions: Cessation of CNIs as used in RSPs appear to result in metabolic benefits after heart transplant. Further studies are needed to assess whether these metabolic improvements do result in longer term benefit in survival, CAV, and NF-MACE.
Summary of Results: Patients with PGD had decreased 5-year survival compared to patients without PGD. 5-year freedom from CAV and NF-MACE and 1-year freedom from any-treated rejection were similar in both groups. (see table)

Conclusions: PGD characterized by left ventricular dysfunction and the need for mechanical support/inotropes do less well after heart transplantation. Further understanding of mechanisms of PGD and identifying characteristics that lead to PGD will be crucial to avoid this extreme complication.

<table>
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<th>Outcomes</th>
<th>No PGD (n = 1,314)</th>
<th>PGD (n = 45)</th>
<th>p-value</th>
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<td>5-Year Actuarial Survival</td>
<td>77%</td>
<td>42%</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>5-Year Freedom from CAV</td>
<td>76%</td>
<td>89%</td>
<td>0.058</td>
</tr>
<tr>
<td>5-Year Freedom from NF-MACE</td>
<td>86%</td>
<td>89%</td>
<td>0.524</td>
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<tr>
<td>&gt; Year Freedom from Any-Treated Rejection</td>
<td>83%</td>
<td>84%</td>
<td>0.712</td>
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</tbody>
</table>

CARDIAC STRANGULATION FOLLOWING EPICARDIAL PACEMAKER IMPLANTATION: A RARE PEDIATRIC COMPLICATION
Carreras EM, Campbell AJ, B.C. Children’s Hospital, Vancouver, BC, Canada.

Purpose of Study: Cardiac strangulation may occur following epicardial pacemaker implantation if its lead becomes adherent to the epicardium and wrap around the heart. With progressive somatic growth this lead may constrict the underlying cardiac structures causing mechanical complications and potentially death. The aim of our study was three-fold: To determine the incidence of the pathology, improve the implantation protocol of epicardial pacemakers and develop a protocol for follow-up that included regular reassessment and potential imaging.

Methods Used: All patients who underwent implantation of an epicardial pacemaker from January 1992 to March 2012 were included with hospital health records being used to gather retrospective data including basic demographics, surgical details and cardiac related check-up information for the first 2 check-up dates post-implant, and for every year thereafter. Any post-operative complication that occurred in between the yearly recorded follow-ups were included. Prospectively, the patients that had not received a chest x-ray within the previous 2 years were approached for imaging with a standard two film chest x-ray to assess the leads’ potential for causing cardiac strangulation - reviewed by a blinded radiologist. The primary outcome was mortality related to cardiac strangulation or reoperation for replacement of the epicardial pacemaker system due to mechanical dysfunction. Specific symptoms were also recorded as secondary outcomes, including: syncope, chest pain, arrhythmias and atrioventricular valve regurgitation. A multivariate analysis determined interdependency between the variables and primary and secondary outcomes.

Summary of Results: This study included 87 patients with a 2.2% incidence, and a 1.1% mortality related to this pathology. A characteristic pattern of posterior looping of the ventricular lead was seen in chest radiographs of both patients with cardiac strangulation presenting acutely in both cases.

Conclusions: Our institutional incidence of cardiac strangulation is significantly greater than the previously reported approximation of 0.01%. Our data supports that the 2 cases of cardiac strangulation were not caused by a lack of follow-up but by a lack of effective imaging for diagnosis. This finding is supported by the 7 cases of cardiac strangulation found in the English literature (May 2012).

NON-INVASIVE STUDY OF CAVAL COMPRESSION SYNDROME IN PREGNANCY
Shuen IA\(^1\), Woelkers D\(^3\), Patino C\(^2\). 1UCSD School of Medicine, La Jolla, CA and 2UCSD School of Medicine, La Jolla, CA.

Purpose of Study: Aortocaval compression by the gravid uterus in supine position reduces maternal cardiac output and uteropelvic perfusion, which is relieved by left or right lateral tilt. This is ascribed to reduced maternal cardiac return, but contributions of increased afterload and uterine venous congestion have not been studied. The objective of this study is to determine if lateral tilt alters maternal vascular resistance and uterine artery blood flow.

Methods Used: A cohort of low-risk obstetrical patients 20 to 35 weeks was recruited during routine ultrasound to undergo noninvasive maternal hemodynamics and uterine artery Doppler studies. Subjects were studied in supine and > 45 degree left and right tilt positions. Hemodynamics were measured by electrical impedance cardiography (Anschulon, Cardioitronics, Inc) which included cardiac output (CO), systemic vascular resistance (SVR), and blood pressure (MAP). Uteroplacental blood flow resistance was estimated by pulsatility index (PI) and systolic (SV) and diastolic (DV) blood flow velocity. Fetoplacental flow perfusion was estimated by systolic to diastolic velocity ratio (S/D). Comparisons between groups were made with Kruskal-Wallis test or repeated measures ANOVA, significance p<0.05.

Summary of Results: 32 pregnant women were recruited with complete data for 26 subjects. Median gestational age was 27.5 weeks and median BMI was 28.5. There were no significant differences in CO in left or right lateral tilt compared to supine, although MAP and SVR were significantly reduced (p<0.001). There were no differences in uterine artery PI, SV, or DV, or umbilical S/D in either lateral position compared to supine. Subgroup analysis demonstrated a trend toward improved CO in obese subjects in right lateral tilt (p=0.0854) but no differences in uterine artery indices by degree of obesity.

Conclusions: In a mixed cohort of various gestational ages, there were no differences in maternal CO in lateral positions. Observed decrease in MAP and SVR in lateral tilt is significant but possibly an artifact of the arm cuff position, so the contribution of increased SVR to caval compression syndrome is uncertain. Preliminary data demonstrates trend toward improved cardiac output for obese patients in right tilt as compared to left or supine.

General Internal Medicine and Aging II
Concurrent Session
11:00 AM
Saturday, January 26, 2013

ULTRAVIOLET EXCIMER LASER TREATMENT OF GENERALIZED PSORIASIS: OPPORTUNITIES AND WARNINGS
Butler D\(^1\), Gupta R\(^2\), Huynh M\(^3\), Levin E\(^4\), Leon A\(^5\), Koo J\(^6\). 1University of Arizona College of Medicine, Tucson, AZ; 2University of Southern California, Los Angeles, CA and 3University of California, San Francisco, San Francisco, CA.

Purpose of Study: Psoriasis is a skin disease affecting close to 3% of the United States population. Treatment of localized plaque-type psoriasis with the excimer laser has proven to be an effective and safe treatment because it allows for the delivery of higher dosimetry UVB light to the localized plaques. The increased dosimetry is possible because the excimer laser targets only the psoriatic plaques whereas the standard phototherapy targets the full body, both psoriatic and non-psoriatic skin. This study seeks to determine the efficacy and safety of excimer laser treatment in patients with generalized psoriasis.

Methods Used: A total of 30 patients with generalized psoriasis, as defined by over 10% body surface area involvement with moderately confluent plaques, were enrolled in the 12-week study protocol. Treatments with the excimer laser were performed twice a week for up to 12 weeks. Additionally patients used adjunct topical clobetasol spray and calcitriol ointment alternated every 4 weeks. We followed the induration protocol for initial dosimetry of the laser. This protocol includes skin type and plaque induration characteristics to determine initial dose. We also used the erythema and burn protocol for dosimetry changes on each visit. This protocol uses the time and amount of erythema and blistering from previous treatments to determine dosimetry changes on subsequent visits.

Summary of Results: Interm results reveal 80% of patients receiving excimer laser for generalized psoriasis achieved PASI 75 after 12 weeks of treatment. However, one case showed a patient who suffered both mild and significant burning upon following the erythema and burn protocol. The patient continued to suffer significant burning after decreasing the dose by 15% as stated on the protocol.

Conclusions: Treatment of generalized psoriasis in combination with topical treatment with the excimer laser is both efficacious and safe. However, there is a need for a new protocol for dosimetry in the management of erythema.
and blistering, which considers the variety of sensitivities seen in generalized psoriasis patients as compared to the initial protocol made for recallant, localized plaque psoriasis.

DIAGNOSIS AND OPTIMAL MANAGEMENT OF PATIENTS WITH DELUSIONS OF PARASITOSIS AND RELATED SOMATIC PSYCHOSES

Gupta R, Huynh M, Butler D, Levin E, Leon A. University of California - San Francisco (UCSF), San Francisco, CA.

Purpose of Study: Delusions of parasitosis (DOP) and other monosymptomatic hypochondriacal psychosis (MPH) are conditions in which patients have a specifically defined, false belief that they are infested with parasites or other living/non-living things. Though the underlying pathology is psychiatric, these patients are unlikely to be seen by a psychiatrist, yet they will not recover if their health care provider is unaware of the tools available to successfully treat them. The following review serves to introduce to the community a psychosis encountered in dermatological practice: Delusions of Parasitosis (DOP) and other related encapsulated somatic delusions.

Methods Used: There is a paucity of published journal articles discussing how to interact and properly treat patients with delusions of parasitosis. A literature review was conducted evaluating the differential diagnosis of DOP and the optimal management strategy. A review of the PubMed database of articles was performed utilizing key words such as somatization disorder, delusions of parasitosis, monosymptomatic hypochondriacal psychosis, psychodermatology, and psychogenic skin excoriations.

Summary of Results: Patients with DOP are extremely challenging patients to treat and can often be frustrating to the physician. Though therapists may be exceptionally creative, they are not as intuitive. It was found that, after a thorough differential diagnosis is evaluated, optimal management consists of strategies to establish a strong interpersonal relationship with the patient followed by prescribing select anti-psychotics. Developing a constructive approach to these patients can help patients with these conditions that are not as rare as previously thought.

Conclusions: It is important for dermatologists and other health care providers to understand the nature and the management of patients with delusions of parasitosis and other related somatic psychoses.

ASSOCIATION OF SPIROCHETAL INFECTION WITH MORGELLONS DISEASE

Middelveen MJ, Poruri A, Mayne PJ, Sapi E, Kahn DG, Stricker RB, Atkins Veterinary Services, Calgary, AB, Canada; University of New Haven, West Haven, CT; Laurieton Medical Centre, Laurieton, NSW, Australia; Olive View-UCLA Medical Center, Sylmar, CA and California Pacific Medical Center, San Francisco, CA.

Purpose of Study: Morgellons disease is an emerging multisystem illness characterized by skin lesions exhibiting unusual fibers or filaments. Recent research has demonstrated that this dermopathy is associated with aberrant keratin expression by epithelial and follicular keratinocytes (Middelveen et al. J Clin Exp Dermatol Res. 2012; 3:140). Although a clinical association between Morgellons disease and Lyme disease has been reported, direct evidence for an infectious agent associated with Morgellons disease is lacking.

Methods Used: Four patients with Morgellons disease were randomly selected for the study. Two of the patients were described in detail elsewhere (Middelveen et al. J Clin Exp Dermatol Res. 2012; 3:140). The other patients had clinical findings of epithelial lesions and dermal fibers consistent with Morgellons disease. Serological testing for Borrelia burgdorferi and rapid plasma reagin (RPR) testing for Treponema pallidum was performed on all patients. Dermatological tissue samples were examined using histological staining (Warthin-Starry and Dieterle silver nitrate-based stains) as well as scanning and transmission electron microscopy. Further characterization of organisms was performed using immunofluorescent staining and polymerase chain reaction (PCR) testing specific for Borrelia burgdorferi.

Summary of Results: Three of the four patients had positive serological testing for Borrelia burgdorferi, and all four patients had negative RPR testing. Spirochetes were detected in dermatological tissue of patients with histological staining and electron microscopy. Immunofluorescent staining coupled with PCR demonstrated that these spirochetes were strains of Borrelia burgdorferi. PCR subtyping indicated that the strains were B. burgdorferi sensu stricto. Conclusions: Morgellons disease is associated with Borrelia burgdorferi infection. This finding supports the association between Morgellons disease and Lyme disease and suggests that Morgellons disease may be transmitted by ticks.

DO PATTERNS OF ALCOHOL USE DIFFER AMONG CLINICAL SITES USING THE ALCOHOL USE DISORDERS IDENTIFICATION TEST?

Paksh J, Kester C. University of New Mexico School of Medicine, ALBUQUERQUE, NM.

Purpose of Study: To compare alcohol consumption between a family practice facility and an urgent care facility in Farmington, New Mexico to optimize spending on interventions to prevent consequences of alcohol abuse.

Methods Used: Self-administered AUDIT surveys were distributed to willing participants over 18 years at two clinical sites in Farmington, New Mexico. Surveys were in English and Spanish and could be declined. Proportions of categorical variables were calculated. Standard summary statistics were calculated using standard methods. A convenience sample was selected to easily acquire data to reflect the patient populations in Farmington. Differences in proportions of categorical variables were tested for significance using exact Chi-squared distribution. The Mann-Whitney Wilcoxon test was used to test for statistical significance between sites for numeric variables. A critical Type II error rate of 0.05 and two-tailed tests were used throughout.

Summary of Results: 196 individuals completed the survey. It is unknown how many individuals refused or were illiterate. The median age was 46.08 (range 23 to 76) at PFP site. Median age was 39.5 (range 18-103) at the UC site. Median AUDIT score was 1.0 (range 0-30.0, interquartile range 0-2.0). The proportion of PFP site subjects that were female was 70.49%, vs 65.19% at the UC site (not significant p=0.5709). Subjects using the PFP site (median 48 years) were older than those using the UC site (median 36.5 years). This difference in medians, 11.5 years, was significantly different from p<0.001. Subjects using the PFP site (median AUDIT score= 1.0) were not significantly different than those using the UC site (median AUDIT score=0.0). This difference in medians, 1.0, was not significantly different from p=0.2417. Native American patients used the UC site 95.1% of the time, while other ethnicities used the UC site 61.3% (p=0.001 using an exact p-value and point probability calculation method). Conclusions: The primary goal of the study revealed no significant differences in alcohol consumption between the sites. Site utilization among Native American patients who participated in the survey was statistically significant. Reasons for this difference in using a family practice site as compared to an urgent care facility are unclear, but merit further investigation.

INCIDENCE AND SEVERITY OF MUSCULOSKELETAL INJURIES IN RURAL OVERWEIGHT AND OBESE PEDIATRICS IN IDAHO

Croshere TM1,2, Seegmiller F3, Paul D3. University of Washington School of Medicine, Seattle, WA and University of Idaho, Moscow, ID.

Purpose of Study: Childhood obesity rates have tripled over the past three decades. The current prevalence of childhood overweight/obesity in America is approximately (33%) compared to Idaho (29.2%). Obese children have a theoretically increased risk of sustaining an extremity fracture because of potential variations in their bone mineral density, serum leptin levels, and altered balance and gait. Load bearing activities are generally associated with osteogenesis leading to stronger bones, however, there is a delicate distinction between loads that induce osteogenesis and loads that result in stress fractures and acute soft tissue injury.

Methods Used: A retrospective medical chart review identified 1298 pediatric injuries (ages 2-19 including fractures, sprains, and strains) that were recorded as occurring between July 1st 2009 - July 1st 2012 in rural clinics and emergency rooms in or near Moscow, Idaho. Age, gender, Body Mass Index (BMI), mechanism of injury, type of injury, and location of injury were
obtained for each pediatric injury. The data was analyzed using Statistical Analysis Software (SAS) to identify significant relationships between the data, with particular attention to BMI, musculoskeletal injuries, and the type of activity involved when the injury occurred.

**Summary of Results:** The prevalence of overweight/obese pediatric injuries was (45.1%) compared to the Idaho prevalence of overweight/obesity of (29.2%). A Chi square analysis failed to show a significant relationship between BMI and severity X2 (4, N= 1218) =3.89, p=0.42. However, obese subjects were prone to injury while navigating activities of daily living (p=0.42). However, obese individuals were more likely to suffer an injury performing normal activities of daily living (p=0.041).

**Conclusions:** The data indicates that overweight/obese pediatrics in Idaho are 1.5 times more likely to suffer these types of injuries than their “normal weight” companions. Males were more likely to sustain an injury than females from ages 6-11. The Chi square showed no significant difference between BMI and severity of injury (p=0.42). However, obese individuals were more likely to suffer an injury performing normal activities of daily living (p=0.041).

**Purpose of Study:** The purpose of this study was to determine the extent to which posttraumatic stress is associated with preterm birth and the invisible wounds of war might impact pregnancy and thus the next generation. The primary objective of this study is to determine the extent to which posttraumatic stress is associated with preterm birth.

**Methods Used:** Using Department of Veterans Affairs (VA) administrative data, we analyzed all deliveries (unit of analysis) from fiscal years 2000-2011. We used ICD-9 codes to identify posttraumatic stress disorder (PTSD) pre-dating the delivery and preterm birth. Multivariate analyses of PTSD as a predictor of preterm birth controlled for military sexual trauma (MST) screening data, deployment (to Afghanistan/Iraq), demographics, and co-morbidities.

**Summary of Results:** 13,643 births were analyzed. 2,348 (17%) were in mothers with a diagnosis of PTSD, with 1,504 (11%) having a PTSD-related encounter within the year prior to delivery (“active PTSD”). 20% of deliveries were in women with MST, 1,065 (8%) were identified as preterm. Preterm delivery was significantly higher in those with a diagnosis of PTSD (9.1%) than those without (7.6%), and remained so after adjusting for age, race and deployment status (aOR 1.24, 95% CI 1.05-1.46). Sub-classifying PTSD into active and not active, the association remained significant only for those with active PTSD (aOR 1.28, 95% CI 1.05-1.55). MST was not independently associated with preterm birth, but showed significant interaction with PTSD—deliveries positive for both MST and active PTSD carried the highest risk (aOR 1.40, 95% CI 1.10-1.79).

**Conclusions:** These results, which represent the largest cohort of PTSD-affected pregnancies ever reported, add support to prior studies suggesting PTSD is a risk factor for preterm birth, and suggest subgroups (those with active PTSD or a history of sexual trauma) who may be at particular risk. The moderate 25-40% increase in odds associated with active PTSD is similar in magnitude to the well recognized 20-60% increase seen with advanced maternal age (≥25).

**Purpose of Study:** In March of 2012, several U.S. organizations released updated cervical cancer screening guidelines calling for less frequent screening. We surveyed practicing gynecologists in the Pacific Northwest region to understand their screening practices, gauge their uptake of the new guidelines, and identify reasons why they may not follow the new guidelines.

**Methods Used:** Participants from Washington, Oregon, Montana and Idaho were sent an anonymous online survey on behalf of their state’s medical association. The survey was sent to 947 gynecologists. The survey consisted of nine questions regarding gender, practice setting, community size, cervical cancer screening practices, and reasons for not following 2012 guidelines.

**Summary of Results:** One hundred and twenty three gynecologists (13.0%) completed the survey. The majority was female (75.0%), in private practice (61.0%), and in an urban setting (56.0%). The majority (52.0%) reported that they follow or plan to follow the new guidelines. Reasons cited for not following the new guidelines included concern over missed opportunities for women’s health education (71.0%), patients wanting more frequent screening (56.0%), and concern about missing dysplasia or cancerous lesions (47.5%). Most physicians report starting screening at age 21 (88.5%) and ending screening between ages 65-70 (77.0%). Although the new guidelines call for a 3-year interval between routine Pap tests or a 5-year interval between routine Pap/HPV co-tests, 61.0% of gynecologists recommended annual or biannual screening for patients <30 years, and 68.0% recommended rescreening within 3 years for women ≥30 with negative co-test results. Private practice physicians were more likely than academic physicians to screen patients <30 years annually (36.0% vs 8.0%, p<0.001 by chi-square test) and more likely to repeat a negative co-test within 3 years (69.0% vs 33.0%, p=0.132 by chi-square test).

**Conclusions:** Gynecologists in the Pacific Northwest are beginning to adopt the new guidelines, with a higher proportion of academic physicians...
than private practice physicians changing practice. Concerns expressed by participants provide an opportunity for physician education on the science and data behind the new guidelines.

406

BARRIERS TO RECOGNITION OF CARDIAC ARREST AND DELIVERY OF CARDIOPULMONARY RESUSCITATION INSTRUCTIONS OVER THE TELEPHONE BY EMERGENCY DISPATCHERS

Lewis MM, Stubbs B, Eisenberg M. University of Washington School of Medicine, Seattle, WA and King County Public Health, Seattle, WA.

Purpose of Study: Disputers recognized cardiac arrest in 80.7% (n=360) of cases and DA-CPR was performed in 46.3% (n=205) of cases. Call circumstances that prevented the dispatcher from assessing for arrest were the primary reasons for non-recognition. When arrest was recognized, the most common reason that DA-CPR was not performed was that bystander CPR was already in progress. Median time to recognition of arrest was 74 seconds. Median time to the delivery of the first DA-CPR compression was 176 seconds. The total median time delay in delivery of the first DA-CPR was 84 seconds. 87.7% of calls had at least one delay (n=360) of cases and DA-CPR was performed in 46.3% (n=205) of cases. Call circumstances that prevented the dispatcher from assessing for arrest were the primary reasons for non-recognition. When arrest was recognized, the most common reason that DA-CPR was not performed was that bystander CPR was already in progress. Median time to recognition of arrest was 74 seconds. Median time to the delivery of the first DA-CPR compression was 176 seconds. The total median time delay in delivery of the first DA-CPR was 84 seconds. 87.7% of calls had at least one delay of 5 seconds or greater.

Conclusions: We observed a high rate of recognition of cardiac arrest by emergency dispatchers. Many barriers to recognition of cardiac arrest and delivery of DA-CPR are due to non-modifiable call circumstance factors. Recognition of cardiac arrest may be particularly challenging in cases where the caller provides erroneous or ambiguous information or when agonal respirations are present. Delays in delivery of DA-CPR are common. While most delays are short in duration, cumulative delays are significant accounting for nearly half of the time to the delivery of the first DA-CPR compression.

407

THE ROLE OF CHILD LIFE SPECIALISTS AS A HEALTH CARE TEAM MEMBER DURING INVASIVE PROCEDURES IN A PEDIATRIC EMERGENCY DEPARTMENT

Holland J, Kim J, Lascelle A, Hart D, Duffy D, Goldman R. University of British Columbia, Vancouver, BC, Canada; BC Children's Hospital, Vancouver, BC, Canada; BC Children's Hospital, Vancouver, BC, Canada; University of British Columbia, Vancouver, BC, Canada.

Purpose of Study: Child life services are used in many children's hospitals to help improve the experience of children and families within numerous clinical settings, including the Emergency Department (ED). A child life specialist (CLS) supports the social and emotional needs of children, youth and families while in the hospital setting. This pilot study aimed to assess whether the presence of a CLS increased patient and family satisfaction during invasive procedures in the ED.

Methods Used: Patient satisfaction scores were collected from 61 families in the ED of a tertiary pediatric medical center between June and August 2012. This prospective, observational study used a Patient Satisfaction Questionnaire (PSQ) with a 100 mm visual analogue scale to score satisfaction in five categories, including (1) how well the patient felt their needs were met, (2) quality of care, (3) communication, (4) support received, and (5) overall satisfaction with the experience.

Summary of Results: Patient satisfaction was extremely high with respect to minor invasive procedures in the ED. There was a slight, but not statistically significant, increase in patient satisfaction scores with intervention of a CLS. PSQ scores were as follows: (1) 87 ± 18; (2) 92 ± 10; (3) 90 ± 15; (4) 90 ± 16, (3) 82 ± 22; (2) 92 ± 13; (4) 88 ± 16; (5) 89 ± 14; 95 ± 7 (control group; intervention group, measured in mm, respectively). Further analysis revealed a smaller variance of overall satisfaction scores in the intervention group compared to the control group (p < 0.001).

Conclusions: While encouraging, the high level of patient satisfaction with the services received in the hospital creates some unique challenges in continuing to improve the experience for patients and their families. Notably, the decreased variation in scores when a CLS was present may suggest that the support of a CLS helps ensure that the experience remains consistently positive.

408

THE PERCEPTIONS AND ATTITUDES OF INTERNS, RESIDENTS, AND ATTENDINGS TOWARD READMISSIONS


Purpose of Study: The purpose of the survey is to determine physicians' perceptions on readmission rates, which will help systems determine the best practices necessary to reduce future hospital readmissions.

Methods Used: In order to assess how UCLA interns perceive readmissions we designed a quick, 10-question survey that was administered to interns, residents and attendings within the Internal Medicine (IM) department. After creating an online survey using Google Documents, we administered the survey to all hospitalists in the UCLA IM department. After administering the survey, we started compiling the readmission rates for each physician by going into the EMR at UCLA and looking up the discharge team listed for every admission at RR for the previous year. We completed 5 months of admissions so the data presented reflects the period from July 2011- November 2011.

Summary of Results: Survey results showed that almost all physicians in the internal medicine department at UCLA wanted to be notified of their readmissions and wanted to know their 30-day readmission rates. However, only about 50% of physicians believed that 30-day readmission rates are indicative of better performance. About 75% of physicians believed that knowledge of their readmission rates would lead to changes in practice that would impact future rates.

Conclusions: This data and the remaining survey data suggest that quality improvements can be made by showing physicians their individual readmission rates, creating a system that alerts providers of their readmissions, and educating physicians around preventability and interventions that work.

Hematology and Oncology II

Concurrent Session

11:00 AM

Saturday, January 26, 2013

409

SUBCELLULAR LOCALIZATION OF PID1, A NEW TUMOR SUPPRESSOR-LIKE PROTEIN IN BRAIN TUMORS

Baweja A, Ren X, Erdreich-Epstein A, Children’s Hospital Los Angeles, Los Angeles, CA and David Geffen School of Medicine at UCLA, Los Angeles, CA.

Purpose of Study: Prognosis of highly aggressive brain cancers such as atypical teratoid rhabdoid tumors (AT/RT) and malignant gliomas is still poor. A better understanding of their biology is needed to design improved therapies. Preliminary studies from our lab have observed a growth inhibitory function for phospho-tyrosine interaction domain-containing 1 (PID1) in a number of brain cancers including AT/RT. PID1 has never been implicated in cancer, which raises the promising idea that this gene may reveal a novel biological pathway to exploit in highly aggressive brain tumors. While prior reports indicate that overexpressed PID1-GFP fusion proteins reside in the cytoplasm, in silico analysis reveals that PID1 harbors a putative nuclear...
Purpose of Study: Robbins HF1, Hahn S2. TRANSCRIPTION ACTIVATION DOMAIN

Head and neck sarcomas are rare and heterogeneous tumors

Summary of Results: Confocal microscopy revealed predominant cytoplastic PID1 localization in a peri-nuclear distribution. In all cell lines tested, there was also evidence of nuclear PID1 observed on the orthogonal views of XY, XZ and YZ axes. Subcellular fractionation demonstrated PID1 compartmentalized primarily to the cytoplasmic and membrane-bound fractions.

Conclusions: PID1 represents a signaling molecule with tumor-inhibitory behavior that provides new insights in both pediatric and adult brain tumors. We report that PID1 is localized in the cytoplasmic and membrane compartments in AT/RT and GBM cell lines. Additional experiments are needed to determine if it is also localized to the nucleus. Studying PID1 function may have implications for our understanding of brain cancer and may help devise more effective treatment strategies for these highly malignant tumors.

410 RETROSPECTIVE ANALYSIS OF ADULT HEAD AND NECK SARCOMA: A SINGLE-CENTER EXPERIENCE FROM 2000-2012

Chang A1, Chai X2, Futran N3, Jones R1. University of Washington, Seattle, WA and 2Fred Hutchinson Cancer Research Center, Seattle, WA.

Purpose of Study: Sarcomas are rare heterogeneous mesenchymal tumors which constitute about 1% of adult malignancies. Head and neck sarcomas compromise only about 5 to 15% of all sarcomas. There have been a few sporadic efforts to investigate the treatment, outcome and prognostic factors in these tumors, but such studies have been hampered by their rarity and heterogeneity. To evaluate the treatment and outcome of head and neck sarcoma patients, we investigated multiple variants with emphasis on their impact on overall survival (OS) and disease-free survival (DFS) to identify high risk individuals and prognostic factors to guide treatment decision.

Methods Used: A retrospective search of UWMC Sarcoma Unit Database was performed to identify patients treated between 2000 and 2012 (n=73).

Summary of Results: The median overall survival was 6.79 years with two-year rate and five-year OS rate of 73% (95% CI: 59%-83%) and 60% (95% CI: 44%-73%), respectively. Univariate analysis of the age at diagnosis, treatment, tumor size, surgical margins, and grade, tumor size, tumor location, treatment received, surgical margin status, and past medical history.

Conclusions: Head and neck sarcomas are rare and heterogeneous tumors that are challenging to treat, suggesting that these tumors should be managed by experienced multi-disciplinary teams. In this study, patients >60 years old at diagnosis had worse overall survival. Surgical intervention remains the optimal treatment modality for those with resectable disease, and was associated with significantly better survival in this heterogeneous series. Further work is required to identify the molecular drivers of these tumors.

411 UNRAVELING THE MECHANISM OF A NOVEL TRANSCRIPTION ACTIVATION DOMAIN

Robbins HF1, Hahn S2. University of Washington School of Medicine, Seattle, WA and 1Fred Hutchinson Cancer Research Center, Seattle, WA.

Purpose of Study: The acidic transcriptional activators are an important class of transcriptional activators (TAs) that encompass most yeast TAs as well as important mammalian activators such as p53, cMyc and E2F.

Despite their biological importance, there is still much to be learned about TAs. TAs are modular in structure. They contain a conserved, structured DNA binding domain (DBD) that targets the activator to the correct gene, and they also contain at least one activation domain (AD) that interacts with other proteins involved in initiating transcription. In contrast to DBDs, there is little sequence conservation between different ADs, they are typically unstructured in the absence of a binding partner, and they often interact with multiple unrelated target proteins. This study unravels the AD binding mechanism of the yeast acidic TA Ino2 and contributes to answering several broad questions including 1) How do transcriptional ADs interact with their targets? 2) What makes a functional activator? 3) Are there different classes of ADs?

Methods Used: Mutations were made in the two ADs of Ino2 (residues 1-50 and 96-160). A total of 24 mutant derivatives of these ADs were made and expressed in yeast. Real time PCR was used to quantify mRNA from two separate genes whose expression is dependent on activator function. Western blots were performed to ensure protein expression.

Summary of Results: Analysis of the mutant derivatives revealed several interesting findings. Deletion mutations showed the minimal binding motif necessary to activate transcription was large and encompassed residues that are both conserved and non-conserved in fungi. Alanyl substitutions for hydrophobic and acidic residues showed that both are necessary for activation.

Conclusions: The ADs of Ino2 interact with target proteins in a novel way. Previously characterized acidic ADs in yeast have shown activation to be largely and sometimes exclusively mediated by hydrophobic interactions. This property helps explain the promiscuity of ADs. Previously studied ADs also contained a short minimal binding motif with important residues being highly conserved in fungi. Therefore the importance of acidic residues in the Ino2 ADs, and the large size of the binding motifs are striking. This data may suggest a new class of acidic ADs.

412 TRIMODALITY TREATMENT OF MALIGNANT PLEURAL MESOTHELIOMA

Sottero T1, Kuwano A1, Truong A2, Laramore G1, Stelzer K1, Patel S1.

University of Washington, Seattle, WA; 2UC Davis, Davis, CA and 3Mid-Columbia Medical Center, The Dailies, OR.

Purpose of Study: Malignant pleural mesothelioma (MPM) is a fatal disease lacking a standardized treatment regimen. Treatments range from palliative to aggressive and consist of combinations of chemotherapy, surgery, and radiation modalities. The purpose of this study was to perform a retrospective chart review: The date of the initial MPM diagnosis/follow-up/death, histological subtypes and grade, tumor size, tumor location, treatment received, surgical margin status, and past medical history.

Summary of Results: Of the 114 patients [90 male, 24 female] included in the analysis with a median age of diagnosis of 60.2 years [range: 36.2-85.0 years] and median survival of 13.7 months [range: 1-107 months]. Of the cases for which histological classification was available there were 70 epithelioid, 11 sarcomatoid, and 7 biphasic tumors [median survival: 15.5 vs. 10.8 vs. 14.3 mo, p=0.056].

A total of 47 patients received trimodality therapy, which was associated with improved survival compared to 60 patients that received one or two of the therapeutic modalities [median survival: 22.3 vs. 10.3 mo; p=0.001]. Of the cases treated with radiation, 25 received photon radiation while 31 received neutron radiation [median survival: 24.8 mo vs. 20.2, p=0.15].

Conclusions: Trimodality therapy consisting of induction chemotherapy, EPP, and adjuvant radiation is associated with significantly prolonged survival in patients with MPM. Radiation treatment modality received (photons vs. neutrons) is not significantly associated with outcome.
CHARACTERIZATION OF PROSTATE CANCER ON MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING: CORRELATION WITH HISTOPATHOLOGY

Beroukhim K\(^1\), Tan N\(^1\), Khin H\(^1\), Lu DY\(^2\), Margolis DJ\(^1\), Reiter RE\(^2\), Raman SS\(^3\). \(^1\)UCLA David Geffen School of Medicine, Los Angeles, CA; \(^2\)UCLA David Geffen School of Medicine, Los Angeles, CA; and \(^3\)UCLA David Geffen School of Medicine, Los Angeles, CA.

Purpose of Study: To describe MRI predictors of prostate cancer foci detection on multi-parametric prostate MRI and correlate it to surgical prostate specimen.

Methods Used: A HIPAA-compliant, IRB-approved retrospective study of 29 consecutive patients who underwent prostatectomy from September 2011 to June 2012 was performed. Patients included had prostate cancer diagnosed by prostate biopsy prior to endorectal-coil 3T prostate MRI. Clinical (age, PSA, biopsy data), MR imaging (T2WI, DCE parameters, ADC, MRSI) and pathologic data (Gleason sum (GS), maximum tumor diameter, seminal vesicle invasion, extracapsular extension, pathologic tumor staging) were collected. Blinded results were correlated with surgical pathology using side-by-side comparisons. T-test was performed for continuous variables and X2 test for categorical variables. Multivariable logistic regression analysis was performed to determine predictors of prostate cancer tumor detection.

Summary of Results: Whole mount histological evaluation revealed 78 foci of cancer in 29 patients. There were significant differences in terms of size and Gleason score between detected and missed tumors on MRI (p < 0.0001). Maximum Diameter: Missed Tumors: 696 cm; Detected Tumors: 1.743 cm. Gleason Scores: Missed Tumors: 32 with Gleason Score ≤ 6, 14 with Gleason Score ≥ 7; Detected Tumors: 8 with Gleason Score ≤ 6, 24 with Gleason Score ≥ 7.

Conclusions: Tumors that are missed and detected on MRI differ significantly in terms of size and Gleason score. Tumors that are smaller than 1 cm at their maximum diameter and of Gleason score of 6 or less are unlikely to pose a lethal risk to patients with prostate cancer. This study shows that tumors missed on MRI tend to share both of these characteristics, and are thus unlikely to be factored into clinical decision-making regardless of detection.

NEUROSCIENCE II

Concurrent Session

11:00 AM

Saturday, January 26, 2013

UTILITY OF A CLOCK DRAWING TASK IN IDENTIFYING SPATIAL NEGLECT IN CHILDREN WITH PERINATAL STROKE

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Purpose of Study: To investigate the long-term effect of hypoxia on gene expression and DNA methylation in hippocampal neuronal cells.

Methods Used: Primary murine hippocampal neuronal cells were cultured for 7 days. Hypoxic stress of 1% O\(_2\), 5% CO\(_2\) for 24 hours was applied on Day 2, conditions found to maximize cellular hypoxic stress response without inducing cell death. This was determined by measuring VEGF and EPO using real-time PCR while cell death was assessed using trypan blue staining. Cells were returned to normoxia for 5 days following the 24 hours of hypoxic stress. On Day 7, Methyl-Sensitive Cut Counting (MSSC) was used to identify a genome-wide methylation profile of the hippocampal cell lines to assess methylation changes resulting from hypoxia. RNA-Seq was also done on Day 7 to analyze changes in gene transcription.

Summary of Results: Transcriptome profiling using RNA-Seq revealed 369 differentially expressed genes with 225 being upregulated. These genes contribute to multiple biological functions including cell death and survival, cell proliferation, and organ development. Furthermore, some of these genes form networks shown to affect CNS development and function. Importantly,
the expression level of 52 genes could be correlated to the changes in DNA methylation in their promoter regions. The top 2 functional groups that were categorized in these 52 genes contribute to neurological diseases and developmental disorders \( (p<0.01) \). Of interest, phenotypic analysis showed that neuronal processes were significantly shorter after 1 day of hypoxia, but there was a catch-up growth of these processes after return to normoxia in spite of the lasting epigenetic changes.

**Conclusions:** We conclude that a) acute hypoxic stress has a long-lasting impact on neuronal gene expression seemingly due to DNA methylation changes and b) the catch-up neuronal morphological changes do not necessarily indicate that there are no major changes in gene expression after re-oxygenation for several days after the hypoxic exposure.

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**RNA EXPRESSION PATTERNS IN SERUM MICROVESICLES FROM PATIENTS WITH GLIOBLASTOMA MULTIFORME AND CONTROLS**

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**Purpose of Study:** To come up with a novel non-invasive molecular marker for the diagnosis of glioblastoma multiforme.

**Methods Used:** Microvesicle RNA from serum from patients with de-novo primary glioblastoma multiforme \((N = 9)\) and normal controls \((N = 7)\) were analyzed by microarray analysis. Samples were collected according to protocols approved by the Institutional Review Board. Differential expressions were validated by qRT-PCR in a separate set of samples \((N = 10\) in both groups).

**Summary of Results:** Expression profiles of microvesicle RNA correctly separated individuals in two groups by unsupervised clustering. The most significant differences pertained to down-regulated genes \((121\) genes \(>2\)-fold down) in the glioblastoma multiforme patient microvesicle RNA, validated by qRT-PCR on several genes. Overall, yields of microvesicle RNA from patients was higher than from normal controls, but the additional RNA was primarily of size \(<500\) nt. Gene ontology of the down-regulated genes indicated these are coding for ribosomal proteins and genes related to ribosome production.

**Conclusions:** Serum microvesicle RNA from patients with glioblastoma multiforme has significantly down-regulated levels of RNAs coding for ribosome production, compared to normal healthy controls, however they have a large overabundance of RNA of unknown origin with size \(<500\) nucleotide.