Cardiovascular 1
Concurrent Session

12:30 PM
Thursday, January 24, 2013

1 ADVANCES IN HEART TRANSPLANTATION ACROSS THE MILLENNIUM
Tittle M, Rafei 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 peripartum 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).

Outcome Summary

<table>
<thead>
<tr>
<th>% Prior Placement of Ventricular Assist Device</th>
<th>Era 1 (n = 422)</th>
<th>Era 2 (n = 333)</th>
<th>Era 3 (n = 303)</th>
<th>Log-Rank p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-Year Actuarial Survival</td>
<td>62%</td>
<td>70%</td>
<td>75%</td>
<td>8%</td>
</tr>
<tr>
<td>5-Year Freedom from CAV</td>
<td>69%</td>
<td>75%</td>
<td>83%</td>
<td>&lt;0.0001</td>
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<tr>
<td>5-Year Freedom from NF-MACE</td>
<td>84%</td>
<td>84%</td>
<td>88%</td>
<td>0.724</td>
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<tr>
<td>1-Year Freedom from Any-Treated Rejection</td>
<td>74%</td>
<td>89%</td>
<td>91%</td>
<td>&lt;0.0001</td>
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</tbody>
</table>

2 ABNORMAL SINOATRIAL NODE PACEMAKING ACTIVITY OF ATRIAL-SPECIFIC SODIUM-CALCIUM EXCHANGER KNOCKOUT MICE
Goldstein Z1, Torrente A2, Lamp ST2, Zhang R2, Chyu K2, Philipson KD3, Goldhaber JI2, 1David Geffen School of Medicine at UCLA, Los Angeles, CA and 2Cedars 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 NCX1 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 di-4-anepp 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-aneapp 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,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. Hence, 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 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, Jons-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 ligature 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 RT-PCR was performed to measure mRNA expression of VEGF variants (120, 164, 188) and 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. Instead, in male rats, sIUGR decreased expression of VEGF 164 (72%) and 188 (67%). In female rat RV, MTS significantly decreased VEGF receptor expression (R1: 79%, R2: 79%) while sIUGR 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, Rafiei 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 outcomes in terms 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.

TACROLIMUS-INDUCED DIABETES LEADS TO MORE DIABETIC COMPLICATIONS AFTER HEART TRANSPLANTATION

Ngan A, Rafiei 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 diabetes leads to more diabetic complications and thus increases the risk of using this drug. We compared our tx pts (pts) on TAC-based immunosuppression vs those who were based on CsA.

Methods Used: Between 1994 and 2010, we evaluated 306 heart tx pts and divided them into those treated with CsA versus those treated with TAC at the time of heart tx. 5 year outcomes including survival, tx vasculopathy, non-fatal major adverse cardiac events, and complications of diabetes including retinopathy, neuropathy, and nephropathy were determined.

Summary of Results: Patients treated with TAC 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 treated with CsA immunosuppression. However, in diabetic pts this benefit is lost at 5 years. However, those pts who had controlled hemoglobin A1C (<6.5%), had comparable outcome with those pts treated with CsA.

Conclusions: TAC-based immunosuppression may have outcome benefit in terms of less rejection; however, long-term complications of diabetestes are more prevalent. Therefore, reassessment of the benefit-risk ratio must be evaluated to assess the longer term outcome of TAC-based immunosuppression.

<table>
<thead>
<tr>
<th></th>
<th>TACrolimus</th>
<th>Cyclosporine</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of Diabetic Patients with Neuropathy</td>
<td>6.4% (3/47)</td>
<td>20.9% (10/9)</td>
<td>0.0275</td>
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<tr>
<td>% of Diabetic Patients with Retinopathy</td>
<td>8.5% (4/47)</td>
<td>11.0% (10/9)</td>
<td>0.6305</td>
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<tr>
<td>1 Year Creatinine, Mean ± SD</td>
<td>1.5 ± 0.5</td>
<td>1.5 ± 0.4</td>
<td>1.0000</td>
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<tr>
<td>5 Year Creatinine, Mean ± SD</td>
<td>1.8 ± 0.9</td>
<td>2.0 ± 1.6</td>
<td>0.4288</td>
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</tbody>
</table>

DESCRIPTIVE ANALYSIS OF VENTRICULAR FIBRILLATION WAVEFORM PROGRESSION AND ITS RELATIONSHIP TO SURVIVAL

Schoene P1, Murphy L1, Sherman LD1, Coult J2, Blackwood J2, Fahrenbruch C3, Rea TD4, 5,6. University of Washington School of Medicine, Seattle, WA; 7, University of Washington Department of Bioengineering, Seattle, WA and 8, King County EMS, Seattle, WA.

Purpose of Study: Ventricular fibrillation (VF) is a common cardiac arrhythmia leading to cardiac arrest, a prominent cause of mortality in the US. VF can be characterized quantitatively using ECG amplitude, frequency, and organization. These quantitative waveform measures, when assessed at the start of resuscitation, may be predictive of patient outcome. However, little is known about how these measures change during resuscitation. We hypothesized that they would change over the course of an arrest and that this change may be correlated to survival.

Methods Used: We utilized the Amplitude Spectrum Analysis (AMSA) method to characterize VF during the first 3 potential shock cycles in a cohort of 404 subjects who suffered out-of-hospital VF cardiac arrest and were treated by King County EMS. AMSA was measured just prior to each shock and patients were categorized by starting AMSA tertile. Patients’ AMSA scores improved when their subsequent shock’s AMSA score was in a higher tertile. The primary outcome of interest was survival to hospital discharge.

Summary of Results: Initial AMSA scores were associated with outcome. Survival to hospital discharge was 22% for the lowest AMSA tertile, 52% for the middle tertile, and 72% for the highest tertile (p<0.0001). Between shocks 1 and 2, 72% of patients had AMSA scores that remained unchanged while 14% improved and 14% deteriorated. Between shocks 2 and 3, 75% remained unchanged, 17% improved, and 8% deteriorated. In the middle tertile, between shocks 1 and 2 there was a 42% increase in survival rate for those whose AMSA scores improved versus those whose deteriorated (p=0.010). Among the lowest tertile, there was a 27% increase in survival rate for those whose AMSA scores improved (p=0.013).

Conclusions: Quantitative waveform measures changed over the course of resuscitation and this change was correlated with outcome. Improvement in the measure was associated with higher survival rates, while deterioration was associated with lower survival rates. Future studies should identify factors that favorably influence these waveform measures.
FEASIBILITY OF PULSE OXIMETRY SCREENING FOR CRITICAL CONGENITAL HEART DISEASE AT 2600 FEET ELEVATION
Han LM1, Klewer SE1, Blank K1, Seckeler MD2, Barber BJ1, 1University of Arizona College of Medicine, Tucson, AZ, and 2Cincinnati Children’s Hospital, Cincinnati, OH.

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 over 20 minutes, 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. Therefore 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, Kemna M1, Law V1, 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 record. Relevant 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 atopic condition. All patients with AMR had median absolute eosinophil counts <400 cells/μL (p=0.059), a literature value indicating eosinophilia. Presence of anti-HLA antibodies before and after transplant, low white cell, lymphocytopenia, neutrophil, and eosinophil counts were associated with AMR, but in the multivariable analysis, only presence of pre-transplant anti-HLA-I 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 further investigation.

ENDOCRINOLOGY AND METABOLISM I
Concurrent Session
12:30 PM
Thursday, January 24, 2013
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NITRIC OXIDE-MEDIATED CONTROL OF VASCULAR MITOCHONDRIAL DYNAMICS IN VIVO
Miller M1, Knabl L1, Olivera L1, Reusch JE1, 1University of Colorado School of Medicine, Aurora, CO, 2Denver VA Medical Center, Denver, CO and 3University of Puerto Rico, Bayamon, Puerto Rico.

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) knockout 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; Fission/Fusion: Mitofusin1, Mitofusin2, OPA1, Fis1, DRP1; Autophagy: 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, Mitofusin1 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.

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 KD1, Chait A1, Reardon C2, Getz G2, 1University of Washington, Seattle, WA; 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 V14 transgenic (V14tg) 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. V14tg/Ldlr-/- 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: V14tg/Ldlr-/- 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, V14tg/Ldlr-/- 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.

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 intratumor growth restriction (IUGR) have measured fetal glucose production using whole-body glucose metabolism. The purpose of this study was to directly measure fetal 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 common 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). In 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 (glycogen, amino acids, pyruvate, or glycerol) 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.

DOES SHORT TERM VITAMIN C REDUCE CARDIOVASCULAR RISK IN DIABETES?

Duran-Valdez E1, Gutierrez A2, Schade DS1. UNM, Albuquerque, NM and 1University 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 antioxidant 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 diabetes 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, carbohydrate/fat meal was ingested during each study arm to enhance oxidative stress. Serum vitamin C levels and atherosclerotic risk factors, including hyperglycemia (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.

Summary of Results: Compared to placebo, serum vitamin C levels increased significantly at all dosages. Vitamin C increased fasting glucose and reduced triglyceride levels as well as oxidative stress, inflammation and hypercoagulability.

Conclusions: In conclusion, these data suggest that vitamin C, if indeed it does have antiatherosclerotic 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 antiatherosclerotic mechanism should be identified.

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

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

Purpose of Study: During weight loss, 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 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 B1, Gamst A2, Franklin S1, Schwimmer J1, 4University of California, San Diego, La Jolla, CA and 4University 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 2.3±0.6. 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). After 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 hyper-insulinemia, 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 I
Concurrent Session
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NATIONAL STUDY OF PRIMARY CARE-TREATABLE EMERGENCY DEPARTMENT VISITS AS INDICATORS OF LIMITED ACCESS TO CARE
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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 observations 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 unadjusted 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.

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 to assess perioperative pain. The purpose of this study was to evaluate the Panda’s agreement with the original paper/plastic versions of these tools.
Methods Used: Following REB approval and informed consent/assent, the Panda FPS-R and CAS were clinically evaluated with children in the Post-Anesthetic Care Unit. Post-surgical pain was assessed in younger children using FPS-R (Panda and paper versions), and in older children using CAS (Panda, paper and plastic versions). Each child was randomly assigned to use Panda 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. 

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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 ±0.24 and 95% limits of agreement within ±1.57 to ±9.17. 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 FPS-R scorer and plastic CAS scorer. The bias toward higher 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.

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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 future 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 3 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% (20-20%) to 91% (85-100%); provision of home management plan: 2% (0-10%) to 86% (76-100%); 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.

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


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 moda-

finil 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; and [3] patients with anti-depressants, 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.

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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.
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 guide wire on the first attempt and required an average of 7 needle sticks before forfeiting. Only 3 out of those 8 identified correct anatomic 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 only 2 needle sticks; we also noted correlation with the ability to pass guide wire on the first attempt (65%), 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. 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.

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FINDING THE PERFECT DOCTOR: IDENTIFYING LGBT-FRIENDLY HEALTHCARE PROVIDERS

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Purpose of Study: Lesbian, Gay, Bisexual and Transgender (LGBT) individuals face significant barriers to receiving equitable health care, and they are significantly more likely to avoid receiving necessary medical care compared to heterosexual adults. Little is known about programs that focus on the doctor-patient dyad to alleviate barriers in access to care. Our objectives are to determine what systems are in place at academic medical centers 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. A sample of academic medical institutions of all 138 U.S. LCME-accredited medical schools was selected to represent all states with a medical school. The chief medical officer of each institution was contacted. The key domains of the survey included the existence of procedures to identify LGBT-friendly providers and LGBT-competency training. The survey was conducted as a 15-minute confidential phone interview, and responses were analyzed as dichotomous variables.

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 35% 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 system is that 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 establish 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.

Immunology and Rheumatology

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

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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 time points after reperfusion, and analysis of IL-10 expression was performed 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 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 of 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 expressing B-cell populations, and modulating IL-10 expression in mouse models in order to observe the effects on renal injury.

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IL-17 INDUCES PROINFLAMMATORY CYTOKINE PRODUCTION IN CORD BLOOD MIXED MONONUCLEAR CELLS IN RESPONSE TO GROUP B STREPTOCOCCUS

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Purpose of Study: Human neonates are uniquely susceptible to group B streptococcal (GBS) and other bacterial infections. Neonates have defects in neutrophil activation and movement which likely contribute to their susceptibility to GBS infection. We previously reported that incubation of neonatal neutrophils with the Th-1 cytokine gamma interferon (IFNγ) corrects these defects (J Exp Med 173:767, 1991). In addition, we demonstrated that neonatal mixed mononuclear cells (MMCs) are deficient in the production of IFNγ in response to GBS (Infect Dis 182:974, 2000). The Th-1 cytokine interleukin-17 (IL-17) is a prominent inflammatory regulator that has been described to act on endothelial cells to recruit neutrophils to sites of microbial invasion. We reported last year at these meetings that cord blood MMCs are deficient in IL-17 production in response to GBS stimulation. Here, we examine the effects of added IL-17 to the cord blood MMCs production of cytokines IL-1β, IL-2, IL-8, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12, IL-13, TNFα, and IFNγ in response to GBS.

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Umbilical cord blood was collected from term deliver-
ies. MMCs were isolated and stimulated with GBS (1×10^5) or GBS + IL-17 (100 ng/mL). Cytokine production was measured using in-house developed multianalyte assay employing Luminex Technology.

**Summary of Results:** In response to GBS + IL-17, neonatal MMCs produced significantly more proinflammatory IL-1β, IL-6, IL-8, TNFα, and IFNγ than with GBS alone (n=12; mean: pg/mL): IL-1β, GBS ([133]; GBS + IL-17: (2475); p=0.007); IL-6 ([8192]; 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=0.03]; IFNγ [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 IFNγ. The addition of GBS + IL-17 to neonatal MMCs significantly enhances the proinflammatory cytokine production of IL-1β, IL-6, IL-8, TNFα and IFNγ. This combined Th-1 type cytokine physiological deficiency likely contributes to the enhanced susceptibility of neonates to GBS and other microbial infections.

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

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**Purpose of Study:** Proper control of wound healing is an essential human process mediated by epidermal and endothelial cells, as well as various hematopoietic immune cells recruited by inflammatory mediators. Classically, wound healing is divided into four phases: hemostasis, inflammation, proliferation, and remodeling. Immediately following wounding, thrombocytes aggregate at the injury site to form a fibrin clot. In the first 1-2 days post-injury, inflammatory mediators attract immune cells to the injury where they phagocytose bacteria and debris. The proliferative phase dominates the second week post-injury, characterized by collagen deposition, granulation tissue formation, re-epithelialization, and wound contraction. The final phase of wound healing consists of collagen remodeling and the removal of non-essential cells by apoptosis. Furthermore, because the use of Poly-A RNA-Seq (RNA-Seq) has never been used to describe wound healing, we sought to further our understanding of the intricate wound healing 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 tissue harvested in the basal state and from the wound site on days 1, 4, and 14 post-injury. RNA-Seq and gene ontology (GO) analyses were conducted using Hypergeometric Optimization of Motif EnRichment (HOMER) and Database for Annotation, Visualization and Integrated Discovery (DAVID).

**Summary of Results:** Compared to unwounded tissue, 7273 genes were differentially expressed on day 1, 6462 genes were differentially expressed on day 4, and 605 genes were differentially expressed on day 14. 1329 and 3402 genes were differentially expressed during wound healing progression from day 1 to day 4 and day 4 to day 14, respectively. Interestingly, GO analyses of up-regulated genes on day 1 and day 4 compared to the basal state and down-regulated genes on day 14 compared to day 4 were significantly enriched for immune processes.

**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.

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**EXPLOITING PROTEASE ACTIVITY TO IMAGE AND UNDERSTANDASTHMA**

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**Purpose of Study:** Asthma is an inflammatory airway disease by which intermittent, reversible airway obstruction that affects more than 300 million people worldwide. The presence of extracellular proteases, such as elastase and matrix metalloproteases 2 and 9 (MMP2/9), correlates with lung pathogenesis 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 + alun 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 asthma lungs than in control lungs (>2-fold higher in whole lungs; p < 0.05), but did not have higher FL than control uncleavable ACPPs. Confocal imaging of lung sections revealed that MMP2/9 ACPPs highlighted inflamed airways while elastase ACPPs have diffuse lung signal; both had higher signal than the uncleavable ACPPs. Second-generation, larger ACPPs had cleavage-dependent FL in asthma 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 asthma 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.

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**PLATELET-ACTIVATING FACTOR AND LIPOPOLYSACCHARIDE FAIL TO INDUCE SLAMF7 PROTEIN EXPRESSION IN PMNS ISOLATED FROM PREMATURELY BORN INFANTS**

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**Purpose of Study:** Polymorphonuclear leukocytes (PMNs) participate in innate immunity as effector cells targeting tissue damage and infection. Neutrophil neutrophil dysfunction contributes to the increased risk for syndromes of dysregulated inflammation of neonates born prematurely. Impaired clearance of PMNs from the inflammatory milieu by tissue macrophages is associated with inflammatory damage. The Signaling Lympocyte Activation Molecule family member 7 (SLAMF7) protein is expressed on lymphocytes, natural killer cells, and macrophages. It facilitates communication between these immune cells, activates lymphocytes, and stimulates cytotoxic activity in natural killer cells, however, SLAMF7 is not known to be expressed by PMNs. We hypothesized that PMNs isolated from healthy adults express SLAMF7 but that neonatal PMNs isolated from prematurely born infants do not.

**Methods Used:** We isolated human PMNs from healthy adults, healthy term infants, and from prematurely born infants. We stimulated these PMNs with lipopolysaccharide (LPS; 100 ng/mL) and platelet-activating factor (PAF; 10 nM) for 2 - 18 hours and determined SLAMF7 mRNA and protein expression using next generation RNA-sequencing, realtime RT-PCR, western blotting, and immunocytochemistry.

**Summary of Results:** PMNs isolated from prematurely born infants failed to express SLAMF7 mRNA following PAF stimulation for 2 hours while PMNs isolated from both healthy term infants and adults robustly expressed SLAMF7 mRNA. Furthermore, preterm infant PMNs failed to express SLAMF7 protein during a 24 hour incubation with PAF or LPS while PMNs isolated from healthy term infants and adults robustly expressed SLAMF7 protein by 4 hours after stimulation.

**Conclusions:** PMNs isolated from healthy adults and term infants express SLAMF7 protein following LPS or PAF stimulation. PMNs isolated from prematurely born infants, however, fail to respond to stimulation with SLAMF7 protein induction. We speculate that the failure to express SLAMF7 protein by PMNs isolated from prematurely born infants represents a developmental component of neonatal neutrophil dysfunction and contributes to the characteristic pro-inflammatory phenotype of preterm infants by decreasing clearance of PMNs from the inflammatory milieu by tissue macrophages.
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.

EXPRESSION OF SURFACE APRIL AND ITS RECEPTOR, TACI, IS UPREGULATED ON B CELLS FROM SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS PATIENTS

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Purpose of Study: Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA) are B-cell mediated autoimmune diseases. These patients have increased numbers of autoreactive B cells suggesting defects in negative selection that occurs during the immature stages of B cell development. The proteins APRIL and BAFF have been shown to promote the survival of B cells in mouse models of autoimmune disease and may contribute to the breakdown of negative selection mechanisms. Soluble APRIL and BAFF are elevated in RA and SLE patients and surface forms have been detected on normal and/or malignant B lineage cells. Using flow cytometry, we found surface forms of APRIL and BAFF on peripheral blood (PB) B cells from SLE and RA patients. The aim of this study is to compare surface expression of APRIL and BAFF and their receptors on B cells from SLE and RA patients to normal B cells.

Methods Used: PB samples were collected from normal, RA, and SLE patients. PB samples were stained for seven-color flow cytometry to assess CD19, IgM, APRIL, BAFF, TACI, and BAFF-R. Stained cells were analyzed using a MACSQuant Analyzer (Miltenyi) and FlowJo analysis software (Tree Star). Mean fluorescence intensities (MFI) for surface markers on B cells from RA and SLE patient samples were compared to normal controls by one-tailed, unpaired t-test, p<0.05.

Summary of Results: The MFI of APRIL, BAFF, BAFFR and TACI on CD19+IgM+ B cells of RA and SLE patients were compared to normal PB. Surface APRIL expression was higher on B cells from RA (p=0.0083) and SLE (p=0.0146) patients and TACI was also increased on B cells from RA (p=0.0114) and SLE (p=0.0146) patients.

Conclusions: Expression of surface APRIL and the TACI receptor are higher on B cells from RA and SLE patients as compared to normal B cells. These results show that in SLE and RA the patient’s B cells themselves serve as a reservoir of surface APRIL that provides a potential source of stimulation for the TACI receptors that are also upregulated on these cells. These data implicate surface APRIL and TACI in B-cell mediated autoimmune diseases.

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 an 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.

32
THE EFFECT OF PROBIOTICS ON METABOLIC BONE DISEASE IN PREMATURE INFANTS
Stillwell KC, Underwood MA. UC Davis Medical Center, Sacramento, CA.
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), Probiotiks® (n=30) and placebo (n=30), and a second trial compared Bifidobacteria infants (n=4), Bifidobacteria lactis (n=6), a 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. 23% (n=29) in the probiotic group (36%) and 10 in the placebo group (26%), RR 0.74 (0.4-1.4). 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 phosphorus < 4 mg/dL: 9 in the probiotic group (12%) and 5 in the placebo group (14%), RR 0.69 (0.3-2.46). 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 possible beneficial effect; a sample size of 4000 infants per group would be needed to test this hypothesis.

33
UTILITY OF TORCH INFECTION SCREENING IN SMALL FOR GESTATIONAL AGE INFANTS
Wei D, Barton L, Sardesai S. LAC+USC Medical Center, Los Angeles, CA.
Purpose of Study: The purpose of this study was to determine the utility of TORCH titer 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 titer 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 titer 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 titer 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.

34
PULMONARY HYPERTENSION IN INFANTS WITH OMPHALOCELE
Hutson S1, Baerg J1, Woelk J1, Lavery A1, Hopper A1, Goff DA2, 1Loma Linda University, Loma Linda, CA; 2Loma Linda University, Loma Linda, CA.
Purpose of Study: To describe the prevalence of pulmonary hypertension (PH) among infants with an omphalocele and identify risk factors associated with the presence of PH.

Methods Used: A total of 33/46 (72%) infants with omphalocele admitted to the LLUCH NICU between 1994-2011 had echocardiograms available for review. Demographic data and clinical characteristics were collected by retrospective chart review. Echocardiogram(s) were reviewed by a single pediatric cardiologist for PH based on presence of flattening of the interventricular septum and/or tricuspid regurgitant jet with estimated RV pressure >40mmHg. Data were summarized and compared for the PH versus the no PH cohort using Fisher’s exact test, two-sample t-test, or Mann-Whitney test as appropriate. Significance was set at p<0.05.

Summary of Results: Pulmonary hypertension was diagnosed in 23/33 (70%) infants with an omphalocele. Most infants with PH were female 14/23 (61%) with mean gestational age 35.7 +/- 3.4 weeks. Presence of liver in the omphalocele sac was more prevalent in the PH cohort compared to no PH cohort, 18/23 (78%) vs 3/10 (30%), respectively, p<0.02.

Conclusions: A large number of infants with an omphalocele have findings of pulmonary hypertension. In this small cohort, presence of liver in the omphalocele sac was more common in those with PH. Further prospective studies are required to determine if PH findings are transient or persistent, potentially influencing outcome.

35
DIFFERENCES IN CLINICAL PRESENTATION OF PRETERM INFANTS (BIRTH WEIGHT ≤ 1250 GRAMS) WITH SPONTANEOUS INTESTINAL PERFORATION
Fischer AM1, Durand M1, Vachon L2, Barton L1, Cayabyab R1, 1LAC+USC Medical Center, Los Angeles, CA and 2LAC+USC Medical Center, Los Angeles, CA.

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DISTRIBUTION OF PLASMA LIPOPROTEIN SIZE IN PRETERM INFANTS IN THE FIRST MONTH OF LIFE

Scoble J1, Smilowitz JT2, German J2, Underwood M1. 1University of California, Davis, Sacramento, CA and 2University of California, Davis, CA.

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 < 0.01). Total LDL levels decreased over time (p < 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 intravenuous intralipid and increasing human milk consumption. Markers associated with insulin resistance appeared 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.

CONGENITAL HEART DISEASE IN LOW BIRTH-WEIGHT INFANTS: EFFECTS OF SMALL FOR GESTATIONAL AGE STATUS ON POST-OPERATIVE OUTCOMES

Wei D1,2, Azen C3, Bhoomal S1,4, Hastings L5,6, Paquette L1. 1Children’s Hospital Los Angeles, Los Angeles, CA; 2LAC+USC Medical Center, Los Angeles, CA; 3Children’s Hospital Los Angeles, Los Angeles, CA; 4Children’s Hospital Los Angeles, Los Angeles, CA; 5Children’s Hospital Los Angeles, Los Angeles, CA; 6Children’s Hospital Los Angeles, Los Angeles, CA.

Purpose of Study: The purpose of this study was to determine whether small for gestational age (SGA) infants are protected against some of the morbidities associated with congenital heart disease repair when compared with premature infants of similar weights.

Methods Used: A retrospective review was conducted on infants admitted to the Children’s Hospital Los Angeles Newborn and Infant Critical Care Unit between January 2004 and December 2011. Charts were reviewed for infants with a birth-weight less than 2500g and with a diagnosis of congenital heart disease. Data was collected including gestational age at birth, birth weight, syndromes, gestational age at repair, pre-operative ventilator time, and weight at repair. Primary outcome was survival to discharge home but additional data collected included post-op ventilator days, oxygen use at discharge, trachectomy at discharge, G-tube or NG feeds at discharge, infection post-operatively, rates of necrotizing enterocolitis, and abnormal brain imaging at discharge.

Summary of Results: A total of 136 low birth-weight infants with a diagnosis of congenital heart disease were identified. Twenty-five infants were transferred with incomplete records, twenty-five infants were not offered surgery due to a lethal condition or uncorrectable heart defect, and twelve infants were offered surgery but died prior to surgery. Of the remaining 74 infants who underwent surgery, SGA infants had a higher gestational age at birth (36.8 vs. 32.3 weeks, p=0.001). There were no differences seen with survival to discharge, abnormal brain findings at discharge, being diagnosed with necrotizing enterocolitis, having an infection post-operatively, duration of post-operative intubation time, or being discharged home on oxygen or with a ventilator.

Conclusions: SGA status plays no protective role in the outcome of low-birth weight infants after surgery for congenital heart disease.

EXPRESION OF LMX1B, KERATOCAN, LUMICAN AND DECORIN DURING NEPHROGENESIS

Espinoza AJ, Feenstra JM, Pira CU, Oberg KC. Loma Linda University, Loma Linda, CA.

Purpose of Study: Lmx1b is a transcription factor necessary for the development of kidneys, limbs, eyes, and the central nervous system. In humans, haploinsufficiency of Lmx1b causes Nalp Patella Syndrome. Individuals with this syndrome exhibit impaired kidney function, absent patella and underdeveloped nails. Similarly, Lmx1b knockout mice exhibit disrupted glomerular filtration that blocks urine production and leads to death shortly after birth. During kidney development, Lmx1b directs podocyte differentiation and maintenance. Podocytes are critical for the formation of the glomerular basement membrane, secreting collagens and proteoglycans. Disruption of podocyte function impairs glomerular filtration, as seen in Lmx1b KO mouse kidneys. The molecular pathways by which Lmx1b directs basement membrane deposition remain uncharacterized. Recent microarray studies in the limb have implicated the proteoglycans Keratocan, Lumican, and Decorin (KLD) as downstream targets of Lmx1b. We hypothesized that Lmx1b might also regulate the KLD proteoglycans during kidney development.

Methods Used: To determine the role of Lmx1b in regulating the KLD proteoglycans, we compared the expression patterns of Lmx1b, Podocin, Keratocan, Lumican, and Decorin in the developing chicken kidney (HH 25/30) using whole mount in situ hybridization and subsequent tissue sectioning.

(Continued on next page)
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
Concurrent Session
12:30 PM
Thursday, January 24, 2013
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ROSIGLITAZONE INDUCES THE DEVELOPMENT OF MACROPHAGE M2 PHENOTYPE AND THE SUBSEQUENT EXPRESSION OF ANTIINFLAMMATORY SIGNALS
Botros A1,2, Husain S1, Sakurai R1, Torday J1, Rehan V1,2, Kwong KY2
1Los Angeles Biomedical Research Institute, Torrance, CA and 2Harbor-UCLA Medical Center, Torrance, CA
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 repair and repair after initial M1 activation. Preliminary evidence shows that M2 phenotype is associated with a decrease of BPD risk. Stimulation of macrophage polarization towards M2 may reduce inflammation in preterm newborns and prevent or attenuate the development of BPD. PPARγ, a member of the nuclear hormone receptor superfamily, is expressed in a number of pulmonary cell types and is critical for alveolar maturation. In experimental models of BPD, systemically administered PPARγ agonists have been shown to block BPD. Whether this effect is mediated solely by affecting alveolar epithelial-mesenchymal interactions, or via their effects on inflammatory cells is not known. We hypothesize that PPARγ agonist-mediated protection against BPD is mediated via their effects on alveolar macrophages.

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 μM) for 24h. Subsequently, IL-6, IL-10 and TNF-α expression were assessed using ELISA.

Summary of Results: RGZ causes 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.

B-NATRIURETIC PEPTIDE (BNP) AND URINARY CGMP IN INFANTS WITH CONGENITAL DIAPHRAGMATIC HERNIA (CDH)
Purpose of Study: CDH is a birth defect characterized by pulmonary hypertension (PH) often not responsive to inhaled nitric oxide (INO). Animal and clinical models of CDH suggest alterations in the NO-cGMP signaling pathway but this has not been investigated in human newborns. BNP also signals via cGMP. It has been proposed as a biomarker of persistent pulmonary hypertension of the newborn, but it has been sparsely studied in infants with CDH.

Methods Used: Infants were enrolled in this prospective cohort study if admitted to the UCSF Intensive Care Nursery (5/11 to 8/12). We measured nitric oxide metabolites (NOx, pmol/ml, by chemiluminescence) and cGMP (nmol/ml, by ELISA) from urine obtained at ≤48h and 7d of age (n=14) in infants with CDH ≤48h in healthy term newborns (n=11). cGMP/NOx ratio (pmol/nmol) was calculated. We measured plasma BNP (μg/mL, Triage Meter Plus) from blood obtained at the same time points in infants with CDH (n=15). In CDH, poor clinical outcome was defined as expired or oxygen dependent at 56d of age. Good clinical outcome was defined as survival off oxygen at 56d. We used non-parametric methods for univariate analysis and logistic regression to assess the prognostic effect of BNP level in CDH after adjustment for concurrent INO administration.

Summary of Results: CDH group demographics: 40% female, median gestational age 38 6/7 (range 35 2/7 - 41 0/7). The median cGMP/NOx ratio at ≤48h was 6.6 for healthy controls, 4.0 for CDH with good outcome (n=7) and 2.1 for CDH with poor outcome (n=7), p=0.026. There was no difference at 7d (2.7 vs. 2.9, p=0.56, for good and poor outcome, respectively). The adjusted OR for poor outcome was 1.3 for every 10 unit increase in plasma BNP (p=0.04), but this was no longer significant at 7d (OR=1.0, p=0.8).

Conclusions: cGMP production may be impaired in infants with CDH at ≤48h; differences were more pronounced in more severely affected infants. Higher plasma BNP levels are associated with poor outcome in CDH at ≤48h. These findings suggest a biochemical mechanism for impaired pulmonary vasodilation in severe human CDH.
IUGR was induced by bilateral uterine artery ligation. Contrary to our hypothesis, we conclude that high fat diet influences aromatase mRNA levels. IUGR alone decreased Setd8 mRNA in both male (82%*) and female lung, but not more than IUGR alone. In male rat lungs, 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 lungs, HFD alone increased Setd8 mRNA (132 ± 27%*). In female lung, HFD alone did not alter Setd8 mRNA levels. HFD with IUGR further increased Setd8 mRNA (174 ± 40%*), p<0.05. Conclusions: Our hypothesis that HFD combined with IUGR will decrease lung static compliance in male IUGR rat pups but not female IUGR rat pups.

Methods Used: IUGR (induced by uterine ligation) and control rat pups were exposed to 60% oxygen or room air from postnatal days 3-6. Rat pups were kept with the dam in room air to postnatal day 21 (d21). Pup nutrition was not affected. At postnatal d21, closed chest, lung static compliance was measured using the FlexiVent System.

Summary of Results: In male IUGR lungs, 60% hyperoxia from days 3-6 decreased static compliance relative to sex-matched room air control (79% ± 15%, p<0.05) and sex-matched hyperoxia control (83+12%, p<0.05). In female IUGR rat lungs, 60% hyperoxia from days 3-6 did not affect static compliance relative to sex-matched room air control or hyperoxia control.

Conclusions: These novel findings indicate that the male IUGR rat lung is vulnerable to alterations in lung mechanics in response to mild hyperoxia from days 3-6. Hyperoxia that was not severe enough to affect control lungs. Gene expression of elastin and other lung repair genes is altered in the male IUGR rat lung before, as well as after, hyperoxia exposure. We speculate that IUGR, alters the regulation of expression of lung repair genes, rendering the lung hyper-responsive to a second hit that otherwise does not cause lung injury.

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


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, monomethylation (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 lungs 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 + SID. 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 lungs, HFD alone increased Setd8 mRNA (132 ± 27%*), and HFD with IUGR further increased Setd8 mRNA (174 ± 40%*), p<0.05. Conclusions: To our hypothesis, we conclude that high fat diet has a sex specific effect on Setd8 mRNA levels, with HFD increasing Setd8 mRNA in male rat lung. We speculate that changes in Setd8 mRNA expression will be refected 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.

Poster Session 1
Cardiovascular
2:30 pm
Thursday, January 24, 2013

REDUCING RISK OF CARDIOVASCULAR DISEASE THROUGH DIETARY MODIFICATIONS IN THE DARHAND VALLEY, MONGOLIA

White S. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Hypertension is common throughout the nomadic herding communities in Mongolia. However, access to blood pressure screening and treatment in rural Mongolia is extremely limited, and community members lack information about the disease. To help address this, a blood pressure screening and educational workshop was held in Renchilhumble, Mongolia in hopes of increasing awareness about the relationship between dietary habits and hypertension.

Methods Used: Over four weeks, a health assessment of the nomadic herding communities of the Darhad valley was performed in cooperation with physicians from Renchilhumble Hospital and BioRegions International. Hypertension and a diet high in salt and animal products with minimal intake of fruits and vegetables were found to be widespread problems. Based on information obtained from the medical literature, an educational poster was created describing the benefits of reducing salt and sugar consumption on
cardiovascular health. The poster was utilized during several free workshops, performed inside families’ gers and at annual community cultural events in the bagh (district) one region of Renchinlhumbe.

Summary of Results: More than 100 health screenings were conducted throughout the Darhad Valley. Over half of the 80 families living in the bagh one community participated in educational workshops. Additional herders in the bagh one region attended the poster session at the local Naadam celebration.

Conclusions: Household level teaching allowed for entire families to hear about possible dietary changes and helped address the difficulties with transportation and remoteness that are endemic to this region, and offer a model for future educational campaigns. Additional work is needed to increase the accessibility of healthier food items and to break the community’s reliance on meat, salt, and fat for sustenance. Health professionals in the area also need support in helping their patients develop lifestyle plans to reduce cardiovascular disease risk.

46 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 (Aesculon, Cardiotronics, Inc.) in the supine position. Uteroplacental vascular resistance was estimated by uterine artery Doppler ultrasound (pulsatility index, PI). Fetalplacental 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 multinarial. 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 resistance (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.

47 NEW ONSET LEFT VENTRICULAR HYPERTROPHY AFTER HEART TRANSPLANTATION: WHAT IS THE MEANING?

Osborne A, Rafiei 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 preservation 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.

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 (CAB) 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 CAB 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 CAB 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 affect 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.

48 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, 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
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.

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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 implantation. 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 pectoral 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.

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

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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-breaker 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.

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ADDRESSING HYPERTENSION THROUGH LOCAL DIETARY OPTIONS IN REXBURG, IDAHO

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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 “X” and 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.
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.

In summary, cascading mentorship community outreach program is an effective way to promote the interest of under-represented minority (URM) youth in health careers. 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 participating students. 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 healthcare 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... It 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.

Conclusions: Introduction of cadaver lab to premedical high school and college students is an effective way of promoting their interest in healthcare careers. Cadaver lab should be included in pipeline programs designed to increase diversity in healthcare professions.

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


Purpose of Study: Diversity in healthcare professions 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 of 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.

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

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**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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**AWARENESS OF SICKLE CELL GENOTYPE AMONG NIGERIANS IN THE UNITED STATES**

Shahani S1, Ezeanolue EE1, Oboro 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 resulting in a child with SCD. We surveyed recent immigrants 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/procreational choices.

**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/procreational 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 SC status (85.5%, 59), 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 (87.7%, 64), while awareness before wedding would have the greatest impact on marriage/procreational 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
A COMPARISON OF DIGITAL BREAST TOMOSYNTHESIS AND FULL FIELD DIGITAL MAMMOGRAPHY IN THE DETECTION OF BREAST CANCER

Moradzadeh A, Bassett LW, David Geffen School of Medicine at UCLA, Los Angeles, CA and David Geffen School of Medicine at UCLA, Los Angeles, CA.

Purpose of Study: The purpose of this study is to compare the new 3-dimensional imaging technique, Digital Breast Tomosynthesis (DBT), to conventional 2-dimensional Full Field Digital Mammography (FFDM). In the United States, Breast cancer is the number one cause of death by cancer among Hispanic women, and the second cause of death by cancer in Caucasian and African American women. Utilization of screening mammograms helped to reduce mortality rates for women ages 40-69 by 44%. However, there are limitations to conventional mammograms. Overlapping fibroglanular tissue can conceal a tumor, thereby hindering a Radiologist’s interpretation and can result in a recall rate of over 10% for women who have undergone screening mammograms.

Methods Used: Benefits of 3D DBT compared to 2D FFDM will be assessed. It is believed that within the next 10 years Digital Breast Tomosynthesis will replace conventional 2D Digital Mammography.

Summary of Results: Utilization of DBT is associated with a reduction in both false negatives and false positives caused by overlapping tissue. DBT was shown to reduce the call back rate for suspicious masses by an average of 10%. Breast tissue density did not compromise DBT’s ability to detect breast cancer. FFDM alone had a breast cancer detection rate of 82.6% compared to 98.3% for FFDM+DBT, across a range of breast tissue densities (Uchiyama N, et al). This exemplifies DBT’s superiority in breast cancer detection, regardless of the breast tissue density type.

Conclusions: Digital Breast Tomosynthesis is now becoming more widely used in the United States. DBT utilization will increase cancer detection regardless of breast tissue density, while reducing the call back rate by 10%. There may be concern of revealing too much information about the breast and result in an increased number of biopsies, however, a similar argument was made several years ago when the push was being made from film mammograms to digital mammograms. The information from the survey we will be performing should provide reasonable approaches for the development of professional practice guidelines in implementation of Tomosynthesis into practice.

A FINANCIAL COMPARISON SUPPORTING MULTIDISCIPLINARY OBSTETRICS SIMULATION OVER TRADITIONAL NURSING EDUCATION IN LABOR AND DELIVERY EMERGENCY MANAGEMENT

Stone S, Daniels K, Halamek L, Pack A, Lucille Packard Children’s Hospital at Stanford, Palo Alto, CA; Stanford University School of Medicine, Stanford, CA; Stanford University School of Medicine, Palo Alto, CA and Lucille Packard Children’s Hospital at Stanford, Palo Alto, CA.

Purpose of Study: A multidisciplinary approach to education has been shown to benefit providers and patients alike. There is evidence that simulation based training results in more successful retention of knowledge for adult learners compared to traditional methods. However, a cost analysis of a multidisciplinary simulation approach to obstetrical nursing education has not been published to date. The purpose of this study was to perform a cost analysis comparing traditional labor and delivery nursing skills education to a multidisciplinary simulation program.

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.

EMERGENCY MEDICAL IDENTIFICATION USE IN ADULTS WITH DIABETES

Nguyen H, Soller C, Bouchonville M, Kapsner P. UNM Health Sciences Center, Albuquerque, NM.

Purpose of Study: Emergency medical identification (ID) is recommended for use by patients with diabetes. Prior studies show awareness of medical ID and its importance among emergency providers. There have been few studies on this topic and little is known about its use in the adult diabetes population. The purpose of this study is to characterize adherence of medical ID use, types used, and reasons for non-adherence among adult patients with diabetes.

Methods Used: Questionnaires were given to patients at a diabetes clinic 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)

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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, low availability of mental health services for uninsured or low-income patients, and low availability of primary and mental health care providers sensitive to depression-like symptoms in Latinos, and cultural stigma often result in underdiagnosis 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

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Purpose of Study: Prehospital selective cervical spine immobilization (CSI) is still a relatively new concept. In our EMS system, protocols for CSI 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 CSI 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 CSI 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 immuno-suppressant 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 kidney 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 medica- tion 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 immunosuppres- sant medication regimen and a mobile phone medication tracking applica- tion 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?

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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 hours spent on a retrospective study from idea genesis to manuscript publi- cation is an important metric for clinicians, students/trainees, as well as administrators in academic medical centers. It will allow appropriate allo- cation of funding for research-based activities including human capital, re- search 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 retro- spective 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.
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

Wackertharth 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.

DELAYS ASSOCIATED WITH INPATIENT ADMISSIONS FROM THE EMERGENCY DEPARTMENT

Larsen C1,2, Colling D1,2, 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 medical administration. 12% were due to a prolonged time for an inpatient bed 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 attending 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 transporting the patient and going to the floor 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.

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<thead>
<tr>
<th>Year</th>
<th>N</th>
<th>Systolic BP</th>
<th>Diastolic BP</th>
<th>TChol</th>
<th>HDL</th>
<th>Tcho / HDL</th>
<th>LDL</th>
<th>TG</th>
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<tbody>
<tr>
<td>2009</td>
<td>118</td>
<td>134 ± 16</td>
<td>82 ± 10</td>
<td>194 ± 43</td>
<td>40 ± 12</td>
<td>4.85 ± 1.6</td>
<td>130 ± 37</td>
<td>132 ± 32</td>
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<tr>
<td>2011</td>
<td>190</td>
<td>129 ± 19</td>
<td>82 ± 10</td>
<td>188 ± 38</td>
<td>47 ± 13</td>
<td>5.96 ± 1.2</td>
<td>129 ± 32</td>
<td>108 ± 81</td>
</tr>
</tbody>
</table>

Unpaired t test

| t | df | p | NS | 0.07 | 0.001 | 0.003 | 0.015 |

2-Year Changes in Wellness Program Participants

Poster Session 1

Hematology and Oncology

2:30 PM

Thursday, January 24, 2013

CARING FOR THE WOOD-WORKERS: TWO-YEAR OUTCOMES OF A LUMBERYARD WELLNESS INCENTIVE PROGRAM

Raymond LW1, Pankowski F2, Shiflett H2, Hall D2. 1Univ of North Carolina, Chapel Hill, Charlotte, NC and 2Carolinas HealthCare System, Charlotte, NC.

Purpose of Study: We tested the hypothesis that a wellness incentive program in a family-owned rural South Carolina lumberyard would improve blood pressure and serum lipoprotein levels of program participants. The lumberyard is self-insured for health care costs.

Methods Used: All men and women working at the lumberyard were invited to participate in the wellness program. Non-fasting serum concentrations of total cholesterol (TChol, mg/dL), high-density lipoprotein (HDL), and triglycerides (TG) of participants were compared for years 2009-2011. LDL was calculated by Friedewald’s equation. Annual results to be shared with personal physicians were sent to each participant in individual letters which included information on cholesterol balance, cardiovascular risk and recommendations. Body Mass Index (BMI) and blood pressure (BP) were recorded during annual health fairs, followed by individual onsite counseling. An onsite fitness facility was added in 2009. Incentives were reductions in health care premiums based on smoking cessation, BP, BMI, lipoproteins and, more recently, glycated hemoglobin. Smoking cessation was judged by self-report without cotinine measurements, and users of smokeless tobacco were asked to report themselves as smokers.

Summary of Results: BMI rose non-significantly between 2009 and 2011 (28.7 +/- 5.95SD to 29.2 +/- 6.2) reflecting both enrollment of new program participants and attrition of others.

Conclusions: A workplace wellness incentive program was associated with improvements in systolic blood pressure and some lipoproteins despite lack of change in BMI. The possible roles of smoking cessation and other specific behaviors remain to be analyzed, as will be trends in glycated hemoglobin.

2-Year Outcomes in Wellness Program Participants
ABIRATERONE-ASSOCIATED DELIRIUM: RECURRENCE WITH RE-TREATMENT
Raymond LW1,2, Carr JP3, Only C1, Yoonmans J1, Salmon 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 unreachable 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 unfit 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 urinated 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 repeatedly 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, psychotic and in need of their inpatient care. Quetiapine (Q) was prescribed, but he became agitated and confused on HD II-3, speaking in multiple languages and requiring security to restrain him. He responded to increased Q dosage and benzodiazepine. Psychiatric re-evaluation on HD II-5 found him reconstituted but still hyperkinetic with an expansive affect. He was again discharged to the home of his daughter, to be followed by oncology, psychiatry and family 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 AB-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 disproportionate 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 communities 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 organizations, 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 screening services. 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 members 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.

ABIRATERONE-ASSOCIATED DELIRIUM: RECURRENCE WITH RE-TREATMENT
Raymond LW1,2, Carr JP3, Only C1, Yoonmans J1, Salmon JS1, 2Carolina HealthCare System, Charlotte, NC and 2University of North Carolina at Chapel Hill, Chapel Hill, NC.

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Conclusion: We suspect that an underlying bipolar affective disorder may have been unmasked by AB, versus a primary AB-induced delirium. No such adverse effects of AB have previously been described.
Awareness of family 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, Bendi M1, Goodwin A2, Geller IB, Oppa T3, Allison K1, Elmore J1, UW, Seattle, WA; VT, UVM, Burlington, VT and Dartmouth, 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 agnostic 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 MYOCYSIS FUNGOIDES

Krishnasamy S1, Pinter-Brown L2,24, Sergio A3, Chiu M1,4, UCLA, Los Angeles, CA; UCLA, Los Angeles, CA; UCLA, Los Angeles, CA and David Geffen 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-9 202.8) 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 need to be done 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 E1,2, Hamilton S2, Lai L2, Lee A1,2, Inglewed 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.

METFORMIN USE AND RECURRENCE IN PATIENTS WITH ORAL CAVITY/OPHARYNGEAL SQUAMOUS CELL CARCINOMA

Sanaiha Y1, Thompson C2, Elashoff D3, Kim B1, Wang M2, Si. John M2, 1Dana-Farber Cancer Institute, Boston; MA and 2University 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 confers protection against recurrences of head and neck cancers. A 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 S, 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.

Conclusions: The 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 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

Aludun C, N, Loe IM, Stanford, Stanford, CA.

Purpose of Study: Premature 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
To examine the effect of prenatal methamphetamine exposure, we conducted a study in which we measured several outcomes.

Summary of Results: Compared to FT, PT had higher scores (more problems) on CBCL Total Problems, mean 49 (SD 11) vs 41 (7), Internalizing, 49 (11) vs 42 (8), Externalizing, 48 (11) vs 41 (8), and GEC, 54 (15) vs 44 (8), and lower IQ, 102 (14) vs 110 (13), all p<.001. The overall model with GEC as mediator and all predictors (GA, SES, gender) accounted for 56% of the variance, p<.001. In model 2, GA was associated with Total Problems score, accounting for 19% of the variance, and IQ, R²=0.10, all p<.001. The overall model with IQ as mediator and the same predictors was unchanged with R²=19%, p<.001. These findings are consistent with previous reports, 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.

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EARLY ADVERSITY AS A MEDIATOR OF THE EFFECTS OF PRENATAL METHAMPHETAMINE EXPOSURE: ON NEUROBEHAVIORAL DISINHIBITION: RESULTS FROM THE INFANT DEVELOPMENT, ENVIRONMENT, AND LIFESTYLE STUDY


Purpose of Study: To examine the effect of prenatal methamphetamine (MA) exposure, mediated by postnatal environmental adversity, on neurobehavioral disinhibition (ND) in the multicenter, longitudinal Infant Development, Environment, and Lifestyle (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 used to assess the outcome. Structural equation modeling was used to establish an association between prenatal MA exposure and ND; covariates used included birth factors, child IQ, R²=0.1, p<.001. The overall model with GEC as mediator and all predictors (GA, SES, gender) accounted for 56% of the variance, p<.001. The overall model with IQ as mediator and the same predictors was unchanged with R²=0.19, p<.001. These findings are consistent with previous reports, 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.

82

Can Readmission For Neonatal Hyperbilirubinemia Be Prevented?

Vora F, Schanler R-2, 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±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±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=.11, p=.19), the relationship between the AAP threshold and actual bilirubin at discharge and readmission was significant (r=.48, P < 0.001). TheAAP 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.

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EARLY IMMUNIZATION RATES AMONG CHILDREN WITH TYPICAL DEVELOPMENT AND AUTISM SPECTRUM DISORDERS

Angkustsiri K-2, Li DD, Hansen RL-2, 1UC Davis MIND Institute, Sacramento, CA and 2UC Davis Medical Center, Sacramento, CA.

Purpose of Study: The relationship between vaccines and autism spectrum disorders (ASD) has been of great interest to families and health providers. This study compares the immunization practices of preschoolers with ASD and typical development (TD).

Methods Used: Immunization records were abstracted from 240 (161 ASD, 79 TD) children between the ages of 24.1-54.4 months participating in the Autism Phenome Project from April 2006 to August 2011. Seventy-eight percent were male. Immunizations were considered up-to-date based on the California state requirement for children ages 18 months to 5 years (3 doses of Hep B, 4 DTAP, 4 PCV, 3 IPV, and 1 MMR). We did not include HIB due to the national HIB vaccine shortage from 2007-2009. Varicella was not included due to the possibility of naturally acquired immunity.

Summary of Results: Immunization rates in ASD children (80.7%) were slightly lower than in TD (82.5%), but this difference was not statistically significant (p=0.775). One (0.6%) ASD child had not received any immunizations. These rates were comparable to those reported in the 2011 National Immunization Survey, which range from 80.4% for HIB to 95.5% for DTAP. The national rate for children who received no immunizations was 0.8%.

Conclusions: Despite the lack of evidence supporting any causal relationship of vaccines to ASD (Institute of Medicine, 2011) many parents remain concerned and some choose to delay or avoid vaccines. Immunization rates in preschoolers with ASD in our sample were lower than TD, although this was not statistically significant. Our study, although not designed to specifically address a causal relationship, does not support an association between vaccines and ASD. In most cases, the immunization practices reported in this study represent behavior during the first 18 months of life, prior to receiving an ASD diagnosis. Further study looking at differences in vaccine acceptance during the 4-6 year booster period is warranted.

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TEACHING CHILDREN HEALTHY FOOD CHOICES THROUGH ACTIVITIES AND VISUAL DISPLAYS

Jenkins DK. University of Washington School of Medicine, Seattle, WA.
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 theorectical 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 and 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.

ENCOURAGING PEER-TO-PEER YOUTH ACTIVISM TO FIGHT DRUNK DRIVING IN CODY, WYOMING
Sunsret M. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: This intervention was intended to decrease drunk driving through youth mobilization and empowerment strategies. In 2011, there were 200 driving under the influence (DUI) offenses in Park County, WY - 33% of all legal offenses in the county last year. The average blood alcohol content of the offending drivers was 0.155. 14 of those charged were minors. Of the county’s 37 motor vehicle accidents last year, 36 involved alcohol.

Methods Used: A literature review was conducted, finding support for interventions targeting adolescents to decrease adulthood problematic drinking behaviors. The chosen project was the creation of a student club that emphasizes peer-to-peer education and youth-organized activism. It was decided to start a Cody chapter of the prominent national organization Students Against Destructive Decisions (SADD), as no chapters existed in the area. The public library was chosen to host the club from its teen room and a willing librarian was found to act as an advisor. A SADD startup packet was obtained and annotated with suggested activities and fundraising ideas. Advertising fliers were distributed to local churches and youth groups, as well as to student athletes during their sports physicals. An interactive discussion was held with interested teens, which covered startup information and established a strategy for the participants to continue building the club.

Community Health I
Concurrent Session
3:30 PM
Thursday, January 24, 2013

VIDEO-BASED ROLE PLAYING: AN INNOVATIVE APPROACH TO QUALITATIVE DATA ACQUISITION AND HIV/STI PREVENTION AMONG MEN WHO HAVE SEX WITH MEN IN LIMA, PERU
Harrison D. UCLA David Geffen School of Medicine, Los Angeles, CA.

Purpose of Study: The objective of this study is to use video-based improvisation to understand common patterns of interpersonal negotiation of sexual risk behavior among men who have sex with men (MSM) and transgender women (TW) in Lima, Peru. MSM and TW have a disproportionately high rate of sexually transmitted infections compared to the rest
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-verbal communication.

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.

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HEALTH BEHAVIORS & PERCEPTIONS OF SPANISH SPEAKING EMPLOYEES IN WASHINGTON

Casimiro 1,2, Kahan M 3, Hannon P 1, Harris J 1, 2, 3, 1 University of Washington, Seattle, WA; 2 University of Washington, Seattle, WA; 3 University 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).

Summary of Results: On average, Spanish speaking employees (SSE) reported drinking more soda compared to English speaking employees (ESE) (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.

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CHILDBIRTH OBESITY: SOURCES OF MOTIVATION TO BE HEALTHY

Sihotang C, Gutierrez W, Tung A, Westerberg M, Debay 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 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.

Conclusions: 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.

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.

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.

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EXCESSIVE GESTATIONAL WEIGHT GAIN INTERVENTION IN TONASKET, WA

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

Purpose of Study: Excessive gestational weight gain (GWG) is increasingly prevalent in the United States. Pregnant women in Tonasket are no exception. According to the Okanogan County Health Department, in 2004, only 43% of pregnant women maintained adequate weight control, a rate less than the state’s and the 3rd lowest in the state. The purpose of this project was to raise awareness of the importance of healthy GWG, to provide tools for pregnant women to track their weight gain during pregnancy and to attempt to prevent excessive GWG through healthy diet and exercise.

Methods Used: A literature review was conducted to determine the most effective method to deliver information to pregnant women with lasting effects, and the statistics on the increased risks of adverse outcomes that are associated with excessive GWG. A presentation of healthy GWG was presented to pregnant women and their support persons in the childbirth classes. In addition, nurses were trained to deliver GWG information in future classes. An individualized brochure for pregnant women was also created and distributed to pregnant patients in the North Valley Family Medicine (NVFM) and in the childbirth classes at North Valley Hospital (NVH).

Summary of Results: Seven people including pregnant patients, their support persons and nurses attended the healthy GWG presentation at NVH childbirth class. Individualized brochures at the 6th grade reading level were developed and were well received by physicians, childbirth education nurses and pregnant women in the NVFM and NVH in Tonasket. The brochure materials were provided to NVFM and NVH childbirth classes, which adopted the brochure as part of their educational materials.

Conclusions: Because many women are concerned about the health of their babies during pregnancy and are in frequent contact with health care providers, pregnancy is an especially valuable period in which to promote healthy lifestyles. By increasing awareness of healthy weight gain during pregnancy and advocating a healthy diet and staying physically active, this project has additional impacts beyond preventing excessive weight gain in pregnant women. Pregnant women may adopt healthy lifestyles in the long run, educate their families and serve as role models for their children.
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 quantitative and qualitative 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 goat project provides buck 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 livelihood projects in rural Kenya. Poverty reduction through income-generating sustainable projects addresses one of the social determinants of health. The strongest indicator of success is that PCT and the community have been heavily involved in developing workshops and disseminating knowledge for each component of the projects.

A STRATEGY TO INCREASE SKILLED ATTENDANT BIRTHS IN KENYA

Tucker K1, Tomedi A2, Mwanthi M1. 1University of New Mexico’s School of Medicine, Albuquerque, NM; 2University of Nairobi, Nairobi, Kenya and 1University of New Mexico, Albuquerque, NM.

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 delivery 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. The pre-intervention percentages of ANC patients who delivered at a health facility at the intervention and control facilities were 19.5% and 20% respectively. 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 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 (Coomrod 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 of 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 Hispanic families in Anchorage; November- Employment Opportunities in Anchorage. We planned future monthly meetings that include two elements: 1) A potluck and 2) A themed educational pursuit for Hispanic families in Anchorage; November- Employment Opportunities in Anchorage.

Conclusions: El Grupo de Apoyo Social is a social support group led by Spanish speaking members of the Anchorage community who meet monthly with the purpose to cultivate Hispanic fellowship. As social support has been demonstrated to significantly predict nearly all health outcomes (Wang HH et al., 2003), it is anticipated that health risks associated with acculturation may be ameliorated.

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

Lam J3, Kaufman M2, 1University of Washington School of Medicine, Seattle, WA and 3University 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. Secondly, 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=63), 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
Dealing with “El Cambio de Vida”: Promoting Menopause Awareness in the Latina Community of Lynden, WA

Chohlas-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 created specifically for this community were given to attendees 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 the message 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 main 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 LE1, Parks L2, Mendez M2. University of Washington School of Medicine, Seattle, WA and Columbia 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 (CVCCH), 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 Beebe 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 oncoproteins 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 variable 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 40 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 oncopgenic 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.
A multiplex antibody binding assay was used to detect Western Regional Meeting Abstracts These data support a model by which M1 macrophages, & 1,2 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 IgG.

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: The identification of MCPyV specific IgM and IgG is a novel discovery. IgM expression may indicate persistent antigenic stimulation, while IgG expression may be evidence of lymphoid neogenesis, mucosal tumor involvement, or protect against tumor progression. Additionally, the presence of IgA to viral capsid in individuals without IgG to the capsid may be evidence of MCPyV exposure in individuals previously thought to lack viral exposure. Future studies should focus on the cause of IgM persistence and investigate the clinical significance of the differential IgA expression observed in this study.
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.

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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 813, 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 x 10⁴ cells per well and incubated for 24h. 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 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 mRNA and not wtK-Ras mRNA. Treatment with IMC-3G3 alone resulted in dose-dependent cytotoxic effects against all three cell lines. IC₅₀ (drug concentration that produced 50% inhibition of cell viability) values for U251, SF8628, and SF188 cells were 250mM, 100mM, and 500mM, respectively. Maximal inhibition for U251, SF8628, and SF188 cells occurred at 500mM, 100mM, and 500mM, respectively, resulting in 10% decrease in cell viability for both. Treatment with IMC-3G3 was found to be superior to RT alone in U251 cells.

Conclusions: Although RAI ablation was indicated in all patients in accordance with the American Thyroid Association guidelines, only 63% of patients actually received therapy. Our study has identified age-related, racial and geographic disparities upon which physicians should focus their attention for future studies to provide thyroid cancer patients the highest level of care.

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INHIBITION OF THE PLATELET DERIVED GROWTH FACTOR α SIGNALLING CASCADE FOR TREATMENT OF PEDIATRIC GLIOMAS

Chung M1, Kolkowitz I2, Yang X2, Olow A2, Mueller S2, Haas-Kogan D2. 1David Geffen School of Medicine at UCLA, Los Angeles, CA; 2UCSF School of Medicine, San Francisco, CA and 3UCSF School of Medicine, San Francisco, CA, CA.

Purpose of Study: Pediatric high-grade gliomas (HGG) have a poor prognosis, with >70% of patients dying within two years of diagnosis. Platelet Derived Growth Factor Receptor α (PDGFRα) is critical for PI3K/Akt/mTOR activation and is frequently upregulated in pediatric HGG. We hypothesized that treatment with neutralizing anti-PDGFRα monoclonal antibody IMC-3G3 enhances anti-neoplastic effects of radiation in malignant gliomas. We tested IMC-3G3 as a single agent and in combination with radiation (RT) in vitro in 3 human glioma cell lines overexpressing PDGFRα.

Methods Used: Using clonogenic survival assays, we measured the viability of cells treated with IMC-3G3 alone on adult malignant glioma U251 cells, pediatric glioma SF8628 cells, and pediatric glioma SF188 cells. Cells were treated with varying concentrations of IMC-3G3 only (0nM, 500nM, 1000nM, 2000nM). All conditions were performed in duplicate. We also tested IMC-3G3 in combination with RT in vitro. Cells were treated with 500nM IMC-3G3 and immediately irradiated at 0Gy, 2Gy, 4Gy, 6Gy, 8Gy, and 10Gy with Cobalt-60. Plates were monitored for 9 days or until large clones (>50 cells) were formed, fixed, and stained with 0.5% crystal violet, and counted with a stereomicroscope.

Summary of Results: Treatment with IMC-3G3 alone resulted in dose-dependent cytotoxic effects against all three cell lines. IC₅₀ (drug concentration that produced 50% inhibition of cell viability) values for U251, SF8628, and SF188 cells were 250mM, 100mM, and 500mM, respectively. Maximal inhibition for U251, SF8628, and SF188 cells occurred at 500mM, 100mM, and 500mM, respectively, resulting in 10% inhibition for all cell lines. Treatment with IMC-3G3 plus RT was superior to RT alone in SF8628 and SF188 cells, resulting in 10% decrease in cell viability for both. Treatment with IMC-3G3 was not found to be superior to RT alone in U251 cells.

Conclusions: The anti-PDGFRα monoclonal antibody IMC-3G3 potentiates the cytotoxicity of radiation in SF8628 and SF188 cells, but not U251 cells. Inhibiting the PDGFRα pathway with IMC-3G3 may prevent post-radiation DNA repair from progressing, but further investigation is warranted to elucidate mechanisms involved.
(PMN) 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 to part in failed NET formation.

**Methods Used:** We studied 13 BMT study subjects, 4 adult and 9 pediatric. The indications for BMT included: leukemic 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 pre-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.

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**QUALITY OF ONLINE RESOURCES FOR COLORECTAL CANCER PATIENTS**

Gusnowski EM, Inglewed P. 

**University of British Columbia, Vancouver, BC, Canada and Fraser Valley Cancer Agency, Surrey, BC, Canada.**

**Purpose of Study:** While a majority of colorectal cancer patients use the internet as an information resource, a lack of quality control for web-based resources presents a problem for physicians and patients. This study aims to comprehensively evaluate the quality of online colorectal cancer patient resources.

**Methods Used:** A previously validated website evaluation tool was used to analyze the quality of online colorectal cancer resources for patients. The term “colon cancer” was used to retrieve hits from the search engine Google and the meta-search engines Dogpile and Yippy. A “top 100” website list was compiled using pre-specified inclusion and exclusion criteria. Websites were evaluated regarding administration, accountability, authorship, organization, readability, content and accuracy. Inter-rater reliability was confirmed via kappa statistics and results were analyzed via descriptive statistics.

**Summary of Results:** The term “colon cancer” returned over 750 websites from the search engines. Of the top 100 sites, 93% disclosed ownership, sponsorship, and advertising. Only 17% identified an author and fewer (16%) gave the author’s credentials. 67% cited resources but most information was out of date, with only 33% having updated material within two years. The average grade level of the websites was grade 10. Most sites accurately described symptoms (90%) but few provided accurate stage-specific prognostic (16%) or treatment (26%) information. Prevention methods were accurately represented in 59% of sites. The term “colorectal cancer” produced a top 100 list that differed significantly in content from the “colon cancer” list, despite the common interchange of these terms.

**Conclusions:** As the third most common cancer, it is essential to provide colorectal cancer patients with appropriate and accurate resources to aid in decision-making. While many sites disclose ownership and provide accurate screening information, there are significant deficits. Of concern, many colorectal cancer sites lack authorship, are out of date, are written at a high grade level and lack accurate stage-specific prognostic and treatment information. This study may help to inform the patient-physician encounter and allow physicians to provide patients with tools to evaluate the quality of web-based colorectal resources.

**Inflammation and Infection**

Concurrent Session

3:30 PM, Thursday, January 24, 2013

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**CHRONIC STRESS & SALIVARY BIOMARKERS**

Mallick AL, Bergen A2, Nishiya D, Wei X, Michel D, David SP, 2, Swan GE, Reid MW, 4, Simon AD, 4, Andrews J, 3, Stanford School of Medicine, Palo Alto, CA; 2SRI International, Menlo Park, CA; 3ORI International, Eugene, OR; 4University of Oregon, Eugene, OR and Notre 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-representation of 3’UTR adenylyl uridylyl (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 unfractinated saliva of young adults.

**Salivary RNA and Clinical Covariates of Significantly Differentially Expressed Test Assays**

**Cancer**

**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.

**Higher Incidence of Igg Anti-IgA Antibodies in IgA Deficient Females with Suspected Celiac Disease**

Martins TB1, Iaskowski TD1, Brickell L1, Augustine N2,2, Kumaraviscas A1,2, Teo AE1,2, Hill HR1,2, ARUP Institute, Salt Lake City, UT and 2University 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.

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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 twice the genetic 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 anti-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.

Summary of Results: Filtering options allow for the customization of accuracy to the seminars and were eager to learn more about CMV.

Discussion: Jensen M, Baeksh 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 syndrome of the right knee in a immunocompetent patient.

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 knee. 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.

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 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 for heart failure patients.

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.
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.

**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.

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**BETA BLOCKER EFFECT ON SURVIVAL IN SEPTIC SHOCK**

Means R1, Friese R1, Ibrahim-Zada I1, Weller J2, Jones T.1 (Univ of Arizona, Tucson, AZ and 1St. George’s Univ, St. George, Grenada).

**Purpose of Study:** β-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 endotoxemia. 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 in the subcutaneous tissues of the back. Pumps delivered β-1 selective antagonists (100, 50 or 10 ug/ml esmolol) or an equal volume of saline. Outcome was measured by survival at 120hrs post LPS injection. Kaplan-Meier survival analysis was used to examine mortality differences.

**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 higher mean survival (65.5hrs) than saline (56hrs) but this difference was not significant with our small sample size. Survival rate in the BB group increased after 48hrs compared to that in saline group: 13/26 (50%) in BB group 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.

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**ROLE OF OSTEAOACTIVIN IN REGULATION OF INFLAMMATORY RESPONSE OF MACROPHAGES IN HYPERGLYCEMIA**

Sinha SK1, Nicholas SB2,3,1 Charles R Drew University, Los Angeles, CA and 2UCLA, Los Angeles, CA.

**Purpose of Study:** Studies have demonstrated that diverse inflammatory molecules play a significant role in the setting of diabetic nephropathy (DN). The process of inflammation requires the selective expression of genes in cells of the macrophage lineage. Osteoactivin is a growth factor that has been identified as a negative regulator of the inflammatory and phagocytic activities of macrophages. However, little is known about its role in the inflammatory response of macrophages in hyperglycemia. We tested the hypothesis that high glucose suppresses the expression of osteoactivin in activated macrophages, leading to aberrant cytokine release and impaired phagocytosis and thus promotes chronic inflammation in DN.

**Methods Used:** J-774A.1 macrophage-like cells were cultured in RPMI 1640 supplemented with 1 × antibiotics and anti-mycotic agents, 2mM glutamine and 10mM HEPES. Following 18 hour serum starvation, the cells were treated with D-glucose (5, 25 and 40mM) for 24h. The expression of osteoactivin, CD36 and IL-6 was determined by immunoblotting, and TNF-α gene by qRT-PCR. Concentrations of IL-6 and TNF-α in culture supernatants were assessed by ELISA. The phagocytosis assays were performed by following the internalization of fluorescent labeled killed E. coli cells using a commercially available kit.

**Summary of Results:** Compared to 5mM, high glucose concentrations significantly reduced the expression of osteoactivin (up to 30%, p<0.05) and increased the expression of CD36 and IL-6 protein (up to 13% and 25% respectively, p<0.05). mRNA expression of TNF-α was up regulated (up to 2.0 fold, p<0.05) with increasing glucose concentrations. Further, the secretion of IL-6 and TNF-α into the media was significantly enhanced up to 3-fold (p<0.005). In contrast, phagocytosis was significantly down-regulated (up to 30%, p<0.05) at high glucose concentrations.

**Conclusions:** These results suggest that in DN, hyperglycemia may promote chronic inflammation by enhancing the inflammatory responses and reducing the phagocytic capacity of macrophages through down regulation of osteoactivin.

**GRANT SUPPORT:** NIH/NIMHD Accelerating Excellence in Translational Science U54M007598 (formerly U54RR026138) at Charles R Drew University.

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**SYNDECAN-1 ATTENUATES THE LUNG CANCER MALIGNANT PHENOTYPE, POTENTIALLY VIA RHOA ACTIVATION**

Lim H, Schlesinger S, Buell C, Brauer R, Chen P. University of Washington, Seattle, WA.

**Purpose of Study:** Lung cancer is the leading cause of cancer death worldwide. Syndecan-1 is a cell surface proteoglycan whose loss of expression on lung cancer cells is associated with progression to higher-grade malignancy and correspondingly poorer patient outcomes. We investigated whether syndecan-1 modulates the development of malignant characteristics through RhoA GTPase signaling.

**Methods Used:** We used two variants of the A549 lung cancer cell line: A549.shRNA.Ksdc1 cells, in which syndecan-1 expression is stably suppressed by shRNA, and control A549.shRNA.scr cells, which express scrambled shRNA and have normal levels of syndecan-1 expression. We assessed whether syndecan-1 expression affects RhoA activation levels in these cell lines using a RhoA activation assay. Further, we grew these cell lines in agarose gels with and without RhoA inhibitor to evaluate whether RhoA inhibition enhances cell ability to grow in the absence of anchorage, a characteristic of malignancy. Additionally, we used western blotting to assess the activation of AKT, a cancer cell survival signal, and PTEN, a tumor suppressor.

**Summary of Results:** A549.shRNA.Ksdc1 cells grew larger colonies than A549.shRNA.scr cells in an anchorage-independent growth assay, and exhibited increased AKT activation and decreased PTEN activation, consistent with more aggressive growth. When we examined the RhoA pathway, we found attenuated activation of RhoA in A549.shRNA.Ksdc1 cells compared
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 counteracts 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.

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**IDENTIFICATION OF A NOVEL PREDICTOR OF ANABOLIC/CATABOLIC BALANCE AND NUTRITIONAL STATUS IN CRITICAL ILLNESS: WHAT CAN BE LEARNED FROM ELITE ATHLETES?**

Winkler Z, Wischmeyer P. University of Colorado, Aurora, CO.

**Purpose of Study:** Critically ill patients and patients undergoing major surgery present with a number of unique physiological responses which must be managed appropriately to achieve optimal outcomes. Current research addresses the metabolic and stress response in peri-operative and critically ill patients but, there is a consensus that these responses need to be better characterized. Currently, there is no useful biomarker that can be followed to predict nutrition status and adequacy of nutrition delivery. With a better understanding of patient nutritional and stress markers physicians could target nutritional and pharmacological therapies for their patients based on their catabolic/anabolic balance. This may also potentially decrease hospital length of stay, morbidity, and increase quality of life.

**Methods Used:** To accomplish this goal our 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 kinase, LDH, ACH, GH, testosterone, troponin I, CBC, IL-6, creatinine, CRP and, EPO.

**Summary of Results:** Preliminary data analysis of testosterone, LDH, and creatinine kinase do 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 2.674 and 2.685, respectively. The p-values for this association were 0.031 and 0.026, respectively. In addition, for every ug/dl increase in the log of the mean cortisol level correlated with an increase of the log mean I.L-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 LDH, creatinine, 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, the underlying molecular mechanisms remain unknown. VD is known to accelerate alveolar maturation and improve lung function; however, whether VD’s protective effect against asthma is also mediated via improved upper airway function is not known. Using an in vivo rat model we determined the effects of perinatal VD deficiency on pulmonary function at baseline and following methacholine challenge, and tracheal contractile response to acetylcholine challenge.

**Methods Used:** 4 weeks prior to pregnancy, Sprague-Dawley rats were started on the following 4 dietary regimens, which were continued through pregnancy and lactation: No cholecalciferol added, 250, 500, or 1000 IU/kg cholecalciferol added groups. After delivery, the pups were sacrificed on postnatal day 21. Blood was collected to determine VD (25(OH)D3) levels. Pulmonary function, using whole body plethysmography, and tracheal contracture, using our previously published method (Liu et al, AJP Lung, 2011; 300:L710-7) were determined.

**Summary of Results:** 25(OH)D3 levels were lowest in no cholecalciferol supplemented group, increasing progressively with increasing supplementation. Compared to 250 and 500 IU/kg cholecalciferol supplemented groups, no cholecalciferol supplemented group demonstrated a significant increase in airway resistance, and a significant decrease in airway compliance following methacholine challenge. However, cholecalciferol deficiency-mediated increase in tracheal contractility in cholecalciferol depleted group was blocked in only 500 IU/kg cholecalciferol supplemented group.

**Conclusions:** Perinatal VD deficiency, in addition to altering alveolar epithelial-mesenchymal signaling at the lower airway level, also alters upper airway contractility, providing novel insights to the induction of the asthma phenotype in the perinatally VD-deficient offspring. Perinatal VD supplementation at 500 IU/kg seems to effectively block the effects of perinatal VD deficiency, providing a strong rationale for adequate VD supplementation during the perinatal period for the prevention of childhood asthma (Grant Support: HL107118, HD51857, HD71731).
NEBULIZED NANO-CURCUMIN: A NOVEL APPROACH AGAINST HYPOXIA-INDUCED LUNG INJURY


Purpose of Study: Curcumin (diferuloylmethane) has potent antioxidant 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 useful 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 apotransferrin 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-Fos, and tetrose uptake). Concomitant treatment with nebulized nanocurcumin blocked both the hyperoxia-induced decrease (CEBPαs and PPARγ) and increase (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. These data suggest that perinatal nicotine exposure causes gender-specific, PPARγ-dependent perinatal cigarette smoke exposure-induced asthma, providing a powerful phenotypic model for unequivocally determining the underlying nature of the cell-molecular mechanism for this disease. Grants: NIH HD51857, HD17131.

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

Alvdorf JM, Houston B, McCoy M, Dong L, Wang Z, Dalh MJ, McKnight 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 (RMVF) 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 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 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 preterm birth, 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 deacetylation 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 covariant 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 hyperacetylation (e.g., postnatal HDACi) 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).

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

Liu J1, Naeem E2, Tian J1, Lombardi V3, Kwong K4, Akbari O5, Torday J1, Rehan V1. 1Los Angeles Biomedical Research Institute, Torrance, CA and 2University of Southern California, Los Angeles, CA.

Purpose of Study: We have exploited a nicotine-induced in vivo rat model of asthma to determine if the effect on offspring pulmonary function and mesenchymal markers of airway contractility in both tracheal and lung parenchymal tissue are gender-specific, and whether the protection afforded by the PPARγ agonist Rosiglitazone (RGZ) against the perinatal nicotine-induced effect on offspring lung is also gender-specific. We hypothesize that nicotine exposure will differentially affect male and female offspring airway contractility and mesenchymal markers for asthma; these effects will be normalized by RGZ treatment.

Methods Used: Pair-fed pregnant Sprague Dawley rat dams received placebo (diHenthanes, Nicotine (1 mg/kg, sc.), and Nicotine (1 mg/kg, sc.) + PPARγ agonist Rosiglitazone (RZG) (3 mg/kg, ip.) in 100 μl volumes daily from eclamps to 21-day old pups. Pups were delivered spontaneously and breast-fed ad libitum. At postnatal day 21, lung resistance, compliance, tracheal contractility, and the expression of structural and functional mesenchymal markers (α-SMA, Calponin, Fibronectin, Collagen I and III) of pulmonary contractility were determined by immunoblotting and immunostaining.

Summary of Results: Compared to control, perinatal nicotine exposure caused a significant increase in airway resistance, and a decrease in airway compliance following a methacholine challenge in both male and female offspring, with more pronounced changes in the males. In contrast to this, the effects of perinatal nicotine exposure on acetylcholine-induced tracheal constriction, along with the expression of mesenchymal markers, were observed exclusively in the male offspring. Concomitant treatment with RGZ normalized the nicotine-induced alterations in pulmonary function in both genders, as well as the male-specific effects on acetylcholine-induced tracheal constriction, along with the affected mesenchymal markers.

Conclusions: These data suggest that perinatal nicotine exposure causes gender-specific, PPARγ-dependent perinatal cigarette smoke exposure-induced asthma, providing a powerful phenotypic model for unequivocally determining the underlying nature of the cell-molecular mechanism for this disease.
(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 10-11wks more (PT weaned; n=6). Control lambs were born at term gestation (~3wk after the PT lambs were delivered) and lived for 8-wk more (T=8wk control; n=6). Brain (temporal lobe) tissue was analyzed by immunoblot for ephrinB1 and B ligands as well as EphA and B receptors, using commercially available antibodies.

**Summary of Results:** Protein bands were evident by immunoblot for ephrinB1 and EphA2 receptor in the brain. Protein abundance of ephrinB1 ligand and EphA2 receptor was the same between the PT weaned groups and control lambs. No bands were detected for other ephrinB 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. (HL100002, HL062875, LU-R1).

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**INCREASED IGF-1 EXPRESSION CAUSES ALVEOLAR SIMPLIFICATION IN CRONICALLY 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 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) MV+rebulbulated IGF-1 receptor antagonist, (3) nasal high-frequency ventilation (nHFr) alone, or (4) nasal HFV+IGF-1 receptor antagonist (n=4 each). Treatment was 1d for 3d. We used nasal HFV as the positive gold standard for alveolar simplification. We assessed alveolar formation structurally.

**Summary of Results:** MV for 3d led to thick, cellular walls of distal airspaces and few secondary septa. Blocking IGF-1 receptors during 3d of MV resulted in thinner walls and more secondary septa. In contrast, nasal HFV for 3d led to thin, less cellular walls and many secondary septa. Adding an IGF-1 receptor antagonist during 3d of nasal HFV resulted in thicker and more cellular walls, and fewer secondary septa.

**Conclusions:** We conclude that IGF-1 causes alveolar simplification. A next step will be to measure serum levels of the IGF-1 antagonist to determine how much leaves the lungs and therefore might lead to systemic effects. (HL100002, HL062875, HL07744).

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**MICROARRAY ANALYSIS OF GENE EXPRESSION IN LUNG MACROPHAGES FROM PRETERM NEWBORNS**

Fischer A,1 Chan B,2 Ramanathan R,1 Kwong K2, Minoo P,1 USC School of Medicine, Los Angeles, CA and 1Harbor-UCLA, Torrance, CA.

**Purpose of Study:** Purpose: Inflammation plays a major role in pathogenesis of neonatal chronic lung disease. BPD. The molecular immunology of macrophage macrophages (AMs), a key component of innate immunity, at birth remains poorly understood. We’ve begun to identify genes expressed by AMs of human newborn infants. Tracheal aspirate fluids were obtained from lungs of three infants born at 24, 35 and 40 weeks gestation.

**Methods Used:** Methods: Macrophages were purified by FACS using CD45/CD14 antibodies. mRNA was extracted and gene array was performed using Agilent technology. We then analyzed gene expression in the 24 week infant using the 35 wk and 40wk data as reference.

**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 maturation of innate 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” as asthma.

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**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 Neurotech 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, unless 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 I**

Concurrent Session

3:30 PM Thursday, January 24, 2013

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**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.

**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 maturation of innate 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” as asthma.
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: Fifteen 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

Kim 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 Topka guinea pigs were randomly assigned to one of four experimental groups (grain-based diet vehicle, grain-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 Coulbourn instruments. Changes in five indices of feeding behavior and meal pattern (cumulative food intake, incremental food intake, meal frequency, meal duration, meal size), body weight, and metabolic parameters at hourly intervals post-injection were evaluated. In addition to being able to monitor food intake and the microstructure of meal pattern, the CLAMS system is equipped with a four-station open circuit calorimeter and ventilation system that allows for the measurement of oxygen consumption (VO2), carbon dioxide production (VCO2), respiratory exchange ratio (RER), and metabolic heat production. After a one to three day acclimation, the animals were put through a five-day experimental period in which either 2 mL insulin or 2 mL 0.9% saline vehicle were infused daily into the 3rd ventricle (ICV) of the hypothalamus via guide cannulae implanted using a stereotaxic frame.

Summary of Results: Centrally administered insulin produced decreases in incremental food intake. With males being more sensitive than females. These effects were associated with decreases in meal frequency in males and decreases in meal size in males and females. Insulin also increased VCO2, VCO2, and metabolic heat production in males and decreased RER in females. These insulin-induced changes were markedly attenuated in animals fed a high-fat diet.

Conclusions: The data reveals extensive sex differences in the central insulino-regulatory balance of energy balance, and it is enhanced by effects on energy metabolism and intake that are more prominent in males compared to females. The data also indicates that central insulin resistance can develop from chronic exposure to a high-fat diet.

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

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Purpose of Study: During brain development, the infrapyramidal tract (IPT) of the hippocampal dentate gyrus undergoes stereotyped retraction-like pruning, which histologically resembles axonal retraction. 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 retraction. This finding demonstrates that the process of synapse elimination with subsequent pruning is regulated by molecular mechanisms that are distinct from the established repulsive 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, Npm2, 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.

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

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Purpose of Study: Perinatal birth is associated with neurodevelopmental disabilities. While matter injury is an important etiologic factor; and is likely secondary to disrupted postnatal oligodendrocyte development. Hyoxia inducible factor-1a (HIF-1a) 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 oligodendrocyte development occurs in a physiologically hypoxic fetus during the third trimester, HIF-1a could play a role in perinatal oligodendrocyte development from the NSC population. However, its specific role in supporting oligodendrocyte development, 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 immunostained for HIF-1a in the region of the SVZ. As oligodendrocytes develop, HIF-1a expression is critical for oligodendrocyte survival. Additionally, we investigated the role of HIF-1a knockdown in astrocytes, postmitotic neurons, and oligodendrocytes in the SVZ, hippocampus and corpus callosum. In addition, we utilized inducible HIF-1a knockout mice in which tamoxifen resulted in consequent expression of YFP and bi-allelic HIF-1a exon 2 gene deletion in nestin+ NSCs and their progeny (nestin-CreERT2:YFP:HIF1afl/fl).
nestic-CreERT2:YPF:HiFl/lf brains. However, the percentage of YFP+ oligodendrocytes was significantly reduced in nestic-CreERT2:YPF:HiFl/lf mice at P49 in the corpus callosum (31% vs 42%, p<0.001) 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.

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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 autobody 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.

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FATIGUE IN MULTIPLE SCLEROSIS: RELATED TO FEAR OF FALLING AND PRIOR FALLS BUT NOT TO FUTURE FALLS
Mazumder R1, Cameron M1,2. 1Oregon Health and Science University, Portland, OR and 2Portland Veterans Administration Medical Center, Portland, OR.

Purpose of Study: Fatigue and fear of falling are often perceived as risk factors for accidental falls in people with multiple sclerosis (PwMS). While fear of falling is a known independent risk factor for falls in PwMS, the relationship between fatigue and falls is not well understood. Here, we explore the relationships among fatigue, fear of falling, and recent prior and future falls in PwMS.

Methods Used: This is a sub-analysis of data from a study of imbalance in multiple sclerosis. Subjects were 58 PwMS age 18-80 with Expanded Disability Status Scale scores ≤ 6.0. Subjects completed the Modified Fatigue Impact Scale (MFIS), a validated questionnaire assessing effects of fatigue on daily physical, psychological and cognitive functioning; the Falls Efficacy Scale-International (FES-I), a validated questionnaire assessing fear of falling; a retrospective fall questionnaire; and six monthly prospective fall calendars. Pearson correlation was used to assess relationships between MFIS and FES-I scores. Differences in mean MFIS scores for past and future fallers and non-fallers were assessed with t-tests.

Summary of Results: 53 of 58 subjects completed the study and were included in this analysis. MFIS scores were moderately correlated with FES-I scores (r=0.67). 27 PwMS reported at least one faller (fallers) in the prior 2 months; 21 and 37 subjects fell at least once in the following 2 and 6 months respectively. Mean MFIS scores were significantly different for fallers and non-fallers in the prior 2 months (fallers: 44 ± 17.8; non-fallers: 20.9 ± 4.6; p<0.001) but not for fallers and non-fallers in the following 2 months (fallers: 40.8 ± 23.1; non-fallers: 32.4 ± 16.2; p=0.12) or following 6 months (fallers: 34.4 ± 15.5; non-fallers: 36.6 ± 21.1; p=0.75).

Conclusions: Although perceived fatigue is related to fear of falling and recent prior falls among PwMS, levels of fatigue do not discriminate between those who fall or do not fall in the following 2 or 6 months.

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FUNCTIONAL CONNECTIVITY OF BASAL GANGLIA NETWORKS IN PARKINSON’S DISEASE PATIENTS COMPARED WITH HEALTHY, OLDER ADULTS
Kennel CE1, Berman B2, Shelton E1. 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 (fcMRI) 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 volun-
teers who passed exclusion criteria received physical, neurological, and cogni-
tive examinations, then were scanned at the University of Colorado School of Medicine’s Brain Imaging Center. fcMRI involved five-finger serial tapping sequences paced with audible cues and monitored via observation and electrolyography. 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 SPM8, DPARSF and a MATLAB toolbox for functional connectivity that focused on six BG seeds per hemisphere plus the subject-specific motor cortex region of inter-
est 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, analy-
sing differences between the two groups, and correlating PD disease se-
verity 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 con-
nectivity between PD patients and healthy volunteers for each BG seed, and we are in the process of characterizing these differences.

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STRUCTURAL BRAIN MRI CHANGES FOLLOWING TESTOSTERONE SUPPLEMENTATION IN HEALTHY OLDER MEN
Hua JT1, Rojas DC1, Filley CM1,2, Schwartz RS1, Pelak VS1. 1University of Colorado School of Medicine, Aurora, CO and 2University of Colorado School of Medicine, Aurora, CO.

Purpose of Study: Men with low levels of endogenous testosterone have been shown to have mild impairments in memory, executive function, visuospatial abilities, and verbal fluency. Recent work has suggested that exogenous testosterone may improve cognitive performance in a curvilinear distribution. The aim of this study is to evaluate neuroanatomical transforma-
tions after testosterone supplementation via Voxel-Based Morphometry (VBM),
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 (Brodmann 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-design 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-groups 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 insights into effects of testosterone on the brain.

Surgery Concurrent Session
3:30 PM Thursday, January 24, 2013
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**A “SENSATE” SURFACE REPLACEMENT SCAFFOLD TO MEASURE LOAD CHANGES IN-VIVO DURING CARTILAGE FORMATION**

Rojas J, Ouellette 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 cartilage formation.

**Methods Used:** Previous studies have employed polymer scaffolds as an engineered cartilage delivery 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 for focal defect repair using “biomimetic” scaffolds derived from µCT scans of cadaver bone cores. The goal of this study was to develop femoral surface replacement scaffolds instrumented with shear sensors to measure strains during cartilage formation.

**Summary of Results:** Surface replacement scaffold seeded with adipose derived stem cells (ASCs) has been previously used to grow canine cartilage for focal defect repair using “biomimetic” scaffolds derived from CT scans of cadaver bone cores. The goal of this study was to develop femoral surface replacement scaffolds instrumented with shear sensors to measure strains during cartilage formation.

**Conclusions:** Further analysis of inter- and intra-groups 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 insights into effects of testosterone on the brain.
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=0.12), 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.

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UPPER POLE ACCESS: DOES IT INCREASE THE COMPLICATION RATE FOLLOWING PERCUTANEOUS NEPHROLITHOTOMY?
Ng C, Culpepper DJ, Creech 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=0.775), 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/lower pole access was similar in our population.

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COMPARISON OF RENAL FUNCTIONAL OUTCOMES AFTER PERCUTANEOUS CRYOABLATION
Mai AT, Wallner CL, Huang GO, Ng C, Creech 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, 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 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 compared to PN. 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.

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KIDNEY DONOR RADIATION EXPOSURE PRIOR TO TRANSPLANTATION
Culpepper DJ, Creech JD, Mai AT, Ng CC, Huang GO, Wallner CL, Arnold DC, Olgin G, Engebretsen SR, Schlafier AE, Anderson KM, Baldwin D, Loma Linda University, Loma Linda, CA.

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.

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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

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fixation and the other underwent arthroscopic stabilization. The calcaneo-fibular ligament (CFL) and anterior talofibular ligament (ATFL) were excised from their origin on the fibula. In the first group, a #2 fiberwire 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 stiffness, 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.

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**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 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 ﬁbrocartilage-like interface, thus improving biological ﬁxation of the rotator cuff.

The objective of this study is to compare cell viability and proliferation of MSCs cultured on biphasic and single phase scaffolds.

**Methods Used:** Electrospun scaffolds were cut into 1.8 cm × 1 cm pieces and secured in clamps. Human MSCs were seeded onto the scaffolds at a density of 6×10^4/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.

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

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**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 (SAN) pacemaking node. 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 (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 atri, with the points of initiation clustered within a small area. The leading pacemaker region in KO was 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.
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. The pre-intervention percentages of ANC patients who delivered at a health facility at the intervention and control facilities were 19.5% and 20% respectively. 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 increased when TBAs were recruited and compensated for bringing their clients to local health facilities to deliver.

THE ESET HISTONE METHYLTRANSFERASE IS CRITICAL TO OSTEOblast DIFFERENTIATION AND TRABECULAR BONE FORMATION
Lawson KA1,2, Yang L1, Chamsky HW1. 1University of Washington, Seattle, WA and 2Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA.

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 ratio of skilled-attended births in health facilities in Kenya with assistance from traditional birth attendants (TBAs).

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 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.

**Characteristics of Patients with Late Viral Breakthrough**

<table>
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<th>Age</th>
<th>Gender</th>
<th>Race</th>
<th>Extent</th>
<th>Primed or Non</th>
<th>Viral Load Breakthrough</th>
<th>Viral Load 6 Weeks</th>
<th>Viral Load 12 Weeks</th>
<th>Time to Viral Breakthrough</th>
<th>Resistance Pattern</th>
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**Utility of FDG-PET in the Evaluation of Large-Joint Osteoarthritis**

Kao S, Morshedi M, Patel P, Obrzut S. UC San Diego Health Sciences, La Jolla, CA.

**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 better interrogate the diversity contained within primate populations.

**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, hypercalcemia, 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.

**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 – 0.43 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.

**Heme Oxygenase Activity and Heme Binding are Critical in Early Life**

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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, 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 24h 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 60μM FH/kg BW. After 24h, 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. 24h after exposure to 60μM FH, a cytoxicity of 48% and an 80% decrease in viability were found; whereas, no cytoxicity 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/mg fresh weight, respectively), and LP and AST levels significantly increased 1.1- 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.

**Analysis of the PRDM9 Gene Shows Large Amounts of Diversity and Points Toward Potential Speciation Mechanism in Ancestral 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 evolution of species. 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 in the population level in primates. This is due to the presence of a ~1.5 kbp, 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 platform. 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.
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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.is-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% (2,202 women). The expected cost savings from implementing the reduced anti-globulin screening strategy ranged from S6 - $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 remained cost beneficial when varying 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.

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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 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 BXP3C cells, with wild type K-Ras (wtK-Ras), were seeded in quadruplicate in 96 well plates at 1.2 x 104 cells per well and incubated for 20 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 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 BXP3C 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. BXP3C 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 BXP3C 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 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.

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

Weller SM1,2, Jones JC2, Rosen H3, Crowther G2,3, 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 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 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 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.

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

McCullough J, Thurman J. University of Colorado School of Medicine, Aurora, CO.

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, and 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 perfusion 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 perfusion, 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 perfusion. 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 of 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 expressing B-cell populations, and modulating IL-10 expression in mouse models in order to observe the effects on renal IRI.

155 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 sentinel markers of mitochondrial biogenesis: ETC Complexes, VDAC1, SIRT1, PGC1α, pCREB; Fission/Fusion: Mitofusin1, Mitofusin2, OPA1, Fis1, DRP1; Autophagy: Beclin1, LC3b, p62, BNIP3.

Summary of Results: Acute NOS inhibition significantly decreased mitochondrial ETC (p<0.035) as well as VDAC1 (p=0.0129). Sirt1 and PGC1α content were unchanged. Mitochondrial fusion proteins decreased significantly (OPA1 p=0.0011, Mitofusin1 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.

156 HANDEDNESS IN RASOPATHIES
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Purpose of Study: RASopathies are a group of genetic disorders which often have language, motor, and neurocognitive defects. 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 neurofibromatoses 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 CFC 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 patients 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.

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

Purpose of Study: 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 is often 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 preterm birth, 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; pos/neg gold standard for alveolar formation) (4 each). Treatment was 1/4 (1m) 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 hyperacetylation 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 hyperacetylation may reduce the cognitive and/or severity of lung and brain injury, and perhaps reduce long-term outcomes (e.g., hyperactive Airways and neurodevelopmental impairment) (HL110002, HL062875, HL056401, HD41075, HL07744).

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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 (LKD). 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 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 transplants are similar regardless of insurance type, Medicare patients take longer to list and receive fewer LDK than patients with private insurance.

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RNA EXPRESSION PATTERNS IN SERUM MICROVESICLES FROM PATIENTS WITH GlioBLASTOMA MULTIFORME AND CONTROLS
Sahaie A1,2, Noerholm M1, Balaj L1, Zhu LD2, Skog J1, Breakefield XO1, Carter B1,2. 1UCSD School of Medicine, San Diego, CA and 2Massachusetts General Hospital, Boston, MA.
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 generated 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.

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CHRONIC LUNG ALLOGRAFT DYSFUNCTION: DO DISTINCT SPIROMETRIC PHENOTYPES EXIST?
Zhang A, Derhovanessian A, Belperio J, Weigt S. UCLA, Los Angeles, CA.
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 obliterans (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 BOS phenotypes on survival with Kaplan-Meier plots and used Cox Proportional Hazard models to assess risk factors.
Summary of Results: CLAD is 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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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 miRNA21 (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. Downstaged 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 is 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.
Preliminary assessment was performed when the infant was 2 mg/dL. Secondary outcomes in-...average weight per gestational age (p=0.001). In con-

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 addi-
tionally 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.

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

Shah M, Venkataraman S, Harris P, Alimova I, Arvani V, Griesinger A, Birks D, Schittone S, Donson A, Foreman N, Vihlbakar R. University of Colorado School of Medicine, Aurora, CO.

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.

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LOW DOSE SOYBEAN OIL FOR THE PREVENTION OF PARENTERAL NUTRITION ASSOCIATED CHELOSTASIS IN NEONATES WITH CONGENITAL GASTROINTESTINAL DISORDERS

Calkins KL1, Havranek T1, Kelley-Quon LN1, Gibson L1, Venick R2, Shew S2.
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Purpose of Study: Parenteral nutrition (PN) associated cholestasis increases potential for liver dysfunction and failure in neonates with congenital gastrointestinal disorders (CGD). The aim of this study is to determine if low dose parenteral lipids when compared to standard dose reduces the incidence of cholestatis in neonates with CGD.

Methods Used: Neonates with CGD were prospectively randomized in the first 48 hours of life to 1 (LOW) or 3 gm/kg/d (CON) of soybean oil while receiving PN. The primary outcome was the development of cholestasis with persistent conjugated bilirubin (CB) > 2 mg/dL. Secondary outcomes included growth, late onset sepsis, and mortality. Chi-square, Fisher's exact test, t-test, and Wilcoxon rank test were used where appropriate.

Summary of Results: Preliminary assessment was performed when 26 neonates were enrolled (13 LOW, 13 CON). Despite LOW having a lower birth weight (2.2 vs. 2.7 kg, p=0.05), longer PN course (31 vs. 21d, p=0.07), later initiation of enteral nutrition (18 vs. 11d, p=0.05), and being more premature (36 vs. 38 wk, p=0.05) compared to CON, LOW neonates...
had lower geometric mean (±SEM) CB at study weeks 8 (0.7±0.3 vs. 2.71±3 mg/dL, p<0.05) and 9 (0.5±0.2 vs. 2.81±1.5 mg/dL, p<0.05) and non-significantly lower median percent CB change/week (17%, range, -33.60% vs. 18% (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 not one LOW subject 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 cholesterol 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.

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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.

Methods Used: Virgin female rats were fed either a regular diet (RD) or a HFCD 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 2 (SREBP2) and its target HMGCoA reductase (HMGCR). We subsequently hypothesized that IUGR and mHFCD would each increase hepatic cholesterol and decrease SREBP2 and HMGCR mRNA in rat pups at birth. Further, we hypothesize that the combination of IUGR and mHFCD would further increase hepatic cholesterol and decrease SREBP2 and HMGCR mRNA compared to either IUGR or mHFCD alone.

Methods Used: Virgin female rats were fed either a regular diet (RD) or a HFCD 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.

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 HMGCR mRNA levels. Compared to Con-mHFCD, female IUGR pups from mHFCD dams (IUGR-mHFCD) increased hepatic cholesterol at birth (131±16%, p<0.05). Compared to Con-mHFCD offspring, IUGR-mHFCD decreased SREBP2 mRNA (77+/−8%, p=0.05 in female, and 67+/−7%, p=0.01 in male) and HMGCR mRNA (66+/−7%, p=0.05 in female).

Conclusions: We conclude that IUGR-mHFCD increased hepatic cholesterol and decreased SREBP2 and HMGCR 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 HMGCR expression thereby predisposing to increased hepatic cholesterol levels in IUGR offspring.

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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 clinic’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<0.01) 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 lower 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.

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SPLAT-WHEN ALCOHOL AND CARS COLLIDE: INCREASING AWARENESS OF HIGH SCHOOL ATHLETES ABOUT THE DANGERS OF DRINKING AND DRIVING. Martin Rofael, University of Washington School of Medicine. Seattle, WA

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

Purpose of Study: To educate athletes ages 14-20 about the dangers of drinking and driving. According to the Silver Bow County health department, due to the long-standing alcohol culture related to Butte’s history as a mining town, binge drinking is a big issue among high school students with 50% of Butte’s high school seniors being involved in binge drinking. As a result, fatal car crashes are 10% higher then the national average. High school athletes were targeted because athletic fitness has been shown to be the number one reason teenagers avoid drugs and alcohol.

Methods Used: An interactive session was created targeting high school athletes. Research confirmed that an interactive approach would work best. Students participated in an obstacle course that mimicked a field sobriety test while wearing goggles that simulated a .08 Blood Alcohol Concentration (BAC). Following this course, the students viewed a short lecture that informed them of alcohol’s effects on athletes and on driving. The pictures/videos were obtained from EMS personnel and were of accidents that were the result of drinking and driving. Advertisement for this session was done through the local newspaper, two radio stations, KIXF Channel 4 news, the YMCA, and Facebook. High school athletic directors and sports coaches were also informed about this session. Wal-Mart donated $150 as an incentive for the students that passed the end-of-the-session quiz.

Summary of Results: Fourteen students from the two local highs schools came to this event. Students were astounded to see the difficulty of the obstacle course with the .08 BAC goggles. In the evaluations, all 14 students stated the lecture was interactive and engaging, 12 stated they learned new information, 14 agreed to avoid drinking and driving in the future, 12 of whom stated that this lesson helped influence that decision.

Conclusions: Drinking and driving is a serious problem in Butte, Montana. The long-standing culture of Butte as a mining town is related to the excess of alcohol drinking. It is socially acceptable. Providing teenagers with a
reason to avoid drinking and driving may help raise a generation that fights this social problem rather than encourages it.

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CONCUPSE PREVENTION AND EDUCATION IN EUREKA, MONTANA
Tanabe A. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: Lincoln County has ample outdoor activities that create a possibility of head injury if proper precautions are not taken. The city of Eureka takes pride in the high school football team, a sport notorious for concussions. The purpose of this project is to educate the community on the gravity of multiple concussions for children and to increase awareness and support for keeping injured children safe while recovering from a concussion.

Methods Used: A literature review was conducted to determine the most effective way to present information to children and teens. Scheduled community activities were utilized to introduce material. Presentations and a handout were given to high school students at sports physicals. Information was presented to younger students by teaming up with the local law enforcement’s annual bike safety rodeo. In both instances parents that attended were also presented with more in-depth information.

Summary of Results: Roughly 100 members in the community attended the two events. The attendance, participation, and positive feedback indicate that the information was well received. All students received handouts, as well as the parents 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 Prompt Care 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 to the younger individual; therefore educating children at an early age is essential. Local primary care providers 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.

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AN INTERESTING CLUSTER OF OSTEOSARCOMAS IN THREE ADOLESCENTS
Mehta A, Das S, UNSOM, Las Vegas, NV.

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 oseous 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.

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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 in a Q&A session post-activity. Access to materials and the curriculum used 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 members, 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.

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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 (WM)” 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...
Becoming a FAWM appears to be a feasible pursuit during pregnancy. The updated seroconversion rate and our model suggest that gestational seroconversion to anti-D antibodies before 28 weeks. This seroconversion rate was used to construct a decision tree to analyze the costs and benefits, and under what circumstances, elimination of the second antoglobulin 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 Washington 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 antoglobulin 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% (2/2,029 women). The expected cost savings from implementing the reduced anti-globulin screening strategy ranged from $67.7 million. The cost savings for implementing this strategy in the U.S. for one year ranged from $3.47 billion to $35.6 billion for an elimination strategy. The strategy remained most beneficial when varying 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.

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

Abby R. Dunsmost-Su R., Sylvester K.1, University of Washington, Seattle, WA; 1University of Washington, Seattle, WA. 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 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 antoglobulin 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 Washington 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 antoglobulin 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% (2/2,029 women). The expected cost savings from implementing the reduced anti-globulin screening strategy ranged from $67.7 million. The cost savings for implementing this strategy in the U.S. for one year ranged from $3.47 billion to $35.6 billion for an elimination strategy. The strategy remained most beneficial when varying 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.

Fresno Emergency Medicine department and their WM and Parkmedic programs. A summary of experiences and key outcomes were compiled into a convenient handbook which will allow future pediatric residents at UCSF Fresno to avoid pitfalls and aid their efficient completion of fellowship requirements. Conclusions: Becoming a FAWM appears to be a feasible pursuit during pediatric residency training at UCSF Fresno. It is likely that similar success could be found in residency training for other specialties and at other sites. Each case would uniquely overcome challenges. Ultimately, the designation requires review and acceptance by the WMS, which would validate the previous conclusions.

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

Abby R. Dunsmost-Su R., Sylvester K.1, University of Washington, Seattle, WA; 1University of Washington, Seattle, WA. 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 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 antoglobulin screen for Rh(D)-negative mothers during pregnancy would be cost-beneficial.

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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.
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). Risk factors 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 vtBMD z-scores >5 or eGFR <15 ml/min/1.73 m2 were excluded. Multivariable logistic and linear regression analyses were performed.

Summary of Results: N=2600 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 logiAVC score). At exam 1, osteoporosis (vtBMD 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=2973 with exam 2 AVC scores, exam 1 vtBMD 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 vtBMD is associated with AVC on both a cross-sectional and prospective basis. These findings suggest a mechanistic link between bone 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.

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

Sullivan CE1,2, Wietrzek TL1, Kim J1, Sta Teresa A1, Dai D2, Hudkins K2, Alpers CE2, O’Brien KD1.1 University of Washington, Seattle, WA and 2University of Washington, Seattle, WA.

Purpose of Study: Diabetes is associated with a 2- to 3-fold ↑ in risk for congestive heart failure (CHF) that is independent of coronary atherosclerosis, hypertension or obesity. Cardiomyopathy can be induced in black and brown brachyuric (BTBR) mice either by: a) superimposing complete leptin deficiency (ob/ob mutation) 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 4 weeks on diets (P=0.11), 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±6 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% ↑ in heart weight (P<0.0001) at necropsy and a 24% ↑ in LV mass index (P<0.0001) by echocardiography. Echocardiography also showed that DD-fed BTBR ob/+ mice had both impaired systolic function (23% ↓ in fractional shortening, P<0.0001), and impaired diastolic function (30% ↓ in E/Aa ratio, P=0.001).

Conclusions: Thus, 16 weeks feeding of a “diabetogenic” diet to BTBR ob/+ mice resulted in a 22% ↑ in cardiac hypertrophy, as well as echocardiographically-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.

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

Ideens C1,2, Albers E3, Law S1,2, Law V1,2, Kernma M1,2, Seattle Children's Hospital, Seattle, WA and 3University of Washington School of Medicine, Seattle, WA.

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 group (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 Fisher’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.

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

Miller TA, Joss-Moore L, Lane RH, Puchalski MD. University of Utah, Salt Lake City, UT.

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 pulsimeters 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.

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CONTENTION: STATUS 2 PATIENTS DO NOT NEED TO UNDERGO HEART TRANSPLANTATION


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.

Endocrinology and Metabolism II

Concurrent Session

12:30 PM
Friday, January 25, 2013

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THE USE OF A BEDSIDE GLUCOSE MONITOR IN HYPERINSULINEMIC EUGLYCEMIC CLAMPS

West A1, Chow K2, Downey M1, Cree-Green M1, Nadeau K1. 1Children’s Hospital Colorado, Aurora, CO and 2Rosalind Franklin University of Medicine and Science, North Chicago, IL.

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 2-3 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 less 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 an 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® (1.09 mg/dl, SD bias=2.81 mg/dl), because the YSI measured plasma vs. whole blood. The major limitation of the Stat Strip® was that readings depend on the angle at which the meter was held and speed of blood absorption by the test strip, as indicated by the higher coefficient of variation (1.97% vs. 1.32%).

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.

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BETA-CELL FUNCTION IS IMPAIRED IN YOUTH TREATED WITH SECOND-GENERATION ANTIPSYCHOTICS

Ngai Y1, Nguyen D2, Chanoune J3, Devlin AM4, Panagiotopoulos C2. 1Faculty of Medicine, University of Toronto, Toronto, ON, Canada and 2University of British Columbia, Child & Family Research Institute, Vancouver, BC, Canada.

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 SGA-naive 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 SGA-naive, 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 stage, degree of psychiatric illness, psychiatric diagnoses, and other medications. The median treatment duration was 17 months (range 3-91) in the risperidone
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 (β = −0.540, P < 0.001). Quetiapine-treatment was negatively associated with insulinogenic index (β = −0.426, P = 0.007) and ISSI-2 (β = −0.433, P = 0.008).

Conclusions: Quetiapine-treatment in youth is associated with overall impaired 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

Yap J, Gately Z, Wilson A, Westerberg M, Deby M, Baum M. Loma Linda University School of Medicine, Loma Linda, CA.

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 in each age group, along with their 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 prevention strategies as early as possible.

Age-specific prevalence of overweight and obese children by age group at SACHS, April 2011 to January 2012

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Prevalence</th>
<th>50% CI Limits</th>
<th>Relative Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>preschool (3-4 yr)</td>
<td>341/72</td>
<td>21%</td>
<td>15%</td>
</tr>
<tr>
<td>elementary (5-9 yr)</td>
<td>287/97</td>
<td>34%</td>
<td>28%</td>
</tr>
<tr>
<td>preteen (10-15 yr)</td>
<td>268/137</td>
<td>52%</td>
<td>46%</td>
</tr>
<tr>
<td>all</td>
<td>893/366</td>
<td>34%</td>
<td>31%</td>
</tr>
</tbody>
</table>

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CHILDHOOD OBESITY: PARENTAL PERCEPTION OF CHILD WEIGHT STATUS

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

Purpose of Study: Currently, 29% of San Bernardino County children are obese, nearly double the national childhood obesity rate. Research suggests that a potential factor is parental perception of their child's weight. This study evaluates whether parents' beliefs correlate with the child's actual body mass index (BMI).

Methods Used: From San Bernardino County schools, 115 children ages 7-17 attended "Operation Fit" day camp for nutrition and fitness. Campers' BMI and parental surveys were collected. 85 children were "overweight/obese" (OW/OB, BMI ≥85th percentile), and 30 children were "underweight/normal" (UW/N, BMI <5th percentile). Parents answered the question, "Do you think your child is too skinny, too fat, or about right?"

Summary of Results: A cross-sectional survey compared the children's BMI to parents' perceptions of their child's weight (Fisher exact test). Parental perception of their child in the OW/OB group: 45.9% "too fat," 32.9% "about right," p = 0.0001. Parental perception of their child in the UW/N group: 46.7% "about right," 13.3% "too skinny," 6.7% "too fat," p = 0.0001.

Conclusions: Although the majority of parents with overweight or obese children considered them "too fat," nearly a third of those parents thought their children were "about right." The study indicated that many parents underestimate their child's weight. Teaching parents how to accurately gauge their child's health status could prove beneficial in decreasing childhood obesity.

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FITNESS CAMP: PART OF A SOLUTION TO CHILDHOOD OBESITY?

Gutierrez W, Tung A, Sihotang C, Westerberg M, Baum M. Loma Linda University, Loma Linda, CA.

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.

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INTERACTIVE NUTRITIONAL EDUCATION AT THE BOYS & GIRLS CLUB IN FERNDALE, WASHINGTON

Mast B. University of Washington School of Medicine, Seattle, WA.

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 and other websites were accessed for age-appropriate information.

Summary of Results: 15 children attended the activity. All were female. Most knew the nutrition plate 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 masters of household food preparation, evidence shows 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

Johnson S. University of Washington School of Medicine, Seattle, MT.

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 downstream effects of implementation on various laboratory values. A placemat was created to visually demonstrate a typical meal using the plate method. Food group examples were provided, along with portion sizes, carbohydrate and fat content, and seasonal activities around Dillon. A venue was chosen to debut the new placemat and educate interested community members. Lunch was provided, showcasing a meal that followed the plate method guidelines.

Summary of Results: Twelve members of the community attended and provided feedback on the contents of the placemat. Using the diabetic community's input, the placemat was revised to better fit their need. All final materials were given to the dietician to be used as a resource in future diabetic education classes.

Conclusions: Diabetes is a disease whose management requires true lifestyle changes, changes that were overwhelming the diabetic population in Dillon. From the positive feedback received after unveiling the placemats, I believe the diabetic community will work to implement this meal-planning method. Follow-up will be necessary to determine if lab values improve under this method. To make this placemat sustainable, it will need to be implemented into the diabetic education classes and edited intermittently.

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

King LE. University of Washington School of Medicine, Seattle, WA.

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 ways 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 to 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.

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Summary of Results: Results showed that 43 of the 45 patients (96%) displayed heterozygosity for 4-12 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, XXYY 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.

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DIAGNOSIS AND MANAGEMENT OF BOHRING-OPITZ SYNDROME CAUSED BY DE NOVO ASXL1 MUTATIONS

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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, Hoischen 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 tumors and an infant with 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 solider tumors, 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.

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STATE HEALTH DEPARTMENTS HANDLING OF SICKLE CELL TRAIT RESULTS IDENTIFIED THROUGH THE NEWBORN SCREENING PROGRAMS

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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 NBS programs; however, 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 survey was identified and sent to all 50 states’ NBS programs by email to determine who performs the NBS, how data are managed, and how follow-up is conducted for individuals identified with AS. This was followed by a phone call to the contact person for each state NBS program when no email response was received.

Summary of Results: Overall, 82% of state NBS programs responded. Most (72%) of programs perform their own tests through the state public health laboratories, although some contract to state or non-government laboratories. In 83% of states, test results are stored in a database, and 98% send the results to either the hospital of birth, the primary care physician on record, or both. A majority (61%) of state NBS programs also send a letter to the parents informing them of an abnormal result, and advise them to follow-up with their child’s pediatrician. For the 39% that do not contact the patient directly, the primary care physician or community based organizations were given the responsibility to inform the family, with 27% of state NBS programs working with community based organizations to assist in follow-up. The number of sickle patients with AS identified through the program varied widely across the states from less than 100 per year to over 10,000 per year.

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.
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 homzygous mutation seen in our patient was also observed in multiple individuals in the cohort of van den Boogaard suggesting a possible genotype-phenotype association.

Mucular 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.

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**ANALYSIS OF THE PRDM9 GENE SHOWS LARGE AMOUNTS OF DIVERSITY AND POINTS TOWARDS POTENTIAL SPECIATION MECHANISM IN ANCESTRAL PRIMATES**

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**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 kbp, 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.

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

Kraicer B, Hirtz SR, Van Meurs KP, Lee HC. Stanford University, Palo Alto, CA.

**Purpose of Study:** Hypothermia (HT) therapy is the standard of care for term newborns with hypoxic ischemic encephalopahy (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). Multi-variable 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 < .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 < .0001), and 10 (AP10) minute Apgar score: 4.7 (SD 2.2) vs. 5.7 (SD 2.1), (p < .0001).

There were 94 (16%) 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 = 0.001); AP10 of 0-3: 31%, 4-6: 14%, 7-9: 6%, (p < .0001). The need for mechanical ventilation was associated with HT (p < .0001), and HIE severity (p < .0001). 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.
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, 1x/wk SC), Epo (400 units/kg, 3x/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-II). Object permanence (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 (946:196 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 and Epo (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).

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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 YW1,2, UCSF, San Francisco, CA; 1UCSF, San Francisco, CA; 1Children’s National Medical Center, Washington, DC; 2University of Washington, Seattle, WA; 3Children’s Hospital and Research Center Oakland, Oakland, CA and 4Santa 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 studies 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 standardly followed after discharge in each of the participating clinics. Information was gathered regarding motor delay, abnormal brain-rectal temperature dissociation among severely encephalopathic infants. 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. We evaluated infants at 18-22 months corrected age using the Bayley Scales of Infant Development (BSID-II). Object permanence (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 (946:196 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 and Epo (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).

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NON-INVASIVE REGIONAL BRAIN TEMPERATURE MEASUREMENTS DURING AND AFTER HIPOTERMIA THERAPY IN INFANTS WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY

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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 and 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.

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ABSENCE OF CEREBRAL AUTOREGULATION IN THE PRETERM LAMB AFTER PRETERM DELIVERY

Czynski AJ1, Blood AB1,2, Loma Linda University, Loma Linda, CA and 2Loma Linda University, Loma Linda, CA.

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 PacO2 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 C1,2, Hartman RE1, Obenaus A1, Blood AB1.1 Loma 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 μg/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.

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EARLY POSTNATAL WEIGHT GAIN AS AN ACCURATE PREDICTOR FOR THE DEVELOPMENT OF RETINOPATHY OF PREMATURITY

Weiner A1,2,2,2, Binwale M1,2, Barton L1,3, Ramanathan R1,2,3, Sardesai S1,3, Cayabyab R1,3,1 LAC+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: Current ROP 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 of ROP Stage 3 or greater in a larger 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 computer-based 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. 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 develop ROP that required treatment.

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DOPAMINE RESISTANT HYPOTENSION AND RETINOPATHY OF PREMATURITY

Catenacci M1, Miyagi S2, Wickremasinghe A1, Lucas S2, De Alba Campomanes A1, Good W3, Clyman R1.1 UCSC, 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 of ROP, no studies have examined the relationship between the etiology and severity of hypotension and subsequent development of ROP.

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, or (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
Idiopathic dopamine-resistant hypotension is an early, significant risk of developing severe ROP ((65% developed severe ROP; Odds ratio: 10 (95% CI: 4-28)). Infants who developed “idiopathic” dopamine-resistant hypotension after age 14 days were at increased 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 predictive 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 association between altered vascular tone and abnormal retinal development.

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THE IMPACT OF PERIOPERATIVE MEDICINE ROTATION IMPLEMENTATION ON ICU OUTCOMES

Purpose of Study: As the role of the anesthesiologist broadens in perioperative care, adjustments to residency program curriculums are expected. ACGME anesthesiology program requirements have proposed increased resident 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 resulted 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. 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 perioperative medicine rotation was effective in reducing ICU average length of stay while managing patients with similar severity of illness. These results demonstrate 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

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<th>Prior to Implementation</th>
<th>Average ICU Length of Stay Days</th>
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VALIDATION OF A TOOL FOR PROMOTING SELF-MONITORING AND SELF-MANAGEMENT IN CHILDREN WITH ASTHMA
Fassl B1, Nkoy F1, Stone B1, Maloney C1, Schatz M2. 1University of Utah, Salt Lake City, UT and 2Kaiser San Diego, San Diego, CA.

Purpose of Study: To improve asthma control and reduce the risk of exacerbations, asthma guidelines recommend ongoing monitoring of chronic asthma symptoms and timely adjustments of preventive therapy. Our 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 assessing 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 concurrent asthma control questionnaire (ACQ) scores (criterion validity), 2) comparing longitudinal changes in AST and ACQ scores (responsiveness), and 3) testing the association between AST scores with quick reliever use and readmission between frequent and non-frequent users (discriminant 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 electronically. Analysis included Chi-square tests and logistic regression.

Summary of Results: 51% (136/266) of patients were enrolled: 1552 individual self-assessments were completed. The correlation between weekly AST and ACQ scores was strong (r=0.89, p<0.01). AST scores showed longitudinal variation similar to ACQ scores. Patients with poorly controlled asthma reported more use of quick relievers than not well- and well-controlled patients: 81%, 26%, and 0.3% (p<0.01). There were 13 (9 ED and 4 inpatient) readmissions 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 survey 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.
SLEEP-RELATED QUALITY OF LIFE AND PHYSIOLOGICAL PARAMETERS IN VETERANS WITH EARLY AMYOTROPHIC LATERAL SCOLIOSIS

Farshidpanah S1,2, Klein WF1, Fargo R2, Dandamudi N2,3. 1Loma 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 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±0.72L 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 (23.5-38) 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 hypercapnic 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 T1,2, 4Loma Linda University, Loma Linda, CA 3Loma Linda VA Healthcare System, 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.

Poster Session II
Adolescent Medicine, General Pediatrics, and Nephrology
2:30 PM
Friday, January 25, 2013

PEdiATRIC PERITONEAL dialysis: A nurse driven anemia protocol

White C, Larksins N, Leechik J. BC Children’s Hospital, Vancouver, BC, Canada.

Purpose of Study: Report on 4 yr outcomes of a nurse led anemia protocol in children on PD based on 2006/7 KDQOI Anemia Guidelines.
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 unmitigating conditions (2) during therapy. Summary of Results: See Table. 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. 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. Details of Results: The children of Hailey are especially susceptible to bike-related death for children ages 1-14. Furthermore, it is estimated that over 700 children die each year from heatstroke and 50,000 die from drowning each year. Among states, Idaho has the highest rate of children drowning. Preventive measures for drowning include the use of helmets and swim lessons. The purpose of this project is to provide basic 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: question and answer style lecture with rewards for correct answers, demonstration of proper life jacket use, and an art contest where the children depicted one or more aspects of water safety. Summary of Results: The event provided eleven children ages 6 to 12 and three childcare providers with information about water safety and risks. All in attendance were very engaged owing to the sugar-free licorice rewards for answering water safety questions correctly. The following art contest 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 nutrition handout was distributed based on these questions. A "Nutrition during Breastfeeding" educational event at CHP was held, at which a cooking demonstration was conducted. Conclusions: The children of Hailey are especially susceptible to bike-related death for children ages 1-14. Furthermore, it is estimated that over 700 children die each year from heatstroke and 50,000 die from drowning each year. Among states, Idaho has the highest rate of children drowning. Preventive measures for drowning include the use of helmets and swim lessons.
Eating healthy, well-balanced diets can be a challenge for post-partum women busy caring for their infants. Despite common trends among mothers regarding nutrition during breastfeeding, nutritional counseling is not often incorporated into patient visits. This inter-active 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.

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ASSESSMENT OF BREASTFEEDING RATES BEFORE AND AFTER “BABY FRIENDLY” DESIGNATION AT PEDIATRIC CONTINUITY CLINIC, LAC+USC MEDICAL CENTER

Laird M1, Kunza B1, Barton L2, Franzky K2, Vasan R2. ‘Keck School of Medicine of USC, Los Angeles, CA; 2 LAC+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 Family 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 six 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.

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, 25.5% at six 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.

Results: To date, 100 surveys were administered. The survey is ongoing and we will continue to collect data as part of the BFHI. We will compare these results to data collected in 2008 when breastfeeding of 46.2% at three months, 25.5% at six months, and 34.1% at 12 months. The survey will inquire when breastfeeding was ended, when breastfeeding was ended, and when breastfeeding was ended, and when breastfeeding was ended, and when breastfeeding was ended, and when breastfeeding was ended, and when breastfeeding was ended, and when breastfeeding was ended. Another aim of the survey is to elicit which BFHI components the mothers found most helpful in sustaining successful breastfeeding.

Conclusions: Pending.

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VIRAL BREAKTHROUGH IN HEPATITIS C

Ferguson JD, Zhou K, Bui S, Saab S. DGROM 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.

Characteristics of Patients with Late Viral Breakthrough

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Gender</th>
<th>Ethnicity</th>
<th>Presence of Breakthrough</th>
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CENTRAL LINE ASSOCIATED BLOOD STREAM INFECTIONS IN PEDIATRIC OUTPATIENTS: PRESENTING SYMPTOMS, EPIDEMIOLOGY, AND RISK FACTORS

Bechthold H1, Wozniak L2, 1 UCLA School of Medicine, Los Angeles, CA and 2 UCLA, Los Angeles, CA.

Purpose of Study: Central line-associated blood stream infections (CLABSIs) require inpatient hospitalization and add to morbidity and mortality. Multiple studies have addressed risk factors of adult hospital-acquired CLABSIs, however few have examined risk factors for pediatric outpatients. Our aim was to characterize the presentation, epidemiology, and risk factors associated with outpatient-acquired CLABSIs in the UCLA pediatric population.

Methods Used: An IRB-approved, longitudinal database to prospectively track CLABSIS in the UCLA pediatric population was created. Medical records were retrospectively reviewed and data was collected for each CLABSI. We are currently collecting the data and will have results in time for the conference.

Summary of Results: We are currently collecting the data and will have results in time for the conference.

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SITAGLIPTIN INDUCED HEPATIC NECROSIS: A CASE REPORT

Cruz VD, Ramos-Matos C, Davis A, Zeitr M, Abel E. University of South Florida, Tampa, FL.

Case Report: Medications are often an 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 afibrile and noted to have scleral icterus, hepatomegaly and ascites. Initial chemistry metabolic 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-maxillary 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 all patients 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
2:30 PM
Friday, January 25, 2013

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A COMPREHENSIVE SURVEY OF MUTATIONS IN THE OPA1 GENE IN PATIENTS WITH AUTOSOMAL DOMINANT OPTIC ATROPHY ‘PLUS’ PHENOTYPE

Ham M1, Smith M2, Osann K2, Kimonis V1. 1 University of California, Irvine, Irvine, CA and 2 University of California, Irvine, Irvine, CA.

Purpose of Study: Autosomal Dominant Optic Atrophy (ADOA) is a common neuro-ocular 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 visual 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 cardiac 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 extraocular symptoms. Statistical analysis was performed of the extraocular 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 (26%), ptosis (13%), and sensorineural hearing loss (63%). 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 extraocular clinical features in ADOA patients, by performing additional neurologic and audiological evaluations.

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A NOVEL STRATEGY TO IDENTIFY BIOMARKERS FOR PROSTATE CANCER

Scapu J1, Kerkoztian S2, Sun Y3, Zhang H1, Squires J3, Li X2,3, Goldstein A1, White O3, Huang F2, 1 David Geffen School of Medicine at UCLA, Los Angeles, CA; 2 David Geffen School of Medicine at UCLA, Los Angeles, CA and 3 Jonsson 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 PC patients, 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 25-35% of men with a negative biopsy have PC that was missed by tissue sampling. Here, we focus on tumor-adjacent, histologically benign prostate tissue to identify biomarkers that can screen patients with negative biopsies containing normal prostatic 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, and PC cell populations.

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.

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MUTATIONS IN THE TETRATRICOPEPTIDE 19 GENE TTC19 ARE A RARE CAUSE OF LEIGH SYNDROME

Atwal PS, Schelley S, Emms 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_967delGACT (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_967delGACT 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 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.

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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, hypotonia and dystonia. The TCTC19 gene encodes tetractiroceptide 19 (TTC19), a CLF 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 TTC19, two of which were in one family. The phenotypic variation and clinical presentation of patients with TTC19 mutations is broad, with initial presentation from childhood to adulthood. In summary, TTC19 is one of a growing number of nuclear genes that affect mitochondrial function and should be included in nuclear gene testing panels for the evaluation of patients with a Leigh syndrome phenotype.

PERIPHERAL NEUROPATHY, LEUKOENCEPHALOPATHY, AND CIRRHOSIS IN A 25 YEAR OLD WOMAN
Mendelssohn 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 neuropathy, leukoencephalopathy, a macrocystic anemia with thrombocytopenia, diabetes mellitus, intermittent lactic acidosisis, 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, electromyogram and nerve conduction studies, nerve and liver biopsies, as well as sequencing analysis for several genes involved in disorders of mitochondrial DNA maintenance. Her symptoms are most consistent with the adult-onset form of Navajo Neurohepatopathy, an autosomal recessive mitochondrial 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. Because 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 possible therapy for human HD based on current human and mouse model studies.

Methods Used: I searched for studies investigating both the effects of creatine 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, survivability and rotarod performance as outcomes measured. Search criteria for human studies: randomized controlled trials, participants diagnosed with a neurodegenerative disease, creatine as the only dietary supplement, creatine tolerability and tests for brain biomarkers affected by creatine as outcomes measured.

Summary of Results: The mouse model studies reviewed show that creatine 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, creatine brain concentrations, and NAA levels, a marker of mitochondrial function, were elevated in creatine supplemented patients, whereas serum 8OHdG 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 progression 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 Oelschlager A3, Mergerian PA4, Avasinoso JR5.
1University of Washington School of Medicine, Seattle, WA; 2Seattle Children’s Hospital, Seattle, WA; 3Seattle Children’s Hospital, Seattle, WA and 4Seattle 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 patients 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 catheterization (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 (non-CIC).

Summary of Results: Eight patients (53%) were managed with CIC and seven (47%) with other methods. There was no significant difference between 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 complications 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 hydronephrosis (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 invasive drainage modalities. Ultimately, a larger, multi-center study is necessary 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 access to TB information using the Information and Communication Technology (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 Paxis, were trained to record, maintain, and distribute spoken health education 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 collaboratively created 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.
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 program and were trained how to use them. Radio Pacis broadcast a 6-minute piece on TB in all of Arau 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 Arau 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 Arau district.

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CLINICAL PRESENTATIONS AND TREATMENTS OF COCCIDIOIDOMYCOSES 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 coccidioidomycosis 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 coccidioidomycosis osteomyelitis based on differentiation of unifocal versus multifocal disseminated disease. Regimens 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 coccidioidomycosis 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: Coccidioidomycosis 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: Coccidioidomycosis 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 predilection 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.

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IUGR DOES NOT AFFECT DNA METHYLATION OF THE PPAR-Y 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) that IUGR will decrease DNA methylation of the PPARγ CpG sparse promoter.

Methods Used: IUGR was induced by uterine artery ligation in 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. In contrast, sites within the CpG sparse promoter were up to 80% methylated in control rat lung. IUGR did not significantly alter this level of methylation at any site in the CpG sparse promoter.

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.

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PREDICTORS OF NEONATAL NEUROLOGIC BIRTH DEPRESSION AND INTRAVENTRICULAR HEMORRHAGE IN PRETERM PREMATURE RUPTURE OF MEMBRANES

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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 gender 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 be at 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.

END-OF-LIFE DECISIONS ENTER A GREY ZONE AT THE EDGE OF VIABILITY

Weiner JA, Kalfbride 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 view differently for preterm infants.

Table 1: Diagnosis, Clinical Stability and Mode of Death for Infants 32 weeks and less

<table>
<thead>
<tr>
<th>Gestational Age (weeks)</th>
<th>Total N=460</th>
<th>Withdrawn, %</th>
<th>Withheld, %</th>
<th>CPR, %</th>
<th>Unrelated, %</th>
<th>Snails, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>22-24</td>
<td>221</td>
<td>43.8</td>
<td>62.5</td>
<td>55.9</td>
<td>52.7</td>
<td>94</td>
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<tr>
<td>25-27</td>
<td>250</td>
<td>25</td>
<td>26.5</td>
<td>21.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28-32</td>
<td>89</td>
<td>31.2</td>
<td>25</td>
<td>17.6</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>23-34</td>
<td>3</td>
<td>91.6</td>
<td>63.5</td>
<td>73.3</td>
<td>77.4</td>
<td>94</td>
</tr>
</tbody>
</table>

INCIDENCE OF BLADDER EVISCERATION IN NEONATES WITH GASTROSCHISIS

Dimond L,1,2 Paquette L,1,2 1University of Southern California, Los Angeles, CA and 2Children’s Hospital Los Angeles, Los Angeles, CA.

Purpose of Study: Gastroschisis is a congenital condition in which portions of the GI tract herniate outside 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 gastroschisis 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 gastroschisis 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 evacivered 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. The differences in rates of urinary tract complications were not significant between the evacuated bladder and the normal bladder groups.

Conclusions: Bladder eversion occurred in 7.4% of gastroschisis 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 eversion confers no additional risk on neonates with gastroschisis, at least during the early years of life examined in this study.
LONG-TERM GROWTH OF SURVIVORS OF CONGENITAL HEART DISEASE

Aguiar DC, Raif 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; Tetalogy of Fallot (TOF), transposition of great arteries (TGA) and VSD from the UCDMC electronic medical record. 34 children with TOF, 35 with TGA and 163 with VSD were identified with measurement 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 body weight between 2-10y of age. Each lesion has a different pattern of abnormally, with either significantly increased body mass, or decreased weight gain over this period. The long-term consequences on long-term metabolic risk and cardiovascular health merits further investigation.

Poster Session II
Surgery
2:30 PM
Friday, January 25, 2013

INTERNATIONAL PUBLICATION TRENDS IN PLASTIC AND RECONSTRUCTIVE SURGERY

Mitchell E, Workman A, Gupta S. Loma Linda University, Loma Linda, CA.

Purpose of Study: As globalization 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 IMPRS 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 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.).

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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.

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THE LONGEST JOURNEY IS FROM THE HEAD TO THE HEART

Hollbrook ER1, Thompson J2, 3University of Arizona, Tucson, AZ and 4University of Arizona, Tucson, AZ.

Case Report: Introduction

Approximately 50% of intravascular missiles enter the venous circulation, and have the potential for central migration toward the heart. We present a case with embolization of a bullet from the head to the distal pulmonary bed. We then reviewed our own institutional experience and the world’s literature to help determine the best treatment strategy for patients with projectile embolization to the pulmonary artery.

Case Report: A 25-year-old male sustained a gunshot wound to the left eye. Computed tomography (CT) scan of the head disclosed rupture of the left globe and lens, complex fractures of the boney structures, and a 5 mm, well-circumscribed metallic foreign body consistent with a bullet fragment in the right superior aspect of the posterior fossa just caudad to the tentorium. Aside from the head injuries, there was no evidence of additional trauma. Soon after arrival to the emergency department, a right lateral ventricular external drain was placed into the calvarium. In order to monitor the progression of the cerebral injury, repeat CT scan of the head was performed a few hours later, and the bullet fragment was gone. Chest x-ray revealed a dense object in the region of the pulmonary artery that had not been present on the prior chest film. CT scan of the chest showed that the bullet fragment was now in the left lower lung field (figure 1). There was consolidation of the lung parenchyma in the area of the bullet fragment. Broad spectrum antibiotics that had previously been started were continued. Several days later, the patient was transferred to another institution for continued neurologic treatment. At the time of transfer the patient had no complications due to the retained bullet.

Discussion: Review of our institution’s medical record revealed two additional cases of bullet fragments having embolized from penetrating head injuries to the pulmonary arteries. Both patients were managed conservatively, and had no pulmonary sequelae at 2 years and 18 months respectively. Assessment of the world’s literature demonstrates that controversy still exists as regards the need for and appropriate timing of extraction of projectiles that have embolized to the pulmonary circulation.

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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...
Our 3D analysis suggests that cranioscoliosis can be quantified by measuring the tragia and recording the difference in position in both AP and SI directions. We propose that cranioscoliosis is a sign rather than a diagnosis and may be present in many craniofacial conditions.

Conclusion: Our 3D analysis suggests that cranioscoliosis can be quantified by measuring the tragia and recording the difference in position in both AP and SI directions. We propose that cranioscoliosis is a sign rather than a diagnosis and may be present in many craniofacial conditions.

THE OPTIMAL DURATION OF ANTIBIOTIC PROPHYLAXIS IN PLASTIC SURGERY: A META-ANALYSIS OF 32 PUBLICATIONS

Richardson C, Workman A, Mattison G, Gupta, MD, PhD, FACS S. Loma Linda University, Loma Linda, CA.

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.

Conclusions: A comparison of the data for antibiotic prophylaxis demonstrates a possible decrease in post-operative infections for the single dose prophylaxis and the extended course of antibiotics in comparison to no antibiotics 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.

240 A RETROSPECTIVE COMPARISON OF TWO DIFFERENT CT URETERAL LENGTH MEASUREMENT TECHNIQUES

Chung CS1,2, Engebretsen S1, Arnold D1, Wallner C1, Huang G2, Creech J2, Mai A1,2, Ng C1,2, Culpepper D1,2, Baldwin D1, Loma Linda University Medical Center, Loma Linda, CA and Loma Linda University School of Medicine, Loma Linda, CA.

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.

241 EFFECT OF PREOPERATIVE WASHES ON SURGICAL SITE INFECTION RATES

Mroczek B1,2, Afshar K1,3, Skippen P1,3, Skargard E1,2,3, Child and Family Research Institute, Vancouver, BC, Canada; BC Children’s Hospital, Vancouver, BC, Canada and 1University of British Columbia, Vancouver, BC, Canada.

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 on SSI 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 on SSI 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 on SSI rates between studies. Several reviews show no effect on SSI rate when preoperative washes are 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, nor 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.

242 REVERSED NEEDLE PASS CLEAR-CORNEAL OR LIMBAL INCISION SUTURING TECHNIQUE USING THE 3-THROW (1-1-1) ADJUSTABLE SQUARE KNOT

Bernard S1, Narvaez J1, Jones T1, Zumwalt M2, Mahdavi P3, Loma Linda University School of Medicine, Loma Linda, CA and 2Loma Linda University School of Medicine, Loma Linda, CA.

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
The reversed-needle pass combined with the 1-1-1 knot is a

We designed a game show that utilizes questions in form

A randomized, controlled, and double blinded study was

1,3 Improving knowledge of childhood nutritional needs and
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 gaps regarding child nutrition. Training comprised of didactic lectures on infant and young children 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 1st 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.

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 gaps regarding child nutrition. Training comprised of didactic lectures on infant and young children 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.

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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.

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.

Community Health II
Concurrent Session
3:30 PM
Friday, January 25, 2013

I CARE TO KNOW: AN INNOVATIVE EDUTAINMENT PROGRAM TO INCREASE HIV SCREENING AMONG ADOLESCENTS AGED 10-18 YEARS IN NIGERIA

Ezeanolue EE3, Aranotu CS2, 1University of Nevada School of Medicine, Las Vegas, NV and 2Year 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 (2) minimum 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 (5) Eight participants are selected to represent each school in the Edutainment Game Show. Other participants act as audience and supporters (6) five schools are selected for each game cycle over 8 weeks and the competition are recorded at a TV station (7) All participants receive a gift pack of school essentials provided by sponsors (8) Game series are played on statewide television (9) The final round is played on live TV and awards are presented by influential individuals including governor, other high level government officials, Bishops, private individuals and celebrities such Beauty Queens and Football Stars (10) A new cycle of 5 school begins.

Summary of Results: 75 schools have participated and 3000 adolescents screened for HIV since 2009. Other people have been influenced to screening for HIV by participants including their parents. The program has expanded with a community based version and a specific version focused on pregnant women, a part of an implementation grant funded by the US National Institute of Health.

Conclusions: Innovative approaches to HIV screening can lead to an increase in community acceptance of screening; number of people screened; private sector participation; and reduce stigmatization.

THE EFFECTS OF REGULAR AND DECAFFEINATED COFFEE ON VOIDING SYMPTOMS IN YOUNG HEALTHY VOLUNTEERS

Chung CS1,2, Baker K2,3, Distelberg B2, Staack A2,1, Loma Linda University, Loma Linda, CA; 2Loma Linda University, Loma Linda, CA and 3Loma Linda University School of Medicine, Loma Linda, CA.

Purpose of Study: The purpose of this study is to investigate the effects 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. 55 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 11, all participants were asked again to refrain from any caffeine consumption and remained on the same diet and fluid regimen that they started on. Day 15 concluded the study for each participant. Analysis included a multivariate repeated measures analysis on variables that related to bladder health and voiding (the ICSC, ICPI, UDI-6 as well as the voiding log).

Summary of Results: The caffeinated coffee group saw a significant increase in urinary volume. There was a lag effect noticed here in that the effects on urinary volume did not wane 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: Increased caffeine intake is the sole variable in the increase of urine output volume and voiding urgency when comparing between those drinking caffeinated coffee and those drinking decaffeinated coffee.
BUILDING A TB SUPPORT AND ADVOCACY GROUP - VENTANILLA, PERU

Burnell 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, momentous 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.

Conclusion: 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

Gurule FS1, Dharas S1, Escareno R1, Skipper B1, Pentler A1, Chillon L2.

1University of New Mexico School of Medicine, Albuquerque, NM and 2University of New Mexico, 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 absenteism 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 local residents, a general pediatrics faculty attending, and a developmental specialist. Services provided in the clinic target patients in their homes. The home visit team consists of a pediatric resident, a general pediatrics faculty attending, and a developmental specialist. Clinic patients targeted for home visits are at high-risk for medical, psychosocial, developmental, or behavioral concerns. Services provided in the home include well-child checks and vaccinations. Each resident is given a post-visit survey identifying their pre-visit goals, whether their goals were met, and how they felt overall with the visit. The team also debriefs before and after each home visit to discuss what was learned.

Summary of Results: From 2009 to 2012, 14 residents and 1 medical student were surveyed on 28 home encounters. Learners’ goals included: 1. Integrate with family in the home environment; 2. Determine how patient's developmental/behavioral findings are affected by the environment in which they grow; 3. Discover barriers that exist in the home making it difficult for families to access medical care; 4. Assess living situation and the needs of the family; 5. Provide more targeted anticipatory guidance based on observed safety issues in home. Post-visit assessment showed 100% of learners were satisfied with the visit, felt that it enhanced their understanding of the patient, felt that it provided better continuity of care for the patient, and allowed the patient to feel more comfortable. Some residents expressed concern that home visits made it more difficult for parents to raise concerns (e.g., mother-in-law present, language barrier without access to interpreter network, parent uncomfortable showing their home to learner).

Conclusion: In line with previous literature on the use of home visits during residency training, we find our residents eager to understand the home environment of their patients and find the overall experience to be meaningful and enriching. Future studies will investigate the impact of these home visits on resident perceptions and behaviors in the long-term.

DERMATOLOGIC NEEDS ASSESSMENT OF UNDERSERVED DISTRICT IN ALBUQUERQUE, NEW MEXICO

Brown M. University of New Mexico School of Medicine, Albuquerque, NM.

Purpose of Study: There is a need for dermatological services for residents of the “International District” in Albuquerque, New Mexico. The International District is primarily home to Native American, Hispanic, and Vietnamese immigrants with a relative lack of access to dermatological services. In order to successfully provide volunteer dermatological services to patients in this district, the prevalence and distribution of dermatologic disease in this population must be elucidated.

Methods Used: Age, insurance status, and primary diagnosis of 3625 dermatologic patient visits from 2008-2012 was obtained from the University of New Mexico UNM Care data base. Patients who had listed the zip code 87108 (International District) as their address were included in the study. Insurance Status was mapped to a binary variable “Likely User” which estimated potential usage of the clinic. Patients with Medicare, Medicaid, state, university, or self-pay insurance status represented a ‘likely user.’ Probable use of clinic resources was simplified into one of three categories: medical, surgical, or cosmetic.
categorical activities were determined by literature review of most common dermatological diagnosis in skin of color and assigned to each unique diagnosis. Statistical calculations were made with Statgraphics Centurion XV version 15.2.06; Microsoft Excel 2007 was utilized for data management. Two-tailed tests and a Type I error rate of 0.05 were employed throughout.

**Summary of Results:** 3625 subjects were included in this study. The likely user group (median, 55 years) was significantly older than the unlikely user group (median, 51 years, p<0.001). Likely users presented with tinea or malignant neoplasm more often than unlikely users (p<0.001). There was no statistically significant difference in skin cancer prevalence between the groups.

**Conclusions:** Patients likely to utilize a volunteer dermatology clinic in the International District represent a slightly older patient population and more often presented with tinea or malignant neoplasm more often than unlikely users. There was no statistically significant difference in skin cancer prevalence between the groups. These findings represent the first dermatologic needs assessment of an underserved population in the International District and will help to appropriately provide volunteer clinic services.

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**PERCEPTUAL AND ADAPTIVE LEARNING MODULES PRODUCE LONG-TERM LEARNING OF PATTERNS IN DERMATOLOGY**

Altieri L1, Gu Z2, Craft N2, Kellman P3, Kranske S4, David Geffen School of Medicine, UCLA, Los Angeles, CA; 1UCLA-Olive View Medical Center and Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Los Angeles, CA and 4UCLA, Los Angeles, CA.

**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 statistically higher than the scores 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.

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**PERUVIAN COMMUNITY MEMBER'S KNOWLEDGE, ATTITUDE AND PRACTICE OF EMERGENCY MEDICAL CARE**

Goldstein MD1, Donaldson RF2, David Geffen School of Medicine at UCLA, Culver City, CA and 2Harbor-UCLA Medical Center, Torrance, CA.

**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 x 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.
Western Regional Meeting Abstracts

Health Care Research II
Concurrent Session

3:30 PM
Friday, January 25, 2013

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BARRIERS TO CLEAR COMMUNICATION FOR PEDIATRIC PRIMARY CARE PROVIDERS WHEN USING PHONE INTERPRETERS: A FOCUS GROUP STUDY
UCSF Fresno Medical Education Program, Fresno, CA and 1Children's 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 medical interpreters 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 able 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, deferring the interpreter about the patient situation before the encounter starts, and using Google Translator.

Conclusions: Clear communication is crucial in a primary care setting that serves at-risk children and adolescents when using medical phone interpretation in primary care. Our study’s preliminary findings highlight that healthcare providers and parents have significant barriers to clear communication for phone medical interpretation. Developing strategies to aid providers and parents to overcome these barriers is crucial to effective communication.

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EFFECT OF PULMONARY REHABILITATION ON SLEEP AS MEASURED BY ACTIGRAPHY
Shah H1,2, Dundamudi N1,2, Fargo R1,2, Elliston K1. 1VA Loma Linda Healthcare System, Loma Linda, CA and 2Loma Linda University Medical Center, Loma Linda, CA.

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 after completion of the program. A repeated measures paired t-test was used to assess for difference in sleep parameters before and after PR.

Sleep measurements obtained by actigraphy included total time in bed, total sleep time, onset latency, sleep efficiency, wake after sleep onset (WASO), and number of awakenings.

Summary of Results: Ten patients completed PR. Two patients who were hospitalized or were ill at time of repeat actigraphy were excluded. Data presented are from the remaining 8 patients. Patients who completed PR had a significant improvement in sleep efficiency (81% vs 64%, p<0.05) and wake after sleep onset (45 minutes vs. 111 minutes, p<0.05). There was a trend towards improvement in total sleep time from 304 to 379 minutes, although not statistically significant (p=0.06). The number of awakenings and sleep onset latency were not different.

Conclusions: Patients who complete PR have improvement in their sleep quality. More specifically, patients have better overall sleep efficiency and spend less time awake at night after initially failing to sleep. Thus, improved sleep is another benefit of pulmonary rehabilitation.

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EVALUATION OF A HEALTH EDUCATION PROGRAM IN UGANDA USING PRE-TEST-POST-TEST RESEARCH

Purpose of Study: To evaluate a medical student designed health education curriculum for the improvement of sexual health and life skills in adolescents in Uganda, and to investigate if teaching could be successfully transferred to local nursing aides, so as to facilitate program sustainability.

Methods Used: A quasi-experimental one-group pre- and post-test research design was used to evaluate knowledge acquisition. Data was collected from nursing aides and secondary school students. A 10-15-item questionnaire was used to evaluate knowledge acquisition. The curriculum employed lectures, decision-making activities, and group discussions. Nursing aides were taught the curriculum first, then secondary school students were taught either by the researchers or by nursing aides in an effort to investigate if the program could be sustained by local residents.

Summary of Results: Questionnaires were obtained from 34 nursing aides and 158 secondary school students. The nursing aides’ mean score on the sexual health pre-test was 60%, and 69% on the post-test, which increased significantly (p=0.0150). Their mean score on the life skills pre-test was 42%, and 65% on the post-test, which increased significantly (p<0.0001). The secondary school students’ mean score on the sexual health pre-test was 43%, and 50% on the post-test, which increased significantly (p<0.0001). Their mean score on the life skills pre-test was 41%, and 60% on the post-test, which increased significantly (p<0.0001). There was no significant difference in test score improvement between secondary school students taught by the researchers and those taught by nursing aides.

Conclusions: Although the mean post-test scores were low, statistical analysis showed the health education curriculum significantly improved nursing aides’ and secondary school students’ knowledge of sexual health and life skills. Future work will include investigating how the curriculum can be improved to further increase knowledge acquisition and if knowledge acquired is retained long-term. Since there was no significant difference in score improvement between students taught by the researchers and those taught by local nursing aides, the training program provided to the nursing aides was sufficient to standardize curriculum delivery, and suggests the program can be continued by them.

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BIOMETRIC MONITORING IN FOUNDRY & PLASTIC PIPE WORKERS: 2010-2011 RESULTS IN AN INCENTIVE-DRIVEN PROGRAM
Raymond LW1,2, Pankowski J1, Yanni A1, Hall D1. 1Carolinas HealthCare System, Charlotte, NC and 2Univ of North Carolina, Chapel Hill, Charlotte, NC.

Purpose of Study: Health care costs were 17% below projections in a family-owned foundry and plastic pipe manufacturer after start-up of an onsite clinic to provide treatment for minor illnesses. Another clinic was added at a second site. The clinics also provide health counseling by mid-level clinicians in wellness programs which include incentives for specific risk factor reductions. Risk factor results are analyzed in this report.

Methods Used: Non-fasting blood samples of program participants were analyzed for lipoproteins and glycated hemoglobin (HbA1c). Results were
comparatively for years 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 lifestyle 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% per cent 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)

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**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 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 that may act as reservoirs for continued infection.

**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 in this and other low transmission endemic regions, and will contribute to the formulation of more effective strategies to control malaria.

**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) 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.

**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 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.
**Purpose of Study:** Congenital heart disease is one of the leading causes of infant deaths in the developed world. Current screening consists of prenatal ultrasound and postnatal physical exam, which combined, diagnoses <50% of congenital heart disease. Pulse oximetry is an effective, non-invasive screening tool that can identify more newborns with critical congenital heart disease. The purpose of this project is to describe the challenges and lessons learned while implementing pulse oximetry screening at Community Regional Medical Center (CRMC) in Fresno, CA, the state’s second busiest birthing center.

**Methods Used:** We reviewed medical literature on newborn pulse oximetry screening and found resources from screening programs across the country.

**Summary of Results:** The evidence for pulse oximetry screening was presented at 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 AT1,2, Rodriguez MF1. 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>
</tr>
<tr>
<td>Providing Practical Avenues for Universities to Implement Interventions</td>
<td>71.4% (5/7)</td>
<td>75% (3/4)</td>
</tr>
<tr>
<td>Leveling of power dynamics</td>
<td>71.4% (5/7)</td>
<td>50% (2/4)</td>
</tr>
<tr>
<td>Resources and funding</td>
<td>28.6% (2/7)</td>
<td>50% (2/4)</td>
</tr>
<tr>
<td>Sustainability</td>
<td>42.9% (3/7)</td>
<td>0% (0/3)</td>
</tr>
<tr>
<td>Dissemination of results</td>
<td>28.6% (2/7)</td>
<td>50% (2/4)</td>
</tr>
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**Conclusions:** The results serve to inform both parties as they begin to develop and implement programs consistent with the mission of EXPORT. From this data, next steps include revising Project EXPORT to include interventions based on the themes which surfaced through the interviews.

**Infectious Diseases**

Concurrent Session
3:30 PM
Friday, January 25, 2013

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

Weller SM1,2, Jones JC3, Rosen H12, Crowther GC1, 2University of Washington School of Medicine, Seattle, WA and 3University 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 products, 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 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.

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 isolated. 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 genes. 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.

THE EFFECTS OF BREASTMILK ON INFANT MICROBIOMES THROUGH PROMOTION VS INHIBITION OF BACTERIAL GROWTH

Finn E, Gustafson C, Frank DN, Janoff EN. University of Colorado, Denver, CO.

Purpose of Study: The development of an infant's intestinal microbiota has important health implications. 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, 6 and 12 months. Based on results of high-throughput ribosomal DNA sequencing to define the populations of colonic bacteria over time, we found that Escherichia-Shigella genus (E. coli) was present in variable concentrations in different infants over time, some high (10-40% of bacteria) and other low (0-10%) at 1 month of age. Using a well-characterized strain of E. coli of intestinal origin, we assayed the ability of milks from women with children colonized with high and low numbers of E. coli to modulate the growth of the bacteria over 2 hours. 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 the 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.

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: Candidemia 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 without (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.

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 obstetric 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 in 2005-2006; only 40% seen by a pediatrician who coordinated care for these infants to ensure compliance with Zidovudine prophylaxis; 30% completed appropriate diagnostic test by 6 months; and five pediatric infec-
tions were documented (20%). From 2007-2011, 100 infants were born to HIV-infected women; post-delivery follow up by a pediatrician increased from 40% to 100%; Documented zidovudine prophylaxis increased to 100%; appropriate diagnostic test performed by six month of age increased from 30% to 100% and no pediatric infection was documented.

Conclusions: Our data suggests that an integrated approach to care of 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.

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 cytomegalovirus (mCMV) infects the developing mouse temporal bone resulting in SNHL in an age dependent manner.

Methods Used: BALB/c mice underwent intracranial injection 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 kHz), 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 abundant in the temporal bone at the 1st week in the P3 mice, but mostly devoid of GFP labeling by 2 weeks postinfection. 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.

269 VIRAL ETIOLOGY FOR ACUTE WHEEZING EPISODES IN CHILDREN WITH HIGH RISK FOR ASTHAMA
Friedman B1,2, Thomas E1, Tilley P1, Goldman R1,2; 1BC Children Hospital University of British Columbia, Vancouver, BC, Canada; 2; Child & Family Research Institute, Vancouver, BC, Canada; 3BC Children Hospital, Vancouver, BC, Canada.

Purpose of Study: To document the viral etiology of acute wheezing epi-
isodes in young children and to evaluate the virally-induced illness in children with or without predisposition for asthma.

Methods Used: Children 6 to 36 months of age who presented to Emer-
gency 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), para-
influenza, enteroviruses, human rhinovirus (HRV), human metapneumovirus (HMPV), human coronaviruses, adenoviruses and bocavirus. Asthma predis-
position 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%), Bovirus in 13 (13%), Paninfluuenza 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.

270 GERMINAL CENTER T FOLLICULAR HELPER CELLS (GC TFH) FROM NAYE 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-1 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 dis-
sected and 5-10’s 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 CD4, CCR5, 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 X4 and R5 HIV-1. Nevertheless, heightened permissiveness of TFH does
not fully account for levels of productively infected follicular cells in vivo, nor for preferential replication of RSV virus in vivo.

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DETERMINANTS OF ROTAVIRUS-SPECIFIC ANTIBODY RESPONSES TO ORAL VACCINE IN SERUM IN INFANTS

Habernehl GK1, Rahkola IT1, Frank DN2, Janoff EN2. 1University of Colorado School of Medicine, Aurora, CO and 2University of Colorado Anschutz Medical Campus, Aurora, CO.

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 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 2.9 IgG/mL virus, added dilutions of serum (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 (Innvotrogen)/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 IgG and IgA 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 IgA 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 IgG 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 IgG 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

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ARTHROGYROPSIS, RENAL DYSFUNCTION AND CHELOSTASIS (ARC) SYNDROME: A NEW PATIENT CASE REPORT

Brennan M1, Slattery L1, Esplin E2, Enns GM1, Hudgins L1, Manning M1,2. 1St. Jude School of Medicine, Stanford, CA and 2St. John’s University Medical Center, Stanford University Medical Center, Stanford, CA.

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 gene, a conserved region of the VPS33B gene. Missense mutations are rarely seen in this condition. Expression and functional studies are underway to better characterize these findings. This case highlights the multiorgan system involvement in ARC syndrome and helps to further characterize this rare condition.

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NEUROBLASTOMA IN AN INFANT WITH SEVERE ARTHROGYROPSIS: CAN A PARANEOPLASTIC PROCESS CAUSE FETAL AKINESIA?

Clark RD, Bartley JA, Gold J, Merritt TA. Loma Linda University School of Medicine, Loma Linda, CA.

Case Report: A female infant was born to a 32-year-old healthy primigravida at 39 weeks gestation by planned c-section after a pregnancy complicated by diminished fetal movement, polyhydramnios, joint contractures, and large lateral and third ventricles. Birth weight was 2885 grams and APGAR scores were 2,6,9. The baby required mechanical ventilation at birth and later a tracheostomy. A left femur fracture was noted at birth. The face showed micrognathia and a small nose. There was little spontaneous movement of the body or face and joints were rigid. The elbows were fixed in flexion and wrists were dorsiflexed, hands were fisted with adducted thumbs and single palmar creases. Hips were dislocated, flexed initially, later severely abducted, and knees were extended. There were no plantar creases. CK and microarray were normal. Head MRI showed diffuse cerebral and cerebellar atrophy with decreased NAA/Cr and NAA/Cho in basal ganglia and thalami on MRS. 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 MIBG study diagnosed neuroblastoma. Catecholamine levels were slightly elevated. At 2 months of age, she has abnormal persistent vertical eye movements and extreme muscular hypertonia but 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 underreported because neuroblastoma is 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 paraneoplastic myopia die before their tumors are diagnosed. We suggest that neuroblastoma may be an uncommon and under-recognized cause of severe arthrogryposis.

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EXPANDING THE ADAMS-OLIVER SYNDROME PHENOTYPE: A MAJOR ROLE FOR MINOR FEATURES

Esplin ED1, Algaze C2, Lowenthal A2, Tacy T2, Selamet Tierney E2, Hudgins L1, Stanford University Medical Center, Stanford, CA and 2Stanford University Medical Center, Stanford, CA.

Case Report: Adams-Oliver syndrome (AOS) is a rare syndrome characterized by aplasia cutis congenital (ACC) and terminal transverse limb defects (TTLD). We report a male infant with this condition with cutis marmorata telangiectasia congenital (CMTC) and truncus arteriosus (TA), highlighting the wide phenotypic variability of this condition. Born at 39 weeks following an uncomplicated pregnancy the patient was noted to have a very large area of ACC overlying the sagittal suture. Hypoplastic toenails were noted along with mildly shortened 2nd digits of both feet. CMTC was present involving primarily the trunk. CT scan revealed a large midline, sagittal-parasagittal skull defect in the frontal and parietal regions. An echocardiogram demonstrated Type II TA, secundum atrial septal defect and a right aortic arch. The clinical criteria for AOS emphasize the association of ACC and TTLD, each of which can present in a spectrum of severity. Our patient meets these criteria for AOS, having rather severe ACC and subtile TTLD along with the less common features of CMTC and congenital heart disease (CHD) in the form of TA. Review of AOS cases found about 20% of patients exhibiting CMTC and a similar proportion demonstrating CHD. Our case is rare among AOS cases, being among about 7% which
17p11.3 Duplication Revisited: Delineation of the Core and Variant Phenotypes

Carry CJ, Dobyns WB, UC SF/Fresno, Fresno, CA and University of Washington, Seattle, WA.

Purpose of Study: 17p11.3 is a gene rich region 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.

Summary of Results: This is a highly diverse phenotype with inter- and intrafamilial 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, cerebellum, vermis and cranial nerves. 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. The weight 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.

Two Siblings with Adducted Thumb Clubfoot Syndrome (ATCS), A Rare Cause of Distal Arthrogyrosis

Li B, Slavotinek A. UCSF, San Francisco, CA.

Purpose of Study: Reaching an underlying syndrome diagnosis in children with distal arthrogyrosis 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 in the girl was reported to be consistent with a myopathy and a muscle biopsy 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), kyphoscoliosis and neurofibromatosis (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 sclera, 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 arthrogyrosis and that a raised CK measurement can be present in children with this diagnosis.

Understanding growth failure in Costello Syndrome: Increased energy intake and resting energy expenditure

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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, papillomatosa 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 helpful 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.

Handedness 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...
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 primes do not show as strong a bias toward right handedness and some primes 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.

Neonatology – General III Concurrent Session
3:30 PM
Friday, January 25, 2013

UP-REGULATION OF SONIC HEDGEHOG BY FIBROBLAST GROWTH FACTOR: THE ROLE OF TFAP2C, A DOWNSTREAM INTERMEDIATE
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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 ularnization 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.

HEMERYTHROCYTE OXYGENASE ACTIVITY AND HEME BINDING ARE CRITICAL IN EARLY LIFE
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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 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 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 decreases 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. 213-823 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 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.

SENSITIVITY OF THE MESENTERIC ARTERY OF FETAL AND ADULT SHEEP TO NITRIC OXIDE AND LOW MOLECULAR WEIGHT NITROSOTHIOLS
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Purpose of Study: Although necrotizing enterocolitis 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, demucosal of endothelium, and mounted in wire myography baths. Each vessel was exposed to 125 mM 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

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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/6J 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 ANOVAs 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 E15.5 there was no additional fetal loss but the number of viable fetuses significantly decreased at E18.5 compared to E15.5, 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 ± 1.5 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 perforation 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. epidermidis) 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. epidermidis is effective in adults against both methicillin-sensitive and methicillin-resistant S. aureus. Whether newborn infants become colonized with this S. epidermidis subtype and whether this subtype 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. epidermidis 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. epidermidis. Of the 10 swabs obtained 12-24 hours after admission from a referring hospital, 5 (50%) grew S. epidermidis (Relative risk 2.0, 95% CI 1.0-4.0, p=0.04). The 74 discharge swabs processed to date, 61 infants were colonized with S. epidermidis (80.3%), 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 nosoagastic/orogastric tube days and colonization with S. aureus. At discharge, among the 61 infants positive for S. epidermidis, 6 (9.8%) were co-colonized with S. aureus, while among the 13 infants negative for S. epidermidis, 9 (69%) were colonized with S. aureus (Relative risk 7.0, 95% CI 1.4-32.0, p=0.001). The analysis for esp producing S. epidermidis is ongoing.

Conclusions: The nare of NICU infants more commonly become colonized with S. epidermidis 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. epidermidis is protective against colonization with S. aureus.

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 (LKD). 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 dialedyzed 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, Tiets, 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.

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**INFLUENCE OF RACE/ETHNICITY ON INFLAMMATION, METABOLIC SYNDROME AND KIDNEY FUNCTION**

Sinha SK1, Pan D2, Nicholas SB1,2 1,2, Charles R Drew University, Los Angeles, CA and 1UCLA, Los Angeles, CA.

**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.

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**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=3.24-5.80; 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 with the complication, patients with skin ulcers (OR=1.38; 95%CI=1.81-1.62; 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.

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**ABSENCE OF CD2AP RESULTS IN GLOMERULAR HYPERTROPHY, PODOCYTE LOSS AND GLOMERULOSCLEROSIS**

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**Purpose of Study:** Kidney disease is a major health problem with 7% of the world population having some form of the disease. The presence of albuminuria in kidney disease may be related to injury to podocytes and the development of glomerulosclerosis (GS). CD2AP is a scaffolding protein of the podocyte. This study examines the albumin-to-creatinine ratio (ACR) and glomerular structural parameters in the CD2AP knockout (KO) mouse.

**Methods Used:** In CD2AP-deficient mice and wild type controls urine was collected and kidneys harvested at 3, 4, and 5 weeks after birth. The ACR, podocyte number and glomerular volume were measured. GS was graded as present or not present.

**Summary of Results:** At 3-4 and 5-weeks of age the CD2AP KO mice had a significant increase of ACR compared to the wild type mice, p<0.05. Glomerular volume was also increased in the KO mice at all three ages, 148±51x10^3 μm³ vs 85±15±10^3 μm³, p=0.03; 196±62x10^3 μm³ vs 90±17x10^3 μm³, p=0.01; and 274±129x10^3 μm³ vs 119±24x10^3 μm³, p=0.003 respectively. There was no difference in podocyte number between the wild type and the KO mice at 3 and 4 weeks of age. At 5 weeks there was a significant decrease in podocytes 45±20 for KO mice versus 77±12 for controls, p<0.01. GS was only present in the 5-week old KO mice.

**Conclusions:** The absence of CD2AP results in an increase in the ACR and glomerular volume, a decrease in podocyte number and is associated with GS.

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**PROTECTION FROM COLD ISCHEMIA IN HIBERNATING MAMMALS**

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**WILD TYPE**

**CD2AP-KO**
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 C57BL6 mice and hibernating GSs were exposed to CI in UW solution for 72 hrs. Apoptotic RTCs were scored by a pathologist. Immunoblot analysis was conducted for caspase-3, XIAP, pAkt and pBAD. Inhibition of pAkt in GS RTC results in reduced anti-apoptotic pBAD and increased pro-apoptotic caspase-3 expression.

Summary of Results: RTC apoptosis and caspase-3 activity were significantly increased in mouse and GS kidneys. XIP, 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 RTC were treated with cisplatin (50μM), 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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MONOCLONAL ANTI-INTERLEUKIN-6 ANTIBODIES ATTENUATE DONOR-SPECIFIC ANTIBODY RESPONSES IN A MOUSE MODEL OF ALLO-SENSITIZATION

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Purpose of Study: sensitization to HLA antigens is a major barrier to human organ transplantation. As many as 30% of the patients awaiting transplantation in the U.S. are considered highly-HLA sensitized and are unlikely to receive a transplant. Desensitization procedures have emerged to deal with this problem, but can be inconsistent and for some, completely ineffective. Interleukin 6 is a pleiotropic pro-inflammatory and immune regulatory cytokine that impacts the development and maturation of cytotoxic T-cell, B-cell, and antibody producing plasma cells. A monoclonal antibody to the IL-6R (Tocilizumab) was recently FDA approved for treatment of rheumatoid arthritis. Although suggestive data exist, the use of anti-IL-6R for alloantibody suppression has not been established. Here, we report on a mouseized rat-anti-mouse IL-6R (mMR16-1) for attenuating donor-specific antibody (DSA) responses.

Methods Used: C57BL/6 mice were sensitized with skin allograft from a HLA.A2 transgenic mouse, and treated with intraperitoneal injections of mMR16-1 or control antibody. DSA responses were monitored weekly for 5 weeks by measurement of serum anti-HLA.A2 antibodies in a flow cytometric antibody binding assay. In addition, we measured levels of serum amyloid A (SAA) known to be regulated by IL-6 and IL-6R levels and markers of apoptosis in spleens of treated and control animals.

Summary of Results: Results show that mMR16-1 significantly reduced DSA IgM, IgG2a and IgG1 responses, respectively, while normalizing serum amyloid A, (p<0.01 vs. control). mMR16-1 injections increased mononuclear cell apoptosis in the spleens, as detected by annexin V staining and TUNEL. Serum IL-6 & IL-6R levels were elevated in treated animals consistent with observations in humans. In conclusion, anti-IL-6R inhibits de novo DSA responses and suppresses inflammatory markers (SAA).

Conclusions: These observations indicate that the IL-6L-IL6R interactions are important in sensitization and DSA development. Therapies targeting the IL-6/IL-6R pathway may be important in modifying human transplant sensitization leading to better therapies for desensitization and treatment of antibody-mediated rejection.

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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 a 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=5.65; 95%CI=4.70-6.80; p<0.001), cocaine (OR=4.38; 95%CI=3.66-6.27; 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.

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THE INCREASE IN IL-33, CD4 T CELLS AND CXCL1 PRECEDES THE RENAL FAILURE AND TUBULAR INJURY IN A 4 WEEK MODEL OF CISPLATIN-INDUCED ACUTE KIDNEY INJURY (AKI) IN MICE

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Purpose of Study: We have previously described the role of the IL-33/CD4 T cell/CXCL1 axis in a 3 day model of cisplatin-induced AKI. Purpose of study was 1) to measure the IL-33/CD4/CXCL1 system and tubular injury in a model of 4 week, low dose cisplatin-induced AKI in mice and 2) to determine the effect of cisplatin on lung cancer in a model that closely...
Mice were injected with lung cancer cells into the flank. The effect of the injection resulted in the development of lung metastases. The conclusion of the study indicated that patients with ESRD treated with RP and subsequent renal transplant experienced unique urologic complications but demonstrated excellent oncologic and renal functional outcomes. Patients with undetectable ultrasensitive PSA levels, negative margins and low or moderate grade disease may proceed to transplantation after a minimum wait of 6 months following RP. Patients that underwent subsequent renal transplantation were further reviewed to determine oncologic and renal functional outcomes following transplantation.

The increase in IL-33/CXCL1 inhibition on the cisplatin-induced AKI and tubular injury suggested that these proteins may play a causative role in the AKI and tubular injury. IL-33/CXCL1 proteins were increased at 1 week: IL-33 (pg/mg) was 150 in vehicle-treated 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/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.

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OUTCOMES OF KIDNEY TRANSPLANTATION FOLLOWING ROBOTIC PROSTATECTOMY

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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 ultra-sensitive PSA levels, negative margins and low or moderate grade disease may proceed to transplantation after a minimum wait of 6 months following RP. The purpose of this study is to review the outcomes of patients undergoing kidney transplant following RP.

Methods Used: A retrospective review of 15 ESRD 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 ESRD 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 ESRD patient that was completely continent following RALP (> 1 liter of urine per day) became incontinent (2-3 ppd) following transplantation.

Conclusions: Conclusion: Patients with ESRD treated with RP and subsequent renal transplant experienced unique urologic complications but demonstrated excellent oncologic and renal functional outcomes.

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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. Miss staged tumors can cause overtreatment or undertreatment 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 pre-op 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 overstaging cT2 and cT3 patients (37.3% 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 pathologic 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 pathological 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.

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COST ANALYSIS OF COMMON PLASTIC SURGERY PROCEDURES: GEOGRAPHY VERSUS ECONOMICS

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Purpose of Study: Breast augmentation, mastopexy, abdominoplasty, blepharoplasty and rhytidectomy 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 procedure costs 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, real estate rental and 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 hemostast by innovative nitrogen detoxification of microfibrillar chitosan, a biodegradable polyglucosamine polymer that requires depyrogenation 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 hemostast 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 fleeces 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 fleeces to levels acceptable for surgical implantation (~<20 EU/mL).

Conclusions: Proof that our new resorbable hemostast 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 L2-3 and 5 L4-5 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 cannulated 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 a 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.
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.
hypotension. In response to an incident of perioperative hypoglycemia in our institution, this study aimed to undertake a prospective audit of preoperative clear liquid fasting in our pediatric population.

Methods Used: We calculated clear liquid fasting during a one month period in children aged 1-17 years admitted sequentially to our procedure rooms as the time interval between reported time of last liquids and procedure room entry time (N=434). All cases on the elective slate scheduled for general anesthetic that could be accessed were included. Patients fasting from clear liquids longer than twice the recommended time (4 hours) were categorized as over fasted.

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).

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.

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DOCUMENTATION AND RECOGNITION OF ABNORMAL BLOOD PRESSURE IN CHILDREN
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Purpose of Study: Abnormal blood pressure in childhood is associated with continued abnormal blood pressures and increased cardiovascular risk in adulthood. Thus, recognition and control of elevated blood pressure in children is crucial in reducing cardiovascular morbidity over time. The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents states that children 3 years and older should have their blood pressure measured during every health care episode. Our objectives are to determine if blood pressures of children 3 years and older are being routinely measured, if abnormal blood pressures are being recognized, and if abnormal blood pressures are being assessed and managed.

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: Out of 945 patient 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 blood 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.

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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 nongovernmental 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 deworming; 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.

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DECREASED KIDNEY WEIGHT AND GLOMERULAR HYPERTROPHY 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-lead 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% paraformaldehyde 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 (91.7 µg) was significantly less than that of the controls (105.16 µg), p<0.02. The mean kidney weight of the 330 ppm group did not differ significantly from controls. The mean glomerular volume of the 30 ppm exposed mice was significantly greater (86.8±10.7 mm³) than that of the control group (72.6±10.4 mm³), 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.

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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 (SRNS). We compared the sensitivities and specificities of the clinical biomarkers in predicting non-MCD and minimizing unnecessary biopsies in MCD patients.

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.

IMPACT OF VIDEOCONFERENCE ON STRESS IN HOSPITALIZED CHILDREN

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Purpose of Study: Family-Link is a videoconferencing program at the University of California, Davis Children’s Hospital that connects hospitalized children and their families to friends and family 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 stress-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.

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CLINICAL BIOMARKERS OF LONG-TERM OUTCOME IN CONGENITAL URINARY TRACT OBSTRUCTION

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Purpose of Study: Congenital urinary tract obstruction due to posterior urethral valves (PUV) is the most common cause of chronic kidney disease (CKD) in children. Kidney damage occurs in utero, and kidney disease progresses through childhood and adolescence. The prognostic factors that determine the progression of CKD in PUV patients have not been thoroughly investigated. The objective of our study was 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 anterior urethral findings, intruterine 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-Weier analysis was performed to compare outcomes between groups with and without the clinical biomarker.

Summary of Results: The median 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.

Community Health III

Concurrent Session

8:00 AM Saturday, January 26, 2013

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COST-EFFECTIVENESS ANALYSES OF A PEDIATRIC CRITICAL CARE TELEMEDICINE PROGRAM

Yang NH1, Marcin JP1, Yoo B1, Leigh J2, Dharmar M1, *University of California, Davis, Sacramento, CA and 1University of California, Davis, Sacramento, CA.

Purpose of Study: The CRITICAL CARE TELEMEDICINE PROGRAM at UC Davis Children’s Hospital is an innovative telemedicine program that connects critically ill children at rural community hospitals with a pediatric critical care team at the University of California, Davis Children's Hospital. The goals of the program are to improve access to critical care services, reduce transport times, and improve patient outcomes. The program includes a dedicated telemedicine team, a telemedicine laboratory, and a telemedicine cart. The program also includes a telemedicine team that provides on-call critical care services to rural hospitals.

Methods Used: The cost-effectiveness analyses of the CRITICAL CARE TELEMEDICINE PROGRAM were performed using a Markov model. The model included 3 states: hospitalization, home, and death. The model was used to estimate the costs and outcomes of the CRITICAL CARE TELEMEDICINE PROGRAM compared to standard care. The model was used to estimate the costs and outcomes of the CRITICAL CARE TELEMEDICINE PROGRAM compared to standard care. The model was used to estimate the costs and outcomes of the CRITICAL CARE TELEMEDICINE PROGRAM compared to standard care.
Purpose of Study: To evaluate the cost-effectiveness of critical care telemedicine consultations to children presenting with asthma, bronchiolitis, dehydration, fever, and pneumonia to rural emergency departments (EDs), compared to the current standard of telephone consultations.

Methods Used: Model probabilities and the costs of telemedicine deployment were derived from the Telemedicine Program at University of California Davis Children's Hospital. Between 2003 and 2009, telemedicine was deployed to 8 rural EDs. We developed a decision-analytic model to estimate the incremental cost-effectiveness ratio (ICER) from the societal perspective and to compare the costs and effects of the use of telemedicine and telephone consultation among children. We conducted a probabilistic cost-effectiveness analysis for each diagnosis using Monte Carlo Simulation. Hospitalization cost for each diagnosis was derived from 2009 Kid's Inpatient Database. Effectiveness measure was the transfer of children from the ED to a higher critical care center. Unit of ICER was the incremental “cost per transfer avoided.”

Summary of Results: Probabilistic cost-effectiveness analysis (PCEA) showed that the telemedicine dominates telephone, demonstrating that the telemedicine program is more effective and less costly. Base-case analysis: Proportion of children with “avoided” transfer to a higher center of care was 39.4% among the telemedicine group compared to 12.5% among the telephone group, resulting in an effectiveness of telemedicine of 30.7%. PCEA demonstrated cost of each transfer was lower for the telemedicine group than the telephone group by $6,130-$10,385. Given a willingness-to-pay to avoid one transfer of $10,000, telemedicine is preferred (more cost-effective) among 74% to 87% of the cohort. One-way sensitivity analyses showed ICER estimates were sensitive to the probability of transferring a child with telephone consultation and the effectiveness of telemedicine.

Conclusions: Economic evaluation shows that pediatric critical care telemedicine consultations to rural EDs helps to reduce the transfer rate, and is more cost-effective than telephone consultations among children with asthma, bronchiolitis, dehydration, fever, or pneumonia.

SAFETY AND EFFICACY OF THE LEVONORGESTREL-RELEASING INTRAUTERINE SYSTEM IN TRANSPLANT PATIENTS

Nizamic T1, Amies Oelschlager A1,2, Debiec K2,3, Smith J2,3, Micks E1, Prager S1. 1University of Washington, Seattle, WA and 2Seattle Children’s Hospital, Seattle, WA.

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 allograft 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.
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.

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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 violent crime and injury related death. Both of these are influenced by alcohol misuse. Teen and adult drinking are widespread in the community at both private and public 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 overuse. 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.

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SAVE YOUR OWN SKIN: SKIN CANCER PREVENTION AND IDENTIFICATION PROGRAM IN SARATOGA, WY

Wefel M. University of Washington, Seattle, WA.

Purpose of Study: Skin Cancer is a common cancer in the US predominantly caused by Ultraviolet Radiation (UVR) overexposure. UVR overexposure and skin cancer can be prevented using the Ultraviolet Index (UVI), as a daily guide to proper protection, and through routine self-skin checks for suspicious lesions from prior UVR damage. Saratoga is a rural ranching and recreational community with an abundance of outdoor activities that increase the chance for UVR exposure. The bulk of residents in the valley have already been overexposed to UVR, making early protection and identification of lesions important in detecting and preventing skin cancer.

Methods Used: 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 brochures were 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.

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SPECIALTY DISRESPECT AT A PRIMARY CARE SCHOOL: STUDENT PERSPECTIVES

Alston MT, Cawse-Lucas F, Kost A, Hughes LS, Wheeler T. 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 directional impacts of SD on career choice.

Methods Used: The authors used statistical software and univariate analysis to explore survey responses collected between 2008 and 2012, including demographic, quantitative, and free text data. A team of five researchers developed a coding protocol via the immersion crystallization method. Three members then coded the excerpts, resolving coding disparities via consensus.

Summary of Results: 865 students responded to the survey, with 195 providing free text responses. 80.7% of respondents reported experiencing SD in the previous year. 15.1% stated a significant impact on specialty choice, with an additional 15.8% stating a moderate impact. Several themes emerged concerning the occurrence of SD, nature of SD comments, impact of SD, and student responses.

Conclusions: Despite this school’s strong support for primary care, SD occurs with similar prevalence and distribution to other institutions in the literature. Student commentary suggests that a majority of specialties engage in SD, 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.

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PREDICTIVE FACTORS OF 30-DAY READMISSIONS FOR HEART FAILURE PATIENTS

Ambile C, Edgington S, Xu H, Ong M. UCLA, Los Angeles, CA and 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.

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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: Fourteen 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

PHARMACOLOGIC INHIBITION OF NF-kB IN COMBINATION WITH TAXANE-BASED CHEMOTHERAPY FOR TREATING ADVANCED THYROID CANCER
Berklin A, Haugen B, Wood W. University of Colorado School of Medicine, Aurora, CO.
Purpose of Study: Nuclear factor-kB (NF-kB) 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 NF-kB 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). Atpoposis was studied using the Promega 3/7 Caspase Assay kit (24 hours; 0-10 nM docetaxel, 100 nM bortezomib).
Summary of Results: Bortezomib and docetaxel act synergistically to inhibit 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, 50 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.
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.

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BIOCHEMICAL STABILIZATION OF GLUCAGON BY POLYPHENOLS FOR BIHORMONAL CLOSED LOOPS TREATMENT OF TYPE 1 DIABETES

Bakhtiani 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 neurogenerative 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 (TTh), 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 or otherwise rapid spontaneous degradation.

Summary of Results: TTh 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 A630 nm, far from curcumin’s peak absorbance. The results of this assay corroborated the TTh 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 curcumin. Prior studies have shown that acid pH is known to favor rapid fibrillation of glucagon, while a pH of 10 nearly eliminates such fibrillation but instead promotes glucagon degradation. 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.

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PERCEPTIONAL DISPARITIES AFFECT TYPE 2 DIABETES CARE AMONG ZUNI INDIANS

Sulahria AJ, Carroll C, Mals R, Burge MR, Shah V. 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 is a major health concern. Although high-quality medical care and support for adhering to healthy lifestyles can prevent diabetes-related complications, Zunis experience significant barriers to accessing such care and self-management support, and as a result, they suffer more complications, and experience lower quality of life and shorter lifespans, than other Americans. Nevertheless, the role of perceived notions about diabetes care among the Zuni remains unknown. We hypothesize that perceptions about the ease and/ or difficulty of diabetes care will impact clinical measurements of diabetes care effectiveness.

Methods Used: We recruited 59 subjects with previously diagnosed T2D from the Zuni Health Initiative (ZHI). A 110 question survey exploring attitudes, knowledge and perceptions about diabetes was administered to all subjects, and routine clinical analytes were obtained. Completed surveys were 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±2.0% 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.

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RELATIONSHIP BETWEEN TESTOSTERONE AND LIPIDS 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 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 (H, NHW, 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 TT/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 = -0.094,0.02), and BMI increased (β=-0.05 (95% CI =-0.08,-0.02)). 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.
While the precise etiology of DME has yet to be fully elucidated, there is a wide array of factors that may cause and/or exacerbate retinal damage from macular edema. In turn, modifying these risk factors may lead to better outcomes in DME management. As new therapies for persistent DME emerge, it is important to consider these risk factors in the future treatment of diabetic patients.

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**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, triglyceride, 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 total of 8235 patients, with 96% male, were included in the study. 29% of them had CAD, and 10.5% were smoker. Other comorbidities included stroke: 14.3%; diabetes: 41.7%; hypertension: 75%; CHF: 9%. The mean values of BMI, TC, LDL, HDL, TG were 28.4, 164.3, 97.2, 41.5, 128.5 respectively. The mean ratio of TC/HDL and TG/HDL was 4.28 and 3.68. These parameters among the five groups are shown in the table.

**Conclusions:** A previous cohort study of population with ages of 50 to 70 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.

**General Internal Medicine and Aging 1**

**Concurrent Session**

**8:00 AM**

**Saturday, January 26, 2013**

**325**

**ASSOCIATION BETWEEN HIGHER FASTING SERUM GLUCOSE LEVELS AND THE PATTERN OF LOWER REGIONAL GRAY MATTER VOLUMES IN COGNITIVELY NORMAL ADULTS**

Barrett J1,2, Burns C1, Thiyyaguru P3, Li A1, Parks S1, Profas H1, Lee W1, Fleisher A1, Kassnick A1, Chen K1, Reiman EM3,4,5,6 Banner Alzheimer’s Inst, Phoenix, AZ, 2 UA COM, Tucson, AZ, and 3 UA, Tucson, AZ.

**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. Studies have demonstrated lower gray matter volumes in AD-related areas. Additionally, negative correlations between peripheral insulin levels and regional GMV are seen in insulin resistant subjects in the middle temporal gyri, an area associated with verbal fluency and declarative memory. The current study investigated whether elevated fasting glucose (FSG) 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 template to obtain GMV maps from MRI and to examine correlations between higher FSG levels and lower structural MRI GMV measurements in 118 cognitively normal, non-diabetic individuals 64±6 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 gyri confirmed findings seen in insulin resistant subjects. These associations are also seen in AD-related areas in both carriers and non-carriers.

**Conclusions:** Higher FSG 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 fluoroxyglucose positron emission tomography neuroimaging.

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**UTILITY OF FDG-PET IN THE EVALUATION OF LARGE-JOINT OSTEOARTHRITIS**

Kao S, Moreshed M, Patel P, Obruzt S. UC San Diego Health Sciences, LA Jolla, CA.

**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, osseseous metastases, hypercalkemia, 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 ρ = 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 (ρ = 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
Chen K, Egertson J, MacCoss M. University of Washington School of Medicine, Seattle, WA.

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 desired 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%) of detection of covered peptides) and DIA detected 27 (52%). Both indicate that “detectability” is 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
Chan EH1, Nakatsu M2, Deng SX3. 1David Geffen School of Medicine at UCLA, Los Angeles, CA and 2Jules Stein Eye Institute, University of California, Los Angeles, Los Angeles, CA.

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, Dossenheim, 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 destained 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. 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.

INCREASING PRESCRIPTION MEDICATION ADHERENCE AMONG VULNERABLE SENIORS
Simpson TG. University of Washington School of Medicine, Seattle, WA.

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. Incentivity in hosting an educational activity was high, so a site at one 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 SANDPOINT, IDAHO
Lammet K. University of Washington School of Medicine, Seattle, WA.

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

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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

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**GRADED OXYGEN SATURATION TARGETS FOR PREMATURE INFANTS IN RELATION TO OUTCOMES**

Arora V1,2, Cayabyab R1, Durand M1, Ramanathan R1,2. 1LAC+USC Medical Center, Los Angeles, CA and 2Children’s Hospital of Los Angeles, Los Angeles, CA.

**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. Our objective was to determine if graded oxygen saturation targets are feasible and can be differentiated toward a mature podocyte phenotype.

**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. 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.
MATERNAL TOBACCO SMOKE EXPOSURE DIFFERENTIALLY ALTERS CANNABINOID RECEPTOR EXPRESSION IN OFFSPRING RAT ADIPOTISE TISSUE

Trevenzioli I, Chengjie J, Wang Y, Fitzhugh M, Albertine K, Lane RH, Joss-Moore L. University of Utah, Salt Lake City, UT.

Purposes of Study: Fetal exposure to tobacco smoke causes obesity in adult humans and rodents. Obesity development depends in part on signal through the endocannabinoid system (ECS). The ECS consists of types 1 and 2 cannabinoid receptors (CB1 and CB2), fatty acid anandamide hydro-lase (FAAhl) 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 rat offspring at weaning.

Methods Used: Pregnant Sprague Dawley rats were exposed to tobacco smoke daily from embryonic day 11 to term. Pups were crossed-fostered to a control dam. At weaning, male and female 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 control rats, and the expression levels of CB1, CB2 and FAAH mRNA levels of male, female and SAT VAT of female rats (90%*) with no effect on male rats. Cnr1 was unchanged in SAT of both genders. However, MTS decreased CB1 protein abundance in both male and female VAT and SAT (40-45%). MTS did not alter Cnr2 (CB2 gene) mRNA levels in VAT but decreased Cnr2 in SAT of female (85%) and male (95%*) rats. Conversely, MTS increased CB2 protein abundance in both genders and depot (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 in 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.

EFFECTS OF ERYTHROPOIETIN AND DARBOPEOTIN ON HUMAN FETAL NEUROGENESIS

Rossol SL, Malik U, Ohls R, McGonaghy S. University of New Mexico School of Medicine, Albuquerque, NM.

Purpose of Study: Erythropoietin (Epo) and darbepoetin (Darbe) are currently being evaluated for their potential as neuroprotective agents for preterm 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. Cells were also plated in duplicate 6 well tissue culture plates containing 10 U/mL Epo, 1,000 ng/mL Darbe, or no erythropoiesis stimulating factors (ESAs). In separate culture plates, cells were also grown on cover slips, for cell phenotyping. Cells reached 70% or greater confluence in 7 to 10 days. RNA was extracted using Trizol and cover slips fixed with 10% formalin. Fixed cells were stained with fluorescent antibodies to identify mature neurons (Nestin), neuronal progenitors (MAP-2), astrocytes (GFAP), and oligodendrocytes (O-1). RNA was analyzed using real time polymerase chain reaction (RT-PCR) with primers and probes to measure Bcl and EpoR gene expression.

Summary of Results: 90-95% of cells were astrocytic, 3-7% were neuronal progenitors, and 1-2% were mature neurons. Oligodendrocytes were not identified. Cells showed a dose-dependent increase in response to ESAs. Cells grown in 10 U/mL Epo increased cell numbers 10-fold (p<0.0001) and cells grown in 1,000 ng/mL Darbe increase cell numbers 13-fold (p<0.0001) compared to no growth factor. Cells grown in ESAs showed increased Bcl and EpoR gene expression compared to controls.

Conclusions: Mixed fetal neuronal cell cultures showed a dose-dependent increase to ESAs, and gene expression of Bcl and EpoR increased when exposed to erythropoietin or darbepoitin. We speculate that ESAs will exhibit similar neuroprotective properties in vivo.

IN UTERO NICOTINE EXPOSURE MODULATES EXPRESSION OF INFLAMMATORY PROTEINS BY BONE MARROW DERIVED MESENCHYMAL STEM CELL: RELEVANCE TO THE INFLAMMATORY RESPONSE

O’Gorman U, Hussain S, Narvaez V, Torday J, Ibe B, Rehan V. Los Angeles Biomedical Research center @ Harbor-UCLA, Torrance, CA.

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 (BMDMs) are important modulators of diseases processes, including chronic lung and heart diseases. Smoke exposure is known to modulate a variety of stem cell responses including increased platelet activating factor (PAF) 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, ip, or RGZ 3mg/kg, p. Treatments were administered once daily from embryonic day 6 until postnatal day 21 (PND 21). The pups delivered at term and were breast fed ad libitum. At PND21 the pups were sacrificed and BMDMScs were isolated. Cell surface marker analysis (immunostaining and flow-cytometry), PAFR binding (ligand binding assay), and protein expression (Western blotting) were performed at passage 3. Prostacyclin metabolites such as 6-keto-PGF1a, 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 increased 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.

Pulmonary and Critical Care II

 Concurrent Session
8:00 AM Saturday, January 26, 2013

CHRONIC LUNG ALLOGRAFT DYSFUNCTION: DO DISTINCT SPIROMETRIC PHENOTYPES EXIST?

Zhang A, Derhovanessian A, Belperio J, Weigt S. UCLA, Los Angeles, CA.

Purpose of Study: Chronic lung allograft dysfunction (CLAD) is the major limitation to long-term survival after lung transplant. 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,
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FOXP3+ REGULATORY T CELLS CONTROL LYMPHOCYTE IL-10 PRODUCTION AFTER ACUTE PSEUDOMONAS AERUGINOSA INFECTION

Namdaran P, Zhu X, McGuire JK. University of Washington School of Medicine, Seattle, WA.

Purpose of Study: While acute inflammation is an essential component of host defense against lung infection, persistent pulmonary inflammation impairs gas exchange, inhibits epithelial repair, and can potentially put patients at risk of multi-organ dysfunction and death. CD4+FOXP3+ regulatory T cells (Tregs) have been shown to be critical in resolving acute lung inflammation, therefore, we aimed to determine how this lymphocyte population influenced cellular production of anti-inflammatory mediators such as IL-10 in an acute pseudomonas model of lung injury in mice.

Methods Used: Mice expressing diphtheria toxin receptor (DTR) under control of the Foxp3 promoter were infected with P. aeruginosa (PA) to induce acute pneumonia. FOXP3-DTR mice were treated with diphtheria toxin (DT) or complete Foxp3+ Tregs prior to and post PA infection. Bronchoalveolar lavage (BAL) fluid and spleens were collected at 4 days post PA inoculation for analysis of T cell cytokine and cell surface marker expression.

Summary of Results: Flow cytometry for intracellular cytokines revealed that the major cell population expressing IL-10 was CD6+ T cells within BAL fluid and spleens of control animals. CD4+FOXP3+ cells also expressed IL-10, though were few in number. With DT treatment, virtually all FOXP3+ cells were eliminated from spleen and BAL fluid. IL-10 producing CD8+ cells were significantly reduced and mice failed to regain weight compared to control mice. An increased percentage of CD122+ and PD1+ expression was noted on CD8+ cells from BAL fluid in DT-treated mice, further suggesting a role for Tregs in CD8+ T cell differentiation. In corroboriation, when naïve FOXP3-DTR splenic T cells were activated with antiCD3 and PA for 4 days in vitro, samples treated with DT displayed significantly fewer FOXP3+ IL-10+ Tregs. Accordingly, IL-10+ producing CD8+ spleen cells in DT-treated groups were substantially diminished as well.

Conclusions: Our results suggest that FOXP3+ Tregs are critical for suppressing the immune response after PA infection, both in vitro and in vivo, by inducing IL-10 production in CD8+ T cells. Our data further suggest that FOXP3+ Tregs may regulate effector CD8+ T cell differentiation and cell surface molecule expression.

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FLUTICASONE PROPIONATE PHARMACOGENETICS: CYP3A4*22 POLYMORPHISM AND PEDIATRIC ASTHMA CONTROL

Stockmann C1, Fassl B1, Gaedigk R2, Nkoy F1, Uchida D1, Reilly C1, Leeder S2, Yost G1, Ward R1. 1University of Utah Health Sciences Center, Salt Lake City, UT and 2University of Missouri Kansas City, Kansas City, MO.

Purpose of Study: To determine the relationship between allelic variations in genes involved in fluticasone propionate (FP) metabolism and asthma control among asthmatic children managed with inhaled FP.

Methods Used: The relationship between variability in asthma control scores and genetic variation in drug metabolism was assessed by genotyping nine single nucleotide polymorphisms (SNPs) in CYP3A4, CYP3A5, and CYP3A7. Genotype information was compared with asthma control scores (0 = well-controlled to 15 = poorly-controlled), determined by using a questionnaire from the National Heart Lung and Blood Institute Expert Panel 3 guidelines.

Summary of Results: Our study cohort was comprised of 734 asthmatic children (mean age 8.8 ± 4.3 years), which were predominantly male (61%) and non-Hispanic Whites (53%). Four-hundred and thirteen (56%) children were receiving inhaled glucocorticoids daily, of which FP was prescribed most frequently (65%). Among the children receiving daily FP, SNPs in the genes CYP3A4, CYP3A5, and CYP3A7 were not associated with asthma control scores. In contrast, asthma control scores were significantly improved among 20 (7%) children with the CYP3A4*22 allele (median 3, range 0-6), as compared to the 201 patients without the CYP3A4*22 allele (median 4, range 0-15) (P = 0.02).
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 CYP3A4 expression in vitro, was accompanied by improved asthma control among FP treated children. Decreased CYP3A4 activity may improve asthma control with inhaled FP.

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**ROLE OF IGF-1 IN FIBROBLAST COLLAGEN GEL CONTRACTION**

Sather MD, Hung C, Schnapp LM. University of Washington School of Medicine, Seattle, WA.

**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)β1; (v) serum free, cells + IGF-1 + TGFβ1; 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 (98.2±1.9 vs. 97.9±1.9; n=4). There was no significant synergistic effect of IGF-1 and pro-fibrotic cytokine TGFβ1 compared to TGFβ1 alone (93.2±3.3 vs. 94.3±3.7; n=4). As expected, a significant increase in contractility was observed in serum-treated 3T3 cells compared to baseline (86.3±2.2 vs. 97.9±1.9; 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.

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**PROGNOSTIC BIOMARKERS IN PATIENTS WITH DOWNSTAGED PanCREATIC CANCER**

Sunijaya D, Kadera B, Li L, Donahue T. UCLA David Geffen School of Medicine, Los Angeles, CA; UCLA, Los Angeles, CA; UCLA Health System, Los Angeles, CA.

**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. Downstaged 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 is 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.

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**COST SAVINGS OF AN ALGORITHM FOR ALLOCATION OF ENDOCRINE SURGERY PATIENTS TO THE APPROPRIATE MEDICAL FACILITY BASED ON PERI-OPERATIVE RISK STRATIFICATION**

Abdulla AG, Buarte PH, Wiggins R, Harari A, Yeh M. 1 UCLA David Geffen School of Medicine, Los Angeles, CA and 2 UCLA Health System, Los Angeles, CA.

**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 thyroid lobectomy, total thyroidectomy, and parathyroidectomy in each of these settings were collected from the UCLA Medical Center Financial Services department under appropriate IRB approval. The 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 total thyroidectomies, there was a 29% cost savings in the community inpatient facility and a 51% cost savings in the outpatient facility (p < 0.0001). For parathyroidectomies, there was a 7% 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.
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 concentrations in whole brain homogenate and plasma were 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.

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TRENDS IN HOSPITAL COSTS ASSOCIATED WITH ESOPHAGECTOMY FOR CANCER: ESTIMATES FROM THE NATIONALWIDE INPATIENT SAMPLE (2001-2009)
DiPardo BJ, Diggs BS, Dolan JP. Oregon Health & Science University, Portland, OR.

Purpose of Study: The age-adjusted incidence of esophageal adenocarcinoma has increased more than 17-fold since the 1940s and continues to rise. Meanwhile, health expenditure in the United States has also steadily increased; surgical expenditure alone is projected to reach 7.3% of the US GDP by 2025. Esophagectomy is the definitive treatment for esophageal cancer but is a complicated, expensive operation associated with significant morbidity. This study aims to use administrative data from 2001-2009 to examine esophagectomy cost relative both to inflation and to the increasing cost of hospital services.

Methods Used: The Nationwide Inpatient Sample, containing records of approximately 8 million hospital abstracts per year, was searched for patients admitted for cancer-related esophagectomy between 2001 and 2009. Hospital charges for these stays were retrieved, and costs were estimated by applying the aggregate hospital cost-to-charge ratio. Cost data were corrected for inflation by indexing to the 2009 Consumer Price Index (CPI). To evaluate trends with respect to health care costs, esophagectomy costs were also indexed to the 2009 CPI for hospital services.

Summary of Results: Records were retrieved for 33,088 esophagectomies performed between 2001 and 2009. The absolute average cost has increased from $40,288 in 2001 to $55,088 in 2009 (p < 0.001). Correcting for inflation, the increase in cost is not significant. Correcting for hospital services inflation, the average cost decreased from $58,751 in 2001 to $55,131 in 2009 (2009 hospital services inflation-adjusted dollars, p < 0.001).

Conclusions: The cost of esophagectomy is decreasing relative to the inflation in hospital service costs. As this analysis evaluates the cost of entire hospital stays, decreased post-operative morbidity is a possible contribution to this trend. As the incidence rate of esophageal cancer continues to rise, it will become increasingly important to minimize costs, and it is encouraging that esophagectomy cost is decreasing relative to the broader trend in hospital services.

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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 (CECS). 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 IMP in CECS 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 Tukey’s 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 impendence 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.

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FEMALE GENDER PREDICTS POOR OUTCOMES WITH EXTRACOPOREAL MEMBRANE OXYGENATION
Lancaster E, Frank P, Laufer D, Satou N, Tamrat M, Shenm R, Benharash P. David Geffen School of Medicine at UCLA, Los Angeles, CA.

Purpose of Study: It has been established that women have poorer outcomes than men following cardiac surgery. Because of the technological advances and increased use of extracorporeal membrane oxygenation (ECMO), we aimed to evaluate if female gender served as a risk for poor outcomes in ECMO as well. We also describe ECMO usage at our institution and identify additional risk factors and criteria that would optimize ECMO outcomes and provide patient-centered therapy.

Methods Used: We performed a retrospective review of a prospectively maintained institutional database to identify adults requiring ECMO from 2008 to 2011. Risk factors assessed include indication for ECMO, age, gender, days on ECMO, renal failure, BMI, preoperative CHF, and previous myocardial infarction, with survival to discharge as the primary endpoint. Chi squared test was used to determine p values.

Summary of Results: There were 104 instances of ECMO in 94 adult patients (64% male) with indications, demographics, and mortality presented
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.

### MIDTERM OUTCOMES FOLLOWING OPEN AND ENDOVASCULAR REPAIR OF RUPTURED ABDOMINAL AORTIC ANEURYSM

**Forte D, Tran N.** University of Washington School of Medicine, Seattle, WA and University of Washington School of Medicine, Seattle, WA.

**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 hypertension, 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 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 mid-term 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 in 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.

### A MODEL OF COST EFFECTIVE SURGERY IN A RESOURCE POOR SETTING

**Rattray K,1 Gollogly P,2 Tom T.1 University of Washington, Seattle, WA and 1Children’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 Y ears (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 avertin 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.

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**EDUCATING SENIORS ON FALL PREVENTION IN EASTSOUND, WA**

**Senecal C. University of Washington, University Place, 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 group card game was also offered at all lunches.

**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.
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.

Summary of Results:

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. Mean age of patients was 64 years and mean BMI of 2,300 people, 50% of which self-identify as Hispanic. In order to assist Hispanic women with GDM 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 any of those appropriate patients 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

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EDUCATION AND SUPPORT FOR HISPANIC WOMEN WITH GESTATIONAL DIABETES IN BREWSTER, WA

Harms MA. University of Washington School of Medicine, Wenatchee, 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 any of those appropriate patients 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

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COMMUNITY EXERCISE STATIONS TO IMPROVE OBESITY AND PHYSICAL INACTIVITY

Handran C. University of Washington, Seattle, WA

Purpose of Study: Shelbyville is the county seat of Tooele County, has a population of 3,376 and ranks 36th 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 promote 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 exercises were made with community input and tailored for different fitness levels to incorporate on the walking trail. 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.
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 modifying lifestyle choices. 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 diabete s is an important step in ending the intergenerational cycle of obesity and diabetes fueling the current epidemic.

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**SYNTHETIC β-GLUCOGALLIN REDUCES SORBITOL LEVELS IN TRANSGENIC MICE OVEREXPRESSING ALDOSE REDUCTASE IN THE LENS**

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, recent clinical trials of 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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**PAPILLARY THYROID CARCINOMA ARISING IN STRUMA OVARI**

Navabi K1, Bouchonville M1, Burge M1, Jaghfi F1, Spafford M2, Saxon S2, Kapsner P3.1.University of New Mexico Health Sciences Center, Albuquerque, NM and 2.University 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 6×8×5.5 cm with evidence of surrounding lymphadenopathy but no local invasion. Preoperative tumor 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, a rare tumor for which there is a relative scarcity of data guiding appropriate management. 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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**MALIGNANT PHEOCHROMOCYTOMA - A DIAGNOSTIC AND TREATMENT DILEMMA**

Jaghab J1, Navabi K1, Burge M1, Bouchonville M1, Schade D1, Davis M2, Kerr H1, Kapsner P1.1.UNM Health Sciences Center, Albuquerque, NM and 2.UNM 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, 17×22×9 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 pentetetido 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 a 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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**CHRONIC PARATHYROIDIS: A DIAGNOSTIC CONSIDERATION IN THE HYPOCALCEMIC PATIENT FOLLOWING SURGICAL CORRECTION OF PRIMARY HYPERPARATHYROIDISM**

Patel-Trujillo R, Schade D, Kapsner 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 (110-60ng/mL). Other labs included a 24-hour
CONGLERATE PULMONARY FIBROSIS: MICA, SILICA, BOTH OR NEITHER? 15-YEAR FOLLOW UP

Raymond LW. 1 Univ of North Carolina, Chapel Hill, Charlotte, NC and 2 Carolinas HealthCare System, Charlotte, NC.

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%)

Resting arterial PO2 = 79, PCO2 = 40, pH = 7.37, alveolar-arterial oxygen difference = 18.

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.
When used without an additional pressor during the peri-intubation period. The rest were given phenylephrine at different times and with the use of other vasopressors during the hypotensive period. In the 17 patients given phenylephrine in the peri-intubation period, there was an increase in SBP and DBP within 30 minutes of treatment (p<0.01), but did not have a significant change on HR.

**Conclusions:** When used without an additional pressor during the peri-intubation period, phenylephrine improved SBP and DBP, but did not change HR. Overall, there does not seem to be a clear systematic practice concerning the use of phenylephrine in improving hypotension and tachycardia in the peri-intubation period.

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**TOBACCO CESSATION EDUCATION FOR ASIAN/PACIFIC ISLANDERS IN SEATTLE, WA**

Shi M, University of Washington, Seattle, WA.

**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 is 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 community and will be providing further follow up.

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**A THEMATIC ANALYSIS OF HEALTH-RELATED QUALITY OF LIFE IN LUNG TRANSPLANTATION**

Chen J1, Chen H2, Blanc PD3, Leard LE1, Kukreja J1, Singer JP1, 1UC San Francisco, San francisco, CA; 2Genentech, San Francisco, CA and 3UC San Francisco, San francisco, CA.

**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 in 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=22), 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.

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**STANDARDIZED TESTS AND SIMULATORS IN CRITICAL CARE: ARE WE REALLY TESTING THE STUDENT’S APPLIED KNOWLEDGE?**

Lauffer D, Frank P, Lancaster E, Penharash P. UCLA, Los Angeles, CA.

**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’ performance 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 $\leq 30$ WEEKS GESTATIONAL AGE


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 $\leq 30$ 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 $\leq 30$ 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 at five minutes.

Conclusions: We conclude that based on our findings that there was no direct correlation between pH and indicators of respiratory outcome in the NICU. Our study suggests that despite premature delivery, the initial pH obtained on cord blood gas analysis was not significantly associated with neonatal respiratory course. The importance of early umbilical cord gas exchange on long term premature infant respiratory outcomes remains to be determined, and further studies are required to delineate this relationship.

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.

LIGAMENTOGENIC PROPERTIES OF BONE MARROW StromA CELL SEeded PolyCAPROLACTONE SCAFFOLDS IN VIVO

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Purpose of Study: 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 in vivo.

Methods Used: 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 Picosirius Red to further identify the deposition of organized collagen. Cellular infiltration was assessed via cell counting H&E stained knee sections. Additionally, the sections were qualitatively graded for inflammation on a scale of 1-4 (low to high).

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 seeded scaffolds.
Acellular PCL scaffolds exhibited a decreased inflammatory response and increased organized collagen deposition compared to rBMSC seeded scaffolds. The significant inflammatory response induced by rBMSCs calls for a reevaluation of their suitability for ligament engineering.

Conclusions: Acellular PCL scaffolds exhibited a decreased inflammatory response and increased organized collagen deposition compared to rBMSC seeded scaffolds. The significant inflammatory response induced by rBMSCs calls for a reevaluation of their suitability for ligament engineering.

369 COMPLICATIONS AND LONG TERM FOLLOW UP ASSOCIATED WITH ENDOVASCULAR REPAIR OF BLUNT THORACIC AORTIC INJURY

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Purpose of Study: To assess complication rates of endovascular aortic repair, and time frame 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 with-out 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 was 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 ≤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, 2/21 (9.5%) 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 men 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.

370 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 BCCCH between 2000 and 2011 were retrospectively reviewed for quality and searched for prima facie evidence related to our purpose.

Summary of Results: (1) 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 continuity 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.
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, cruciate ligaments, or tectorial membrane has been 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 tectorial membrane. 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 evidence of damage to the apical ligament (28/30), alar ligament (17/20), and tectorial membrane (25/30) was most commonly associated with AOD. Damage to the transverse ligament (11/27), 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 tectorial membrane 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.

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 incidental and non-incidental 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 1.7cm, and were larger than non-incidental RAAs with mean diameter 1.3cm (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/y for non-incidental RAAs (n = 4), and 0.8±0.3 mm/y 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 2.9cm, and were significantly larger than conservatively treated RAAs with a mean diameter of 1.3cm (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/y, 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.

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 right distal radius fracture 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. Rupture 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.

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, after controlling for certain 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 Score 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 0.8 mm/yr, 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.
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 823 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.

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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 (AITF), infratrochlear nerve (ION), and internal maxillary artery (IMA) was more easily attained by the sublabial approach. ION entry to the infraorbital 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 AITF 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 the retromaxillary space in an attempt to access the anterior skull base: a sublabial anterior maxillotomy and endoscopic Denker’s approach. Although tissue was observed on some samples, it may have been due to the experimental conditions, learning how to effectively communicate with patients and by having early exposure to the clinical aspects of medicine.

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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.
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 enrolled 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.

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DEVELOPMENT OF SIMULATION-BASED TRAINING CURRICULUM FOR BASIC MOTOR SKILLS OF ARTHROSCOPIC SURGERY
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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 attending surgeons on the simulator modules.

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A NEW APPROACH TO TEACHING AORTIC CANNULATION
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Purpose of Study: Surgical simulation in 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.

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USE OF AN INTEGRATED NEGATIVE PRESSURE WOUND THERAPY SYSTEM WITH VOLUMETRIC AUTOMATED FLUID INSTILLATION FOR TREATING WOUNDS WITH AN INFECTION: A CASE SERIES
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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-V*) using a less hydrophobic reticulated open-cell foam (ROCF-V*) dressing for use on patients with an infected wound.

A Dacron graft is perfused via a pulsatile pump to simulate an aorta in a live patient.
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 polyoctenamide (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.® Therapy System, V.A.C.® VeraFlo™ Dressing (KCI USA, Inc., San Antonio, TX); [iProntosan® (B.Braun Medical Inc., Bethlehem, PA).

QUANTITATIVE AND QUALITATIVE EVALUATION OF STEM-CELL DERIVED LARYNGEAL MUCOSA REPLACEMENT
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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 restitute 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 gating 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 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 layer 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 0.049 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.

OPEN VERSUS ROBOTIC RADICAL PROSTATECTOMY: FUNCTIONAL AND ONCOLOGICAL OUTCOMES OF ONE SURGEON
Shah S1, Sonn G2, Kwan L2, Whitted L2, Dennis R3, Reiter R2. 1DGSM at UCLA, Corona, CA; 2DGSM at UCLA, 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

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TRPV4-DEFICIENCY INHIBITS APOPTOSIS DURING URINARY TRACT OBSTRUCTION
Hiatt M1, Ivanova L2, Trinka P3, Matsell 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, composed of the collecting duct and distal tubule, is an early and conserved feature in both clinical and experimental occurrences of urinary tract obstruction. However, the process by which injury to the distal nephron is transduced into an epithelial response is not known. Here we demonstrate that TRPV4, a putative mechanosensory cation channel expressed in the distal nephron, is integral to this process.

Methods 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 transduction 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.

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SELF EFFICACY DOES NOT CORRELATE WITH HOURS OF PARTICIPATION IN A DIABETES RISK REDUCTION PROGRAM FOR ADOLESCENTS AND YOUNG ADULTS
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. 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 RxLM. 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 range = 7). Mean self-efficacy score to make healthy food choices was 4.1, SD = 0.6 (possible range = 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=-0.0008, p=0.997.

Conclusions: Overall, students in RxLM 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.

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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 P1, Zappitelli M1, Sabraei V1, Mammen C3, 1BC Children’s Hospital, Vancouver, BC, Canada; 2BC Children’s Hospital, Vancouver, BC, Canada; 3Montreal Children’s Hospital, Montreal, 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 <0.5mL/kg/h for 6h (I); Stage 2: ΔSCR >2 or U/O <0.5mL/kg/h for 24h; Stage 3: ΔSCR >3 or U/O <0.3mL/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 infants and neonates respectively. 

AKIN Severity Distribution of ΔSCR and U/O Criteria

<table>
<thead>
<tr>
<th>AKIN Stage</th>
<th>ΔSCR ≥1.5</th>
<th>U/O &lt;0.5mL/kg/h for 6h</th>
<th>U/O &lt;0.3mL/kg/h for 24h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>19 (8)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>1 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Stage 3</td>
<td>1 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

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infants and neonates respectively. Of 27 AKI patients, only 1 neonate did not fulfill \( \Delta SCr \) criteria; 4/21 (19%) infants and 3/6 (50%) neonates fulfilled U/O criteria. U/O and \( \Delta SCr \) criteria agreement level was poor (\( k = 0.139, 95\% CI = 0.014 \) to 0.293).

**Conclusions:** Most AKI is captured by \( \Delta SCr \) criteria. There is poor agreement between \( \Delta SCr \) 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.

**EFFECTIVENESS OF A MULTIDISCIPLINARY TERTIARY WEIGHT MANAGEMENT CLINIC AT IMPROVING BODY MASS INDEXES AND BLOOD PRESSURES AMONG MORBIDLY OBESE PEDIATRIC PATIENTS**

Thang CK\(^1\), Whitley M\(^2\), Izadpanah N\(^3\), DeUgarte D\(^4\), Slusser W\(^5\). \(^1\)David Geffen School of Medicine at UCLA, Los Angeles, CA; \(^2\)University of California Los Angeles, Los Angeles, CA; \(^3\)Children's Hospital 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 dietitian, 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 BMI across all patients with an average BMI percentile decrease of 10.0% 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.

**BUILDING A CLINICAL PATHWAY FOR CHILDHOOD NEPHROTIC SYNDROME**

Jobas JI, Mammen C, AlShami A, Sibley M, Matsell D. BC 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 pediatricians.

**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 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.

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**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 increase 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 blood pressure, use of antihypertension 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 (CAGV) 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=0.007) 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 CAGV, and NF-MACE were not significantly different. Once patients (pts) are off CNIs there should be benefit in these metabolic parameters.

**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, CAGV, 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>
<thead>
<tr>
<th>Outcomes</th>
<th>No PGD (n = 1,314)</th>
<th>PGD (n = 45)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<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>
</tr>
<tr>
<td>1-Year Freedom from Any-Treated Rejection</td>
<td>83%</td>
<td>94%</td>
<td>0.712</td>
</tr>
</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 arterial/venous 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 JA, Woelkers D1, Patino C2. 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 uteroplacental perfusion, which is relieved by left or right lateral tilt. This is ascribed to reduced maternal cardiac output, 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, Cardiotronics, 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 blood 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 tilts 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 trends toward improved cardiac output for obese patients in right tilt as compared to left or supine.
and blistering, which considers the variety of sensitivities seen in generalized psoriasis patients as compared to the initial protocol made for recalcitrant, localized plaque psoriasis.

399 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 (MHP) 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 excoriation.

Summary of Results: Patients with DOP are extremely challenging patients to treat and can often be frustrating to the physician. Though therapist interventions are generally associated 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.

400 ASSOCIATION OF SPIROCHETAL INFECTION WITH MORGELLONS DISEASE

Middelveen MJ, Poruri A2, Mayne P3, Sapi E1, Kahn DG, Stricker RB1.

1Atkins Veterinary Services, Calgary, AB, Canada; 2University of New Haven, West Haven, CT; 3Laurention Medical Centre, Laurieton, NSW, Australia; 4Olive View-UCLA Medical Center, Sylmar, CA; 5California 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 using 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.

401 DO PATTERNS OF ALCOHOL USE DIFFER AMONG CLINICAL SITES USING THE ALCOHOL USE DISORDERS IDENTIFICATION TEST?

Paskish 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 for 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=0.5799). 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.

402 INCIDENCE AND SEVERITY OF MUSCULOSKELETAL INJURIES IN RURAL OVERWEIGHT AND OBESE PEDIATRICS IN IDAHO

Croschere TM1,2, Seegmiller J3, Paul D3. University of New Mexico School of Medicine, Santa Fe, NM.

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 sustain an 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, and females were more likely to sustain an injury 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).

Health Care Research III
Concurrent Session

11:00 AM Saturday, January 26, 2013

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THE EFFECT OF PROTON PUMP INHIBITORS ON GLYCEMIC CONTROL IN PATIENTS WITH TYPE 2 DIABETES

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Purpose of Study: Purpose of the study was to replicate previous studies and evaluate the effect of PPIs on glycemic control in patients with type 2 diabetes by comparing A1C values to a similar group of patients with type 2 diabetes not using a PPI.

Methods Used: Methods Used: This study was a retrospective multicenter electronic data analysis using data obtained from healthcare facilities within Veterans Integrated Service Network (VISN) 21. VA patients were included if they had established care within VISN 21 and had type 2 diabetes with an A1C > 6.5%, were using a PPI concurrently with stable doses of metformin or sulfonylurea monotherapy, had more than one prescription fill for metformin, sulfonylurea or a PPI, had at least two documented A1C values, and a medication possession ration (MPR) > 80% for metformin, sulfonylurea or a PPI. Veterans were excluded if they were using insulin, combination anti-hyperglycemic therapy, or oral corticosteroids. We also looked for differences in pre- and post-BMI, serum potassium, or use of other medications known to affect glycemic control between the treatment and control groups.

Summary of Results: Summary of Results: A total of 195 patients were in the treatment group and 2,330 patients were in the control group for the final analysis. There were no significant differences in baseline characteristics between the treatment and control groups. There was a statistically significant decrease in A1C within each group. However, there was no statistically significant difference between the treatment and control group in the post-A1C. There were no significant differences in pre- and post-BMI, serum potassium, or use of other medications known to affect glycemic control between the treatment and control groups.

Conclusions: Conclusion: In patients with type 2 diabetes, A1C improved in both groups but PPI addition did not affect glycemic control. Future randomized controlled trials are needed to determine the value of PPIs as a treatment option for patients with type 2 diabetes.

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POSTTRAUMATIC STRESS DISORDER, MILITARY SEXUAL TRAUMA AND PRETERM BIRTH

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Purpose of Study: Preterm birth is a leading cause of infant morbidity and mortality, yet remains poorly understood. Maternal stress and depression are increasingly recognized as risk factors for poor birth outcomes, but the effect of traumatic stress is less studied. As a growing number of reproductive-age females return from military service, 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: Methods Used: 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 maternal sexual trauma (MST) screening data, deployment (to Afghanistan/Iraq), demographics, and co-morbidities.

Summary of Results: Summary of Results: 13,643 births were analyzed. 2,248 (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: 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 (≥35).

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ADHERENCE TO CERVICAL CANCER SCREENING GUIDELINES BY GYNECOLOGISTS IN THE PACIFIC NORTHWEST

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Purpose of Study: 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: 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: 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% vs 8.0%, p=0.01) 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: 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.

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BARRIERS TO RECOGNITION OF CARDIAC ARREST AND DELIVERY OF CARDIOPULMONARY RESUSCITATION INSTRUCTIONS OVER THE TELEPHONE BY EMERGENCY DISPATCHERS

Lewis MM1, Stubbs B2, Eisenberg M1,2. 1University of Washington School of Medicine, Seattle, WA and 2King County Public Health, Seattle, WA.

Purpose of Study: In order to assess how UCLA internists perceive readmissions, we conducted a survey of perceptions on readmission rates, which will help health systems determine the best practices necessary to reduce future hospital readmissions.

Methods Used: We surveyed all hospitalists in the UCLA IM department. After creating an online survey using Google Documents, we administered the survey to all hospitalists in the UCLA IM department.

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.

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THE ROLE OF CHILD LIFE SPECIALISTS AS A HEALTH CARE TEAM MEMBER DURING INVASIVE PROCEDURES IN A PEDIATRIC EMERGENCY DEPARTMENT

Holland J1, Kim J2, Lascelle A3, Hart D2, Duffy D3, Goldman R1, 1University of British Columbia, Vancouver, BC, Canada; 2BC Children’s Hospital, Vancouver, BC, Canada; 3BC Children’s Hospital, Vancouver, BC, Canada; 4University of British Columbia, Vancouver, BC, Canada.

Purpose of Study: The role of child life specialists (CLS) has grown to include a variety of responsibilities in many 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 minor 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. Patients were asked to participate in the study at the time of their ED visit. Consent was obtained by the child life specialist and all families provided written consent.

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 for minor procedures were as follows: (1) 87 ± 18; 92 ± 10, (2) 90 ± 15; 90 ± 16, (3) 82 ± 22; 92 ± 13, (4) 88 ± 16; 96 ± 6, (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.

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THE PERCEPTIONS AND ATTITUDES OF INTERNS, RESIDENTS, AND ATTENDING TOWARDS READMISSIONS


Purpose of Study: The purpose of the survey is to determine physicians’ perceptions on readmission rates, which will help health systems determine the best practices necessary to reduce future hospital readmissions.

Methods Used: In order to assess how UCLA internists 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.

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

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SUBCELLULAR LOCALIZATION OF PIDI, A NEW TUMOR SUPPRESSOR-LIKE PROTEIN IN BRAIN TUMORS

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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 (PIDI) in a number of brain cancers including AT/RT. PIDI 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 PIDI-GFP fusion proteins reside in the cytoplasm, in silico analysis reveals that PIDI harbors a putative nuclear
export signal. This suggests that PDI1 localization is regulated between nuclear and cytoplasmic compartments, which may have consequences for cell fate. The aim of this study was to determine the localization of PDI1 in brain cancer cell lines.

**Methods Used:** We visualized endogenous PDI1 localization using indirect immunofluorescence confocal microscopy in three brain tumor cell lines: CHLA-06-ATRT primary ATRT cells and U251 and LN229 glioblastoma multiforme (GBM) cell lines. We also performed subcellular fractionation of the same cells and resolved them by SDS-PAGE and western blotting to determine the localization of PDI1 in specific compartments.

**Summary of Results:** Confocal microscopy revealed predominant cytoplasmic PDI1 localization in a peri-nuclear distribution. In all cell lines tested, there was also evidence of nuclear PDI1 observed on the orthogonal views of X, Y, and Z axes. Subcellular fractionation demonstrated PDI1 compartmentalized primarily to the cytoplasmic and membrane-bound fractions.

**Conclusions:** PDI1 represents a signaling molecule with tumor-inhibitory behavior that provides new insights in both pediatric and adult brain tumors. We report that PDI1 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 PDI1 function may have implications for our understanding of brain cancer and may help devise more effective treatment strategies for these highly malignant tumors.

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**RETRIESSIVE ANALYSIS OF ADULT HEAD AND NECK SARCOMA: A SINGLE-CENTER EXPERIENCE FROM 2000-2012**

Chang A, Chai X, Futrau N, Jones R. 1 University of Washington, Seattle, WA and 2 Fred 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 comprise only about 5% 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). Adult patients with primary tumors above the clavicle were included in this study. Retrospective data were collected by chart review of the Social Security Death Index, dates of death were obtained from patient records or by search of the Social Security Death Index. Summary statistics, univariate analysis and Kaplan-Meier survival analysis was performed with predetermined level of significance of p<0.05. The median overall survival was 6.79 years with two-year rate and five-year OS rate of 75% (95% CI: 59%-83%) and 60% (95% CI: 44%-73%), respectively. Univariate analysis of the age at diagnosis, treatment, tumor size, surgery, sarcoma margin status, and other historical data was used to identify possible predictors of DFS or OS.

**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.

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**UNRULING THE MECHANISM OF A NOVEL TRANSCRIPTION ACTIVATION DOMAIN**

Robbins H2, Hahn S1. 1University of Washington School of Medicine, Seattle, WA and 2Fred 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 BDs, 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. Alani 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.
CHARACTERIZATION OF PROSTATE CANCER ON MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING: CORRELATION WITH HISTOPATHOLOGY

Beroukhim K, Tan N, Khin H, Lu DY, Margolis DJ, Reiter RE, Raman SS. UCLA David Geffen School of Medicine, Los Angeles, CA; "UCLA David Geffen School of Medicine, Los Angeles, CA and "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 histopathologic 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: .698 cm; Detected Tumors: 1.743 cm. Gleason Scores: Missed Tumors: 32 with Gleason Score 6; Detected 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 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.

DO THE EYES HAVE IT? APRAXIA & OCULOMOTOR CONTROL IN AUTISM

Miller M, Chukoskie L, Townsend J, Trauner D. University of California, San Diego, El Cajon, CA.

Purpose of Study: Autism research has demonstrated specific deficits in gross motor, fine motor, gait, balance, motor planning and motor coordination, but little research has investigated oculomotor functioning. The data are inconsistent, however several studies have suggested that individuals with Autism Spectrum Disorder (ASD) struggle to imitate timely and accurate saccades.

Many children with ASD also have difficulty performing learned, skilled movements (apraxia). Studies have repeatedly shown a negative correlation between basic motor function and apraxia, however, the association between oculomotor function and apraxia is unknown.

The current study had two hypotheses: that the ASD group would show significant differences from a typically developing control group (TD) in saccade parameters, such as latency and accuracy; and that more severe apraxia would be associated with poorer saccadic control in both the ASD and TD groups.

Methods Used: 40 adolescents age 8-15 (20 ASD and 20 age and performance IQ matched TD) were tested with a battery of standardized tests including the Beery VMI and VMI supplemental tests of Visual Perception and Motor Coordination. Tests measuring IQ and social development were also administered. Saccade parameters were tested with a simple, single target paradigm and measured with the Eyelink 1000 remote eye-tracking system. Apraxia was assessed with a 30-item test designed to evaluate specific subtypes of apraxia as well as basic motor function.

Summary of Results: The ASD group showed increased saccadic latency and decreased accuracy when compared with the TD group. The ASD group also showed deficits on the Beery VMI and Motor Coordination tests and in tests of ideational apraxia. No differences were found in Visual Perception. Finally, ideational apraxia was negatively correlated with saccadic control as well as with measures of social skill.

Conclusions: Deficits in control of eye movements and the association of these deficits with apraxia suggest that eye movement deficits in ASD may reflect a generalized praxic deficit, similar to that previously shown in other components of the motor system. The concurrent association of apraxia with tests of social skills suggests that praxic impairments may contribute to the development of the social deficits that are central to ASD.

HYPOXIA-INDUCED MODIFICATION OF DNA METHYLATION IN HIPPOCAMPAL NEURONAL CELLS

Elkhoury F, Hartley I, Gu X, Poulsen O, Zhou D, Haddad G. University of California, San Diego, La Jolla, CA.

Purpose of Study: While the effects of hypoxia on gene expression have been investigated to some extent in the CNS, we currently do not know what role epigenetics plays in the transcription of many genes during such hypoxic stress. To start understanding the role of epigenetic changes during hypoxia, we investigated 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% O2, 5% CO2 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 stimulus. On Day 7, Methyl-Sensitive Cut Counting (MSCC) 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.

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.

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