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Caloric Restriction and Dietary Curcumin Improve Functional Outcomes of Aging in Mice

Curcumin, from Curcuma Longa, has antioxidant and anti-inflammatory effects that are hypothesized to benefit impaired functional capacity related to normal aging. The following results are from an ongoing study of dietary curcumin alone and in combination with caloric restriction, testing functional and biochemical outcomes in late middle age (MAG) (15 months) and senescent (AG) (20 months) C57BL/6j male and female mice. Mice were assigned in treatment groups to receive: (i) base diet ad libitum (AL), (ii) weight stable caloric restriction (CR), (iii) curcumin in the base diet (7200 mg/kg diet) (CURAL) or (iv) curcumin plus CR (CURCR). At 8 weeks of treatment, all mice were tested for spatial memory and cognitive flexibility. Cognitive flexibility, tested using a serial reversal task, was significantly better for MAG males under CR and CURAL compared to AL but not under CURCR, suggesting an antagonistic interaction. On the other hand, MAG and AG female experimental groups did significantly better than AL. No interaction of CR and CUR was observed in AG males, with CURAL and CR yielding comparable benefits. None of the treatments had a significant effect on hippocampus-dependent spatial memory performance in MAG or AG. These results suggest that when implemented separately, both CR and CUR treatments have an ameliorative effect on impaired frontal cortical function present in late middle age and senescence. These effects were similar across different behavioral tasks and were non-interactive or antagonistic, suggesting that they could involve the same or similar mechanisms. Therefore, curcumin intake may mimic the effect of CR in the absence of diminished energy intake and weight loss.

Determining the Viability of Biomarkers for Oxidative Stress Detection in Clinically Afflicted Cohorts

Intro: In the US, there are more than 5 million Americans living with Alzheimer’s disease (AD) and approximately 500,000 more are suffering from Parkinson’s disease (PD). Oxidative stress (OS) and its deregulation of reactive oxygen species (ROS) have been implicated as a component of neurodegenerative diseases. Accumulation of ROS is accountable for increasing mitochondrial dysfunction that leads to neuronal apoptosis. In addition to ROS accumulation, OS can result in a number of cellular by-products such as Malondialdehyde (MDA), 8-isoprostane, and Advanced Oxidation Protein Products (AOPP). Recent studies also suggest that high levels of testosterone can depress cellular resistance to oxidative stress.

Purpose: The objective of this research is to determine the viability of laboratory assays as a detection tool for the evaluation of neurodegenerative diseases in aging males. Methods: 352 clinical plasma samples from the Texas Alzheimer’s Research and Care Consortium were used in assay evaluation. The samples were collected from either Caucasian or Hispanic males and evaluated based on 6 previously determined disease statuses. The AOPP Assay was used to detect chlorinated oxidation of plasma proteins. For AOPP, plasma samples were performed with a 1:7 dilution factor. Following preparation, the samples were then plated in duplicates and read at an absorbance of 340nm. To correlate with a previous testosterone study, a Testosterone ELISA was conducted with the use of Rabbit Anti-Free T-Antibody without sample dilution. Once plated, the samples were incubated for 60 minutes, washed, and read at an absorbance of 450nm. MDA can be accounted for in OS-resultant lipid peroxidation (LP), MDA levels in the clinical samples were examined using a Colorimetric TBARS Assay. The assay subjected the samples to boiling, centrifuging, and incubation in an ice bath. The supernatant was then removed, plated, and read at an absorbance of 532nm.

Results: The absorbance reading from the AOPP assay and Colorimetric TBARS assay, yielded similar results across all six-disease statuses. Despite the differences in disease status, samples were determined to have triple the amount of MDA concentration compared to the control. Conclusion: The similarity in values and discrepancy from the control indicates that AOPP and TBARS cannot accurately determine OS in banked plasma samples. T-ELISA is currently undergoing further scrutiny with the use of mass spectrometry.
Epigenetic alterations in Brain tissue and Alzheimer’s Disease

Background: Epigenetic factors such as methylation of DNA have shown to impact the phenotype of a cell and irregular methylation of DNA has been correlated with numerous diseases. DNA methylation has been shown to impact the expression of certain genes associated with AD.

Methods: A novel method, methylated DNA immunoprecipitation (MeDIP), is used to study genome wide methylation patterns via high throughput sequencing to assess DNA methylation patterns in brain tissue from individuals diagnosed with AD (N=12) and age matched controls (N=12). MeDIP isolation facilitates an unbiased methylation analysis of the entire human genome by enriching samples for methylated DNA fragments. The MethylMiner kit (Life Technologies) was utilized to precipitate methylated DNA, which was sequenced on the Illumina Hi-seq 2500. In addition, another aliquot will undergo MeDIP and bisulfite treatment. This will allow analysis of methylated cytosines at single base pair resolution across the entire genome. In addition, RNA and miRNA-seq was performed on the Illumina Hi-seq 2500. RNA-seq information obtained provides additional insight on epigenetic impacts on miRNA and RNA levels. Results: Sequence data reveal a genome wide methylation pattern profile, along with gene expression changes that differentiate case from control participants. Conclusions: These data provide insight and help explain a portion of the missing heritability that has yet to be characterized for AD.

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IRB/IACUC# UNTHSC IRB Protocol # 2007—137.

HDL and Cognitive Function in Older Adults: A Systematic Review

PURPOSE: The objective of this systematic review was to address the question, “Is High Density Lipoprotein-cholesterol (HDL-C or HDL) related to cognitive function in older adults?”

MATERIALS AND METHODS: This systematic review included 17 primary research articles: 8 cross-sectional studies and 9 prospective studies that assess the relationship between HDL and cognitive function in older adults. The search for articles was conducted in July 2014 using online library resources at the UNT Health Science Center. The criteria for selection included (1) primary research articles that reported (2) a measure for HDL-C and (3) at least one measure for cognitive function (4) in older adults. Data was extracted using an individual article review form that assessed the research level, quality, and results for each article. Determination of the evidence base rating was based on the results across articles.

RESULTS: The evidence base for the 8 cross-sectional studies did not support a relationship between HDL and cognitive function. However, these articles also did not address a change in cognitive function over time. The evidence from 9 prospective studies did support a relationship between HDL and cognitive function. Six of 9 studies reported baseline HDL levels significantly related to cognitive function. Five studies of 9 demonstrated a relationship between memory and HDL, and controlled for other influential factors, over a time range of 4-7 years. Another study demonstrated a relationship between HDL and language/sensory/motor functions at 16 years. The 4 studies that did not find significant relations had follow-up time periods of 3 years (2 studies), 12 years and 16 years, indicating that relations may be most evident within a limited window of time, and may vary by domain of cognitive function.

CONCLUSIONS: The evidence base for prospective studies indicates a significant relationship between HDL and cognitive function. The results also suggest that some cognitive measures may not be equally informative across populations and/or languages. Future research studies should be a minimum of 4-years and extend beyond 16 years, with uniform sampling intervals. Additionally, future studies should control for domains of cognitive function, known factors that influence HDL-C, employ consistent sample and data collection processes, and include diverse populations.

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Impact of Hypertension, Diabetes, and Dyslipidemia Comorbidity on Cognition among Hispanic Mexican Americans: An HABLE Study

Background: Hypertension, hyperlipidemia, and diabetes mellitus are medical diagnoses that occur at high prevalence rates among the Hispanic Mexican American population. Current research shows that each individual diagnosis is linked to cognitive decline, but this assertion is limited in that these studies have been conducted on Non-Hispanic White populations only. Additionally, an insignificant number of studies have investigated the comorbidity of these diagnoses, and how that may impact risk for cognitive impairment. This study seeks to fill this gap in the literature by determining the association between combinations of these diagnoses and cognitive functioning within a Hispanic Mexican-American population.

Methods: Data were analyzed from 537 Mexican American participants who met diagnostic criteria for hypertension, dyslipidemia, and diabetes mellitus (Group 1, one diagnosis, n = 148; Group 2, two diagnoses, n=219; Group 3, three diagnoses, n=170) from the Health and Aging Brain study among Latino Elders (HABLE). Information from each participant was obtained via clinical interview (including medical history, current medications, and health behaviors), informant interview, neuropsychological testing, blood draw, and physical examination. Consensus reviews were conducted weekly to review subject data, and to establish cognitive and medical diagnoses according to national guidelines. Linear regressions analyses were utilized to examine cognitive functioning, measured through the domains of memory and verbal fluency as the dependent variable, with the independent variable consisting of the number of medical diagnoses (one, two, or three). Covariates included age, gender, and education.

Results: Those in Group 1 displayed poorer performance on measures of immediate (B[SE]= -2.66[1.05], t-test = -2.52, p-value=0.012) and delayed (B[SE]= -1.59[0.77], t-test= -2.04, p-value= 0.041) memory. Differentially, those in Group 2 showed poorer performance on tasks related to verbal fluency (B[SE]=2.33[0.80], t-test=- 2.88, p-value=0.004) and working memory (B[SE]= 0.59[0.24], t-test=2.42, p-value=0.016). Group 3, which encompassed all three medical diagnoses, was not significantly related to any of the cognitive domains that were examined.

Conclusion: These findings suggest that within the Hispanic Mexican American population, domains of cognitive functioning are differentially affected within each group, with Group 3 showing no significant increased risk for cognitive dysfunction. These findings do not support current research, which suggests a higher and more invariable prevalence of cognitive decline, regardless of the comorbidity of these diagnoses. Additional research is needed to investigate the neurological effects of the biological pathways associated with the varying combination of diseases, which may explain the dissimilarity in associated cognitive function.

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IRB/IACUC# 2012-083

p38 acts as an activator of presenilin 1 in the brain of alcoholic rats.

Purpose: Presenilin 1 (PS1) is originally known as a major protein of which mutation is responsible for age-associated brain disorders such as Alzheimer disease. In addition to this property, interaction between PS1 and other proteins has been reported to mediate various brain damages. Our previous studies have demonstrated that repeated exposure to and withdrawal from a high dose of ethanol provokes the over expression of a stress-activated protein kinase p38 in the rat brains. Here, we investigated whether p38 is an upstream activator of PS1 in a manner that impedes cerebellar-related motoric performance. We also investigated whether p38-PS1 link mediates an excitotoxic stress induced by repeated ethanol exposure and withdrawal.

Methods: We employed transgenic mice (p38-KO) lacking p38 in cerebellar neurons and tested motoric performance using Rotarod where a shorter time to fall from rotating apparatus indicates poorer cerebellar function. After Rotarod test, mice were subjected to measure PS1 protein and mRNA level in cerebellum using immunoblot and q-PCR. Separately, young adult male rats (alcoholic rats) received an ethanol program, consisting of 4-week-ethanol diet and 3-week-withdrawal per cycle for two cycles. At the end of the diet program, the rats were tested for Rotarod performance and then cerebellum was used to measure PS1 level. Finally, HT22 (mouse hippocampal) cells were exposed to glutamate with or without a p38 inhibitor to measure PS1 level.

Results: P38-KO mice were opposite to alcoholic rats in that they showed a decrease and an increase in the level of PS1 protein and mRNA, accompanied by a superior and inferior motoric performance, respectively. Glutamate treatment increased PS1 level in a manner that is attenuated by a p38 inhibitor.

Conclusions: These results suggest that p38 activates PS1, contributing to cerebellar deficit of alcoholic rats. They also suggest that p38-PS1 link is readily formed under a hyperexcitatory stress.

Sponsor IAADR
IRB/IACUC# 2012/13-A04/05, 2009.10-08
Results: We found that baseline overall depression (GDS30) was not significantly related to cognitive decline. Specific depressive symptoms were significantly related to cognitive decline, but there were different effects in men and women. Apathy was correlated with increased cognitive decline in men only (p < 0.05).

Methods: We conducted linear regression analysis to determine if baseline depression or depressive symptoms influenced the rate of age-related cognitive decline. Data analyzed were from 634 male and 934 female elderly white, non-Hispanic participants in the Texas Alzheimer’s Disease Research and Care Consortium. Participants included cognitively normal controls (733), subjects with mild cognitive impairment (243) and subjects with Alzheimer’s disease (592). Baseline depression was estimated using Geriatric Depression Scale (GDS30) scores. Baseline depressive symptoms of depression, influences the rate of cognitive decline.

Objectives: Depression and cognitive decline have a complex relationship. The purpose of our study was to determine if depression, or specific symptoms of depression, influences the rate of cognitive decline.

Methods: We conducted linear regression analysis to determine if baseline depression or depressive symptoms influenced the rate of age-related cognitive decline. Data analyzed were from 634 male and 934 female elderly white, non-Hispanic participants in the Texas Alzheimer’s Research and Care Consortium. Participants included cognitively normal controls (733), subjects with mild cognitive impairment (243) and subjects with Alzheimer’s disease (592). Baseline depression was estimated using Geriatric Depression Scale (GDS30) scores. Baseline depressive symptoms included apathy and agitation, as measured in the Neuropsychiatric Inventory Questionnaire (NPI-Q). Cognitive decline was measured by a change in Clinical Dementia Rating (CDR) scores between visits 1 and 3. In these analyses we stratified based on gender and adjusted for age at first visit and education.

Results: We found that baseline overall depression (GDS30) was not significantly related to cognitive decline. Specific depressive symptoms were significantly related to cognitive decline, but there were different effects in men and women. Apathy was correlated with increased cognitive decline in men only (p < 0.05).

Conclusions: Depressive symptoms appear to increase the rate of cognitive decline and may be early signs for neurodegeneration. These symptoms may also be important targets for therapeutics designed to treat, or slow the progression of Alzheimer’s disease. However, the relationship is not simple, as indicated by the divergent results observed in males and females. Further research in this area is warranted; while there are currently no proven treatments for Alzheimer’s disease, depression and depressive symptoms are therapeutically modifiable.

Sponsor: TARCC
IRB/IACUC#: 2007-137

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Pyruvate induction of Nrf2/ARE-regulated Glyoxalase1 and Glutathione Reductase in porcine brain post-cardiac arrest: enhanced methylglyoxal detoxification

Background: After cardiac arrest (CA) and cardio—cerebral resuscitation (CCR), enhanced glycolysis elevates toxic carbonyl methylglyoxal (MG) that contributes to reactive oxidative/nitrosative stress (RONS), enzyme inactivation and death of neurons and astroglia. Post cardiac arrest cognitive deficits may be prevented by pyruvate infusions that boost glyoxalase 1 (GLO1) detoxification of MG and glutathione (GSH) synthesis by glutathione reductase (GR) via Nrf2/ARE (antioxidant response element)—regulated Phase II gene expression.

Hypothesis: Pyruvate—induced cytoprotective mechanisms can curtail brain injury and cognitive deficit after cardiac arrest and resuscitation in pigs.

Methods: Compared to sham non-arrest animals, pigs were subjected to CA/CCR, infused with either 4 mM pyruvate or NaCl for one hour, recovered 4 hours prior to sacrifice. Post-mortem frontal cortical lysates were assayed for Nrf2/ARE binding activity, GLO1, GR, and GAPDH (rate—limiting for MG production) activity, while plasma glutamate concentrations were measured.

Results: Compared with saline controls, pyruvate infused pigs demonstrated increased Nrf2/ARE binding activity (Fig 1) and 3—fold higher GLO1 activity (Fig 2) supporting MG detoxification, while GR (Fig 3) and GAPDH (Fig 4) were similarly stimulated. Plasma glutamate concentrations were reduced by pyruvate (Fig 5), which would support greater brain clearance of excitotoxic glutamate, according to the brain—to—blood glutamate efflux hypothesis.

Conclusions: Intravenous pyruvate induces Nrf2—regulated gene activation for augmented GR, and GLO1 biological activity via mechanisms that may lower glutamate—inflicted excitotoxicity and heretofore untreatable cognitive deficits of post—CA/CCR brain injury. Thus pyruvate infusion may also provide therapeutic benefit for several neurodegenerative disorders of similar etiology.

Sponsor: NINDS
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Poster: M. Andrew Ford
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Relationship between Depressive Symptoms and Cognitive Decline

Objectives: Depression and cognitive decline have a complex relationship. The purpose of our study was to determine if depression, or specific symptoms of depression, influences the rate of cognitive decline.

Methods: We conducted linear regression analysis to determine if baseline depression or depressive symptoms influenced the rate of age-related cognitive decline. Data analyzed were from 634 male and 934 female elderly white, non-Hispanic participants in the Texas Alzheimer’s Research and Care Consortium. Participants included cognitively normal controls (733), subjects with mild cognitive impairment (243) and subjects with Alzheimer’s disease (592). Baseline depression was estimated using Geriatric Depression Scale (GDS30) scores. Baseline depressive symptoms included apathy and agitation, as measured in the Neuropsychiatric Inventory Questionnaire (NPI-Q). Cognitive decline was measured by a change in Clinical Dementia Rating (CDR) scores between visits 1 and 3. In these analyses we stratified based on gender and adjusted for age at first visit and education.

Results: We found that baseline overall depression (GDS30) was not significantly related to cognitive decline. Specific depressive symptoms were significantly related to cognitive decline, but there were different effects in men and women. Apathy was correlated with increased cognitive decline in men only (p < 0.05).

Conclusions: Depressive symptoms appear to increase the rate of cognitive decline and may be early signs for neurodegeneration. These symptoms may also be important targets for therapeutics designed to treat, or slow the progression of Alzheimer’s disease. However, the relationship is not simple, as indicated by the divergent results observed in males and females. Further research in this area is warranted; while there are currently no proven treatments for Alzheimer’s disease, depression and depressive symptoms are therapeutically modifiable.

Sponsor: TARCC
IRB/IACUC#: 2007-137
Toxicity of Amyloid Beta Proteins on SH-SYSY Cells and Determination of an Optimal Dose of Methylene Blue That is Nontoxic to the SH-SYSY Cells

There are many theories that explain the etiology of Alzheimer’s disease but the exact mechanism and pathophysiology of this disease remains unclear. The hallmark of the disease is the identification of amyloid beta plaques in the brains of Alzheimer’s patients during autopsy and tangles of hyper phosphorylated Tau proteins but why and how these compounds mediate their neurotoxicity is still a matter of debate. Knowing the exact mechanisms and the biochemical pathways through which these compounds mediate their neurotoxicity could open a whole new area of research for targeted medical therapy. There have been a lot of studies establishing the neurotoxicity of amyloid beta proteins in different cell lines but there are also studies establishing other factors of neurodegeneration including the tau protein, glutamate toxicity, oxidative stress which makes drawing a conclusion for amyloid beta as the instigator of the disease challenging but there is a general consensus that amyloid beta plays a role in the pathophysiology of Alzheimer’s disease. I investigated the toxicity of amyloid beta proteins on SH-SYSY cells and also determined an optimal dose of methylene blue that is nontoxic to the SH-SYSY cells. SH-SYSY is a human derived cell line used in most labs for scientific research and my decision to use these cells was based on the fact that few studies have been done using these cells to establish amyloid beta toxicity. SH-SYSY cells were plated on a 96 well plate and allowed to grow to confluency, after which the amyloid beta protein was added to the cell culture and incubated for two days. A cell viability assay was then performed on the cell cultures. My findings showed amyloid beta protein is toxic to SH-SYSY cells and the toxicity is dose dependent. I was also able to find an optimal dose of methylene blue that is nontoxic to SH-SYSY cells. Methylene blue has been in clinical use for a long time and some in vivo studies have shown that it can improve cognitive function in rats by increasing the activity of cytochrome c oxidase by up to 25%. With these findings, further investigation into the mechanism through which the amyloid beta protein mediates its toxicity on SH-SYSY cells can be carried out. Also, using the optimal dose of methylene blue that’s nontoxic to SH-SYSY cells, I intend to further investigate if methylene blue can reverse the neurotoxic effects of the amyloid beta protein on SH-SYSY cells.

Sponsor: American Federation of Aging
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Treadmill exercise attenuates aging-related bradykinesia: potential involvement of increased nigral GFR-α1 expression and dopamine tissue content

Given the burgeoning increase in our elderly population, lifestyle strategies that mitigate aging-related impairments are essential. Bradykinesia, a cardinal symptom of Parkinson’s disease (PD), also affects up to 30% of the elderly population. Exercise can ameliorate locomotor impairment in PD models and patients, but the neuroanatomical and molecular basis for these effects have not been delineated. Striatal dopamine loss exceeds 80% at onset of bradykinesia in PD, but the greatest loss ever reported in aging humans or animal models is ~50%. Furthermore, exercise-related improvements in locomotor function can occur without significant effects on striatal dopamine in PD models. Here, we hypothesize that an established treadmill exercise regimen could attenuate aging-related bradykinesia (ARB) in conjunction with increased dopamine and the glial cell line-derived neurotrophic factor (GDNF) receptor, GDNF family receptor-alpha 1 (GFR-α1) in the substantia nigra (SN).

The rationale for this hypothesis is based on observations that striatal infusion of GDNF in aging models increases locomotor activity and dopamine in the SN, but not striatum. Second, GFR-α1 decreases only in the SN in aging. Third, replenishing the quantity of GFR-α1 lost due to aging increases locomotor activity in combination with increased dopamine and tyrosine hydroxylase (TH) expression in SN, but not striatum, in aged rats. A critical component of this hypothesis is that GDNF, which has been shown to increase following exercise, may also increase GFR-α1 expression.

Using our treadmill exercise regimen, we assessed the impact of short- and long-term exercise on ARB and GDNF signaling in aged rats. Our results demonstrate that two rounds of our exercise regimen increased GFR-α1 expression and dopamine in SN of aged rats; a result that reflects the previously reported effect of exogenous GDNF. Notably, a repeated regimen of long-term exercise followed by an equal amount of rest eventually attenuated ARB when compared to non-exercise rats. These studies may be applicable in PD models, in that augmentation of dopamine biosynthesis in SN, instead of striatum, may be an important mechanism of improving locomotor impairment. Finally, our work may delineate molecular targets to enable development of therapeutic strategies that target bradykinesia, particularly in those who may be physically unable or unwilling to exercise.

Sponsor: National Institute on Aging (R01 AG040261-Awarded to Michael F. Salvatore)
IRB/IACUC#: P-12-036 (LSU Health Sciences Center IACUC protocol number)
Two dimensional blue native/SDS-PAGE to identify mitochondrial complex I subunits modified by 4-hydroxynonenal (HNE)

Abstract

The lipid peroxidation product 4-hydroxynonenal (HNE) can form protein-linked HNE adducts, thereby impacting protein structure and function. Mitochondrial complex I (NADH-ubiquinone oxidoreductase), containing at least 45 subunits in mammalian cells, sits in a lipid-rich environment and is thus very susceptible to HNE modifications. In this paper, a procedure for the identification of HNE-modified complex I subunits is described. Complex I was isolated by first dimensional nongradient blue native polyacrylamide gel electrophoresis (BN-PAGE). The isolated complex I band, visualized by either Coomassie blue staining or silver staining, was further analyzed by second dimensional SDS-PAGE. HNE-modified proteins were visualized by Western blotting probed with anti-HNE antibodies. HNE-positive bands were then excised and the proteins contained in them were identified by mass spectrometric peptide sequencing. The method was successfully applied for the identification of two complex I subunits that showed enhanced HNE-modifications in diabetic kidney mitochondria.

Keywords: blue native/SDS-PAGE, diabetes, 4-hydroxynonenal, mitochondria, reactive oxygen species, streptozotocin

Worry in Mexican American Elders: The Role of Age, Gender, and Metabolic Syndrome

1. Purpose: Metabolic syndrome (MetS) is defined as risk factors which increase an individual’s risk for cardiovascular disease and diabetes. Risk factors include: abdominal obesity, hypertension, dyslipidemia, and elevated blood glucose. Research has suggested that worry, independent of anxiety, can contribute to poor health effects such as those seen with MetS. Mexican Americans (MA) have a high prevalence of worry and MetS, however a relationship between these variables has yet to be investigated for this population. The purpose of this study was to analyze the relationship between MetS and worry in the MA population. It is hypothesized that individuals with high levels of worry will be more likely to have MetS and show elevated risk factors. This study also examines the effect of age and gender on levels of worry in this population.

2. Methods: This cross-sectional study used data collected from the Health and Aging Brain Study among Latino Elders. Participants were grouped into a high or low worry category based on their Penn State Worry Questionnaire (PSWQ) score. Odds ratio was calculated for the presence of MetS. Independent sample t-tests were used to analyze the following: differences in MetS risk factors between individuals with high and low levels of worry, and differences in levels of worry based on gender and age.

3. Results: Odds ratio calculation was not significant for the presence of MetS (95% CI 0.443-1.163, p = 0.18) between individuals of differing levels of worry. Participants with high and low worry showed a significant difference in abdominal circumference (p = 0.025) and blood glucose (p = 0.038). Males and females showed a significant difference in total PSWQ score (p = 0.000). There was a significant difference in total PSWQ score between individuals aged 61 and above and those aged 60 and below (p = 0.006).

4. Conclusion: Individuals with a high level of worry did not have an increased likelihood to have MetS compared to individuals in a low worry group. However, when analyzing each risk factor alone, participants in a high worry group had a greater abdominal circumference and higher fasting glucose levels compared to those in a low worry group. The results of this study suggest the association of waist size and blood glucose with elevated levels of worry in the MA population. Results showed that females and individuals under the age of 61 have higher levels of worry compared to males and those over the age of 61, respectively.

Sponsor n/a
IRB/IACUC# # 2012 – 083
Bacteriomicmic Nanoparticles for Immunotherapy against Breast Cancer

Short description: Immunotherapy represents a potential and innovative means to combat cancer. It essentially harnesses the body’s immune system to fight against cancer. Previous literature suggests that cancer vaccines designed against a specific tumor antigen have been efficiently utilized to trigger immune responses against tumor cells. Despite the preliminary evidence in animal models, low immunogenicity is one of the major hurdles in the development of vaccines in humans. In order to surmount this obstacle, several approaches including the use of an “ideal” tumor antigen, appropriate delivery techniques, immune boosting strategies with co-stimulatory molecules are being explored.

Purpose: The purpose of this study was to develop “bacteriomicmic nanoparticles” to enhance adaptive cell-mediated immune responses (CD4+ and CD8+ T cell responses) against tumor antigen as a therapeutic option for cancer treatment.

Materials and Methods: Bone targeted nanoparticles were made using a modified water in oil in water double emulsion solvent evaporation method using an ultrasonic processor UP200H system (Hielischer Ultraschonics Gmbh, Germany). We used membrane preparations of the 4T1 mouse mammary cancer cell line as a tumor antigen and CpG ODN’s as a “bacteriomicmic” stimulant. Fourteen days before tumor challenge BALB/c female mice (6-8 weeks) were pre-immunized with CpG followed by secondary immunization using respective NPs encapsulated with the membrane antigen preparation. Subsequently, mice (n=5) were challenged subcutaneously (SC) with 10^5 tumor cells and the primary tumor size was monitored using vernier caliper and bioluminescence imaging (Caliper Life Sciences Inc., MA, USA). Mice were sacrificed on day fourteen after tumor challenge; spleen cells were used for flow cytometric analysis and primary tumor tissue was used to evaluate effect of NP immunization on tumor growth, survival as well as the immune response (CD4+ and CD8+ T cell) via immunohistochemistry.

Results: We found significant reduction in progression of tumor growth in mice immunized with CpG coated NPs containing tumor antigen (CpG-NP-Tag). Histological analysis confirmed that tumors in CpG-NP-Tag mice were relatively well differentiated and of lower grade in contrast to CpG-Blank tumors. Immunofluorescence (IF) data further revealed that CpG-NP-Tag tumors had lesser proliferation and higher apoptotic activity. Tumor CD4+ and CD8+ T cell infiltration as well as T cell response in spleen was found be higher in CpG-NP-Tag NP immunized mice as compared to the controls (CpG-NP-Blank and NP-Tag).

Conclusions: Primary tumor size, IHC, IF and flow cytometry analysis indicate that CpG-NP-Tag NPs were successfully employed to boost the immune response against tumor cells.

Sponsor N/A
IRB/IACUC# 2013/14-A04
Small Molecule, Tolfenamic Acid Induces the Apoptotic Response of Cis-Retinoic Acid in High-Risk Neuroblastoma Cells

Neuroblastoma (NB) is an aggressive and highly heterogeneous extra-cranial solid tumor found in children. NB accounts for 15% deaths among pediatric cancer patients. 13-cis-retinoic acid (RA) is commonly used as adjuvant therapy during the remission maintenance phase of NB treatment. There is, however, a greater than 50% risk of relapse in high-risk neuroblastoma (HRNB) that necessitates the development of an alternative therapeutic strategy. Specificity protein 1 (Sp1) is a transcription factor that is involved in the regulation of various cellular functions including cell growth, differentiation, and apoptosis. The present study is aimed at investigating the effect of a small molecule and Sp1 inhibitor, Tolfenamic Acid (TA) for enhancing the anti-proliferative effect of RA in HRNB cell lines, LA1-55n and SH-SY5Y. The optimized doses obtained from dose/time-dependent response of individual agents were used for the combination treatment experiments. LA1-55n and SH-SY5Y cells were treated with TA (30 µM) or RA (20 µM) or both for 48 h and tested to assess the effect on cell viability, apoptosis and selected molecular markers- Sp1, survivin, AKT and ERK1/2. Cell viability and caspase activity were measured using the CellTiter-Glo and Caspase-Glo kits. The apoptotic cell population was determined by flow cytometry with Annexin-V staining. The expression of Sp1, survivin, AKT, ERK1/2 and c-PARP were evaluated by western blot analysis. Treatment with TA and RA resulted in significant inhibition of cell viability in dose/time- dependent manner in tested cell lines. Even though the individual agents showed anti-proliferative response, the combination of both agents increased cell growth inhibition in LA1-55n (91.8%), SH-SY5Y (78.2%) as compared to TA alone (LA1-55n: 65%; SH-SY5Y: 51%) and RA alone (LA1-55n: 50%; SH-SY5Y: 33.5%). This anti-proliferative effect is accompanied by a decline in Sp1 and survivin expression. Furthermore, TA and RA combination treatment resulted in a significant increase in apoptotic (Annexin-V positive) cells, caspase 3/7 activation (LA1-55n: 12 fold and SH-SY5Y: 9 fold; p

Targeted Therapy for Non-Small Cell Lung Cancer Using Antibody-Coated Gold Nanoparticles

Purpose: Lung cancer is the leading cause of cancer-related death in the United States among both men and women. Approximately 85 to 90% of all lung cancers are non-small cell lung cancer (NSCLC). Unfortunately, NSCLC is extremely difficult to treat and survival rates are low (the five year survival rate is Methods: AuNPs with pendant –COOH and –OH groups are synthesized by the reduction of gold ions in the presence of a mixture of alkanethiols. A targeting ligand (mAb) is attached to the AuNPs by EDC-coupling. The size and zeta potential of the AuNPs is determined using dynamic light scattering and TEM, and the amount of antibody conjugation quantified via colorimetry. Uptake of AuNP and AuNP-mAb in various NSCLC cell lines with various levels of expression of the adhesion molecule was then performed Results: AuNP-mAb was synthesized, characterized and uptake tested in cell culture. We anticipate next to attach a platinum prodrug and test for use in targeted therapy for NSCLC.
Tolfenamic Acid Induces Therapeutic Efficacy of Chemotherapeutic Agents in Medulloblastoma Cells

Medulloblastoma (MB) is the most common malignant brain tumor of childhood. Currently, MB is treated using a multimodal approach consisting of surgery, craniospinal irradiation, and chemotherapy. Among the most commonly used chemotherapeutic agents are vincristine (Vinc), etoposide (Etop) and Cisplatin (Cis), while doxorubicin (Dox) is also used rarely. All of these agents carry significant delayed consequences for the patients including cognitive deficits. It is imperative that the strategies to improve the therapeutic efficacy of standard chemotherapy will include reduction of side effects in order to have a significant impact for treating MB patients. The primary objective of this study is to determine the effectiveness of a combination treatment to enhance the therapeutic efficacy of chemotherapeutic agents using MB cell lines. We have tested the combination of Tolfenamic Acid (TA), a small molecule and non-steroidal anti-inflammatory drug along with Vinc or Etop or Cis or Dox using MB cell lines, DAOY and D283. These cell lines were purchased from American Type Culture Collection (ATCC), Manassas, VA. TA has been shown to inhibit cell proliferation, induce apoptosis, and decrease the expression of Sp1 and Survivin which play roles in growth and cell survival in MB cells. Our results show that each drug together with TA causes a time and dose dependent decrease of MB cell viability which is more than that of single drug treatment. The cell growth inhibition is accompanied by an induction of apoptotic markers and the decrease in expression of Sp1 and survivin. The preliminary results of this preclinical model are in favor of combining TA with Vinc or Etop or Cis or Dox to achieve maximum therapeutic benefit while limiting the duration of treatment. Further studies are under investigation to precisely understand the underlying mechanisms and to confirm these results via in vivo assays. Addition of TA to current chemotherapy regimen for MB may reduce the dose and amount of time necessary for chemotherapy and therefore potentially reduce the toxicity and side-effects in children.

Sponsor
IRB/IACUC#
AnxA2 contributes to TNBC progression

Purpose:
The National Cancer Institute (NCI) estimates that in 2015, approximately 232,340 women will be diagnosed with new cases of invasive breast cancer and 39,620 will succumb to the disease. Advances in breast cancer research have led to the identification of four molecular subtypes; Luminal A, Luminal B, Triple negative/basal-like, and HER2 (Human Epidermal Growth Factor [Erbb2]) type. Triple-negative breast cancers (TNBC) are identified by the absence of three major receptors that drive most breast cancer: estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER-2); and constitutes 15 to 20% of diagnosed breast cancers. Given the heterogeneity and lack of standard molecular targets, patients with TNBC do not benefit from currently available targeted therapy, such as endocrine or anti-HER2 agents. Therefore, the only systemic treatment option available for these patients is surgery (+/- radiation) and chemotherapy with standard cytotoxic agents. Overall, TNBC is associated with poor prognosis, high mortality rate, and shorter median time to relapse (due to its aggressive tumor phenotype(s)), high recurrence rate, and visceral metastatic spread to the brain and lungs. This presents an urgent clinical need to identify new biomarker(s) that can be used for diagnosis and/or as potential therapeutic targets.

Our previous studies have demonstrated that AnxA2 is abundantly expressed in TNBC and has a reciprocal relationship with HER2 (Human Epidermal Growth Factor Receptor 2/ErbB2) at mRNA and protein levels. We have also demonstrated that AnxA2 and EGFR interact at the cell surface and this association is essential for EGFR mediated downstream signaling events that lead to cancer cell proliferation and migration. Furthermore, we have found that addition of growth factors, like EGF, stimulate the expression of AnxA2 at the mRNA and protein level in cancer cells expressing EGFR and basal levels of AnxA2. Based on our previous published studies and new preliminary data we hypothesize that AnxA2 expression in TNBC provides a selective advantage for TNBC fueling cancer progression. Our investigation will allow us to identify the AnxA2-EGFR relationship as a molecular contributor to TNBC progression.

Materials and Methods:
We serum starved MCF-7 cells overnight and treated with EGF (100ng/mL) at different time intervals. Increased expression of AnxA2 was observed at 48 and 72 hours at the protein level and mRNA. Membrane and cytosolic extraction of metastatic TNBC cell lines was performed for analysis of AnxA2 protein expression. TCGA(The Cancer Genome Atlas) analysis of breast cancer subtypes from clinical samples will also performed for analysis of AnxA2 and EGFR expression in cancer progression.

Results:
Our data indicate that increased expression of AnxA2 was observed at 48 and 72 hours at the protein level and mRNA fold change increased exponentially with EGF treatment. TCGA analysis unveils a significant increase in AnxA2 mRNA expression in comparison with other breast cancer subtypes.

Conclusions:
Our results suggest that AnxA2 increased expression during EGF stimulation of cancer cells with low expression of AnxA2 may be a potential mechanism of the AnxA2-EGFR interaction in TNBC. Increased expression of AnxA2 in TNBC in comparison with other breast cancer subtypes from the TCGA portal demonstrates AnxA2 as a potential biomarker for TNBC.

Sponsor
IRB/IACUC#
Assessment of Bladder Cancer Risk Factors: Central European Health Study

Purpose: Urinary bladder cancer is the ninth most commonly diagnosed cancer in the world and fifth most common malignancy in the United States. Because of the lifetime needs for surveillance, treatment and management of recurrent tumors, it poses a significant economic burden. A pilot case-control study was conducted to explore relationships between established and suspected risk factors and risk of different types of bladder cancer. We preliminarily described distributions of risk factors among bladder cancer cases.

Method: A multi-center case-control study was conducted in three Central European countries during 2012-2013. Cases (n=83) were aged 30-79, diagnosed with primary, histologically or cytologically confirmed incident bladder cancer. Participants were in-person interviewed to collect information on tobacco and alcohol use, second-hand smoking (SHS), history of chemical exposures, medical history and habitual dietary history. We stratified the cases by gender to compare distributions of risk factors in men and women.

Result: Mean age of cases was 62.7 years; there were more males (78.3%) than females (21.7%). 77% of all patients ever smoked, and 65% of the smokers have quit smoking before diagnosis. Among smokers, men were more likely to be heavy smokers than women (p values 66.7% for men and women respectively, p value≤0.05). More male patients ever exposed to potential chemical carcinogens than female patients (58.5% for men and 38.9 % for women, p value=0.20), and the major sources of chemical exposures were from petroleum/gasoline, vehicle exhaust, painting and wood dust. About 14% of female ever used hair dyes. Compared to female, men had higher body mass index (BMI) (27.2 for men and 26.9 for women, p values0.05), and men were more likely to have higher frequency of meat consumption everyday (14.3% for men and 5.6% for women, p value=0.05).

Conclusion: The preliminary results showed different distributions of risk factors among male and female bladder cancer cases. Further case control comparisons are needed to investigate different risk factors associated with bladder cancer across gender and subtype of bladder cancer in this study.

Keywords: bladder cancer, epidemiology, smoking

Sponsor N/A
IRB/IACUC# 2014-067

Development of Curcumin Loaded Nanoparticles and Evaluation of Antitumor Effects on Prostate Cancer Cell Lines

Purpose (a):
Curcumin (CUR) is a low molecular weight, lipophilic, yellow polyphenolic compound of Indian spice turmeric. In recent years, CUR has been shown as an effective antiproliferative agent in many cancer cell lines such as breast cancer and prostate cancer. Due to low water solubility and instability, the formulation of CUR is challenging and this prevents the usage of CUR in anticancer application. Lipid based nanoparticle (NP) delivery system is a promising approach to formulate CUR, in terms of its abilities in formulating lipophilic drugs, improving the drug’s pharmacokinetics and biodistribution, and reducing drug toxicity. The main objective of this study is to develop CUR NPs by optimizing NPs with varying compositions of lipids and surfactants.

Methods (b):
The preparation of nanoparticles was performed by a warm o/w microemulsion system. The drug loading and entrapment efficiency of CUR NPs were measured by using HPLC. Particle size was determined by using photon correlation spectroscopy. The in-vitro cytotoxicity of CUR NPs were performed by using MTT assays in PC3 and DU145 prostate cancer cell lines.

Results (c):
We were able to load CUR into the NPs made of Miglyol 812 and TPGS (1:1, w/w). Particle size was less than 150 nm with polydispersity index<95% and drug loading was >5%. CUR NPs were stable for up to 5 months at 4°C and up to 96 hours at 37°C in PBS buffer (pH 7.4) without significant changes in particle sizes. For both sensitive and resistant PC3 and DU145 cell lines, CUR NPs significantly reduced IC50 values over free drug.

Conclusions (d):
We successfully prepare CUR NPs using lipid-based NPs. CUR NPs significantly improved cytotoxicity of CUR in sensitive and resistant prostate cancer cells compared to free CUR.

Sponsor N/A
IRB/IACUC#
Development of Docetaxel-Loaded Lipid Nanoparticles for Prostate Cancer Treatment

Purpose: Using docetaxel-based therapy (DTX) for treatment for men with castration-resistant prostate cancer (CRPC) showed efficacy on improving overall survival. Despite this promising outcome, toxicities and adverse events of DTX limit the dose and dosage frequency. Moreover, patients develop DTX resistance eventually. Nanoparticle (NP) drug delivery systems offer alternative therapeutic options for the treatment of prostate cancer. The goal of this study is to develop novel DTX NPs to treat CRPC.

Method: Lipid and surfactant were selected using the solubility test. DTX NPs were prepared by an emulsion method. The NPs were characterized in terms of particle size, polydispersity index, short-term stability, drug loading, drug entrapment efficiency, in vitro release study, and cytotoxicity studies in DU145 and PC3 prostate cancer cell lines.

Results: DTX NPs were prepared using a proportionally amount of Migloyl 812 as the oil phase and TPGS as the surfactant phase. All tested NPs had particle size less than 150 nm with polydispersity index of less than 0.35. DTX NPs were physically stable at 4°C over five months and in PBS at 37°C over 96 hours as measured by particle size. DTX NPs had the drug entrapment efficiency over 90% with drug loading over 5%. The cytotoxicity studies demonstrated that there was no significant difference in IC50 values for the sensitive PC3 and DU145 cells between DTX NPs and free DTX. For the resistant PC3 and DU145 cells, DTX NPs significantly reduced IC50 values compared to free DTX.

Conclusions: DTX NPs were successfully prepared and characterized. DTX NPs showed comparable cytotoxicity in sensitive prostate cancer cells, and superior cytotoxicity in resistant prostate cancer cells compared to free DTX. Therefore, DTX NPs have the potential to treat CRPC and overcome drug resistance.

Development of Methylene Blue-Loaded Nanoparticles for Glioblastoma Treatment

Glioblastoma (GBM) is the most common and aggressive primary brain tumor in adults over 45, resulting in an average survival of 15 months post-diagnosis and treatment. While recent research has provided essential information to aid diagnosis and treatment, GBM is known to cause relapse following traditional combinatorial regimens, necessitating the development of more effective and less toxic therapies. Methylene blue (MB), a dye with noted medicinal applications, has received recent consideration as a potential neurotherapeutic due to its ability to infiltrate the blood-brain barrier (BBB) and improve cellular processes within distinct brain cell compartments and types; however, one drawback is an increased administration to produce desired therapeutic effects, leading to excessive brain deposition and potential neurotoxicity. A method commonly used to enhance drug delivery while reducing unwanted side effects is via encapsulation in nanoparticles (NPs) composed of the biodegradable/biocompatible co-polymer, poly(lactic-co-glycolic) acid (PLGA).

In this study, we formulated and characterized MB-loaded PLGA NPs, with a 3:1 molar ratio of sodium oleate to methylene blue at 5mg, based on particle size, drug loading, encapsulation efficiency, and release kinetics. Currently, we are establishing their in vitro effects in two different commercially-available GBM cell lines, according to their responses to commonly-used chemotherapeutics.

Following loading of 5mg MB and their comparison to blank NPs, we obtained NP preparations in the range of 120-145nm, with encapsulation efficiencies from 25-40% and drug loading between 1-2%. Additionally, we have found that 50% of the MB initially added is released at 24 hours, and stays constant up to two weeks, demonstrating sustained drug release.

In conclusion, based on studies that have demonstrated in vitro effects with MB at a minimum of 1μM (~0.3mg) and 150nm particles, our formulation should elicit comparable, if not better, results when treating GBM.
Exosomal AnnexinA2 promotes angiogenesis and breast cancer metastasis

Purpose: Early detection of cancer using circulating biomarkers is a realistic possibility with the discovery of exosomes. Cells under both physiological and pathological conditions secrete a wide array of membranous vesicles containing specific protein and RNA signatures. Exosomes, which are 40-100nm in size, comprise a major portion of these vesicles. Annexin A2 (AnxA2) is a 36 KD Ca$^{2+}$ dependent phospholipid-binding protein up-regulated in many cancer types and implicated in promoting tumorigenesis and angiogenesis. Cancer cells have been shown to secrete more AnxA2 and it is also highly expressed in the exosomes; but the function of exosomal AnxA2 (exo-AnxA2) has never been studied. We hypothesize that exo-AnxA2 promotes angiogenesis and breast cancer metastasis and we propose to explore this in our study.

Methods: Exosomes were isolated from MCF10A progression model for progression studies. For the metastasis studies MDA-MB-231 and its organ specific metastatic variants MDA-MB-831 (brain met) and MDA-MB-4175 (lung met) were used. They were characterized via Western blotting, particle size analyzer, transmission Electron Microscopy (TEM) and Atomic Force Microscopy (AFM). In vitro and in vivo angiogenesis assays were performed to study the role of exo-AnxA2 in angiogenesis. Exo-AnxA2 was either inhibited by use of LCKLSL inhibitory peptide or knocked down in these studies. Tail vein and intracardiac injection metastasis models were used after priming the animals with exosomes to study the role of exo-AnxA2 in breast cancer metastasis.

Results: Characterization of exo-AnxA2 by Western blot and AFM revealed that it is highly expressed in cancer exosomes than exosomes from normal cells. In vitro and in vivo angiogenesis studies revealed exo-AnxA2 to be a potent inducer of angiogenesis and inhibition of exo-AnxA2 significantly inhibits angiogenesis (~3 fold and ~5 fold decrease with LCKLSL vs. control in endothelial assay and matrigel plug assay respectively). Tail vein and intracardiac metastasis models showed that exo-AnxA2 promotes lung and brain metastasis. Knockdown of exo-AnxA2 showed ~2 fold decrease in lung and brain metastasis vs. control respectively, as evident from bioluminescence imaging.

Conclusion: We found that exo-AnxA2 correlates positively with breast cancer progression. Furthermore, we found that exo-AnxA2 is a potent inducer of angiogenesis and breast cancer metastasis indicating a possible role of exo-AnxA2 in tumor- microenvironment signaling and cancer progression.

Sponsor: 1P20 MD006882 from National Institute on Minority Health and Health Disparities

IRB/IACUC#: #2009-001 2013/14-03-A04
100% killing effect in the given range.

Conclusions:

Particles compared to the free drug. Moreover, the rHDL-SAQ particles were both able to achieve 100% killing while the free SAQ did not achieve

Particles were 10 times more effective than free Saquinavir. The effect on the SJNK cells was observed to be 2 fold greater when using the rHDL

The stability of the nanoparticle formulation measured as retention of the drug under experimental conditions indicated that 71% of

Fluorimetric measurements. The chemical composition of rHDL/Saquinavir particles was estimated by standard kits. The average size of the

Purpose: Malignant melanoma (MM) is a type of skin cancer that has a high potential to metastasize to distant organs and cause death. MM is

The third most common skin cancer in the United States and has an incidence of 18 new cases per 100,000. It is more lethal compared to other
type of skin cancers due to its higher rate of metastasis and has a 5 years survival rate of 7-18%. In MM, the levels of hyaluronidase are
overexpressed. Hyaluronidase is an endoglycosidase that degrades glycosaminoglycan and the hyaluronic acid (HA). Therefore, monitoring the
hyaluronidase activity can be used as a contrasting mechanism for its detection. A novel fluorescence polarization based detection of enzyme
activity using a fluorophore with a long fluorescence lifetime can enable a simple wide field molecular analysis of the cancer activities at the

cellular and tissue level. Hyaluronic acid is a large biopolymer (over 1MDa) that is cleaved by the hyaluronidase enzyme to smaller elements.
Monitoring kinetics of HA degradation by fluorescence polarization will be a simple and precise tool reflecting hyaluronidase activity and can be
used for the detection, diagnosis and monitoring of the malignant melanoma.

Methods: A long lifetime fluorophore (ADOTA) with a fluorescence lifetime of- 20 ns was used to label hyaluronic acid. The hyaluronidase activity
was measured as a function of change in the steady state fluorescence intensity and fluorescence polarization. Results: An intact HA will rotate slowly and the fluorescence polarization will be high, on the other hand, the cleaved HA (-300KDa) will
depolarize within the fluorescence lifetime of ADOTA yielding low polarization. The change in the polarization directly reflects hyaluronidase
activity. We found an increase in the fluorescence intensity with increasing time. This is due to release of HOMO-FRET. We also observed a
decrease in the fluorescence correlation time as cleaved hyaluronic acid fragments needs smaller time to rotate.

Conclusions: Thus, preliminary results show the ability of HA-ADOTA probe to efficiently detect hyaluronidase activity. This study will develop a
new technology for the non-invasive detection of the molecular activity of tumor in situ. In future, this technology can be used to construct a
device which can be used in the primary care setting for the detection of melanoma and monitoring the therapy progress.

Sponsor Sigma Xi Grants-in-Aid of Research.

IRB/IACUC# 119

Purpose: Formulating adjuvant therapy of rHDL nanoparticles with saquinavir to combat high-risk neuroblastoma.

Materials and Methods:
The rHDL-Saquinavir nanoparticles were prepared by cholate dialysis method. The entrapment efficiency of Saquinavir was determined by
Fluorimetric measurements. The chemical composition of rHDL/Saquinavir particles was estimated by standard kits. The average size of the
particles was measured by DeLSa Nano particle size analyzer. The stability of particles was estimated by dialyzing the particles at 37°C, for 48
hours at pH 7.4. The cytotoxic effectiveness of the formulation was tested against two HRNB cell lines (SJNK and IMR-5 obtained from Dr F.
Temius, Regina Margherita Children’s Hospital, Turin, Italy)) as compared to that of the free Saquinavir using CCK-8 kit. The Inhibitory
concentration to kill 50% of the cells (IC50) was determined.

Results:
The entrapment efficiency of the rHDL-SAQ particles was determined to be 70%. The chemical composition study indicated that the rHDL-SAQ
nanoparticles were composed of 60% phospholipids, 24% protein, 9% cholesterol, and 7% of Saquinavir. The average diameter of the particle
was 7.3 nm. The stability of the nanoparticle formulation measured as retention of the drug under experimental conditions indicated that 71% of
the drug was preserved. When testing the survival of the IMR-5 cell lines in presence of Free and rHDL-Saquinavir, it was found that the rHDL
particles were 10 times more effective than free Saquinavir. The effect on the SJNK cells was observed to be 2 fold greater when using the rHDL
particles compared to the free drug. Moreover, the rHDL-SAQ particles were both able to achieve 100% killing while the free SAQ did not achieve
100% killing effect in the given range.

Conclusions: The rHDL-Saquinavir nanoparticles were successfully formulated. The particles appeared to be small, stable and non-leaking. In vitro survival
studies suggested that rHDL-Saquinavir formulation is more effective than the free saquinavir. Thus, these studies support the potential of this
novel drug delivery platform for treating HRNB. These studies could be extended to other types of cancers as well.

Sponsor

IRB/IACUC#
Neutron-Activatable Holmium-Containing Nanoparticles for the Treatment of Non-small Cell Lung and Skin Cancers

Purpose:
To improve therapeutic outcomes for patients with non-small cell lung and skin cancers using radiation therapy.

Methods:
Magnetic holmium-165 (Ho) nanoparticles (HoIG) and derivatives containing platinum-based chemotherapeutic drugs (HoIG-Pt) were prepared and then neutron-activated to radioactive holmium-166 ($^{166}$Ho; $E_{\beta_{\max}} = 1.84$ MeV; $t_{1/2} = 26.8$ h) nanoparticles ($^{165}$HoIG and $^{166}$HoIG-Pt, respectively). Cytotoxicities of $^{166}$HoIG and $^{166}$HoIG-Pt were tested against non-small cell lung cancer cells, and in vivo studies were performed. $^{166}$HoIG were also introduced into poly-acrylonitrile (PAN) polymer solutions; these solutions were electrosprun to produce bandages that can be applied directly to tumor lesions after neutron-activation.

Results:
Ho materials were carefully characterized and successfully neutron-activated. HoIG contained approximately 56% w/w Ho. Two $^{166}$HoIG-Pt derivatives showed greater toxicity toward non-small cell lung cancer cells than blank $^{166}$HoIG and free platinum drug. The animal study data collected showed that the radiation and platinum drug act synergistically. HoIG was distributed homogenously throughout the radioactive bandages and the bandage was stable upon neutron-activation.

Conclusion:
Pt-based chemotherapeutic drugs and $^{166}$Ho have been incorporated together in a magnetic nanoparticle for the first time, and then used successfully in human cell culture and animal studies. A novel radiotherapeutic bandage was successfully prepared using PAN solutions and HoIG nanoparticles, and subsequently neutron-activated. The radiotherapeutic bandage is a more flexible strategy than that currently being used in the clinic for the treatment of skin cancer.
Primary Esophageal Adenosquamous carcinoma presenting as a pancreatic tail mass

This is a case report of a case of primary esophageal adenosquamous carcinoma. This report highlights the rarity of this subtype of cancer as well as the difficulty establishing an accurate diagnosis. This difficulty in this case was due to the cancer presenting as a pancreatic tail mass. All information was gathered while on a core surgery rotation with a hospital affiliated with UNTHSC (Dallas Methodist). Results are that this is an aggressive subtype of esophageal cancer that is lacking in the literature due to its rarity. There is an immense need for further research to establish more targeted and effective post surgical care in order to increase prognosis for these patients. There is also a lack of understanding of the pathophysiology in adenosquamous carcinoma, determining if it arises first as adenocarcinoma, squamous cell carcinoma, or independently as both could help determine risk factors and chemotherapy strategies. Known risk factors include diet, like the consumption of hot beverages and foods.

Sponsor
IRB/IACUC# 2015-057

Reproductive Health in Female Members of Cook Children's Life After Cancer Program

Reproductive Health in Female Members of Cook Children's Life After Cancer Program

Purpose: Late effects from cancer treatment have been a topic of growing interest in pediatric oncology. In this study, we assessed the relationship between cancer treatment modalities (radiation therapy and chemotherapeutic drugs) on spontaneous primary ovarian insufficiency (POI) and hormone replacement therapy (HRT) among female pediatric cancer survivors enrolled in the Life After Cancer Program (LACP) at Cook Children’s Medical Center.

Reproductive ability is an important quality of life issue in pediatric cancer survivors. Oncologists can utilize this information to minimize risks during treatment and recommend fertility-preserving steps such as removal and cryopreservation of oocytes and ovarian tissues prior to treatment. Female pediatric patients benefit from being more informed of reproductive late effects as fertility-preserving measures can be pursued prior to initiation of cancer treatment.

Methods: Chart review (n = 194) was conducted of LACP cancer survivors from 1/1/2011 to 6/30/2013. POI was defined clinically as females <40 years old with metrorrhagia or amenorrhea in association with elevated serum FSH levels as determined by individual lab assay method. Bivariate and stepwise logistic regression models assessed associations between treatment-related factors and both POI and HRT. Two-sided statistical tests (significance = 0.10) were performed in the model.

Inclusion criteria as follows:

Results: Mean age of diagnosis = 6.69 years. 25 subjects required HRT. Age at diagnosis, busulfan, ifosfamide, carboplatin, radiation therapy affecting ovaries/uterus, and total body irradiation (TBI) were found to be significantly associated (p < .05) with HRT in stepwise model.

Twenty-three patients developed POI. Age at diagnosis, busulfan, carboplatin, radiation therapy affecting ovaries/uterus, and total body irradiation (TBI) were found to be significantly associated (p < .05) with POI in stepwise model

Conclusions: Findings show certain alkylating agents (busulfan, ifosfamide), heavy metals (carboplatin), and radiation therapy increased odds of HRT and POI among LACP pediatric and young adult cancer survivors. Future analyses are ongoing with an expanded cohort (n = 449).

Sponsor
IRB/IACUC# 2013-210
Therapeutic Leukapheresis in Pediatric Leukemia: The Cook Children’s Experience

Purpose (a):
In Pediatrics, acute leukemia is the most common cause of hyperleukocytosis, as defined by WBC above 100K. In children, hyperleukocytosis is associated with early morbidity and mortality due to leukostasis-related complications such as intracranial hemorrhage and pulmonary distress. Additionally, tumor lysis syndrome, a dreaded complication due to high rate of cell turnover, can especially occur if chemotherapy is initiated without leukoreduction. Currently, therapeutic leukapheresis (LK) serves as an adjunctive therapy for select population presenting with hyperleukocytosis and/or leukostasis-related symptoms. Although LK is commonly used for this purpose, specific guidelines regarding when to use LK are not well-established. The purpose of this study is to evaluate the efficacy of LK and to determine the specific patient population that will benefit the most from this procedure. To our knowledge, this is the largest study conducted on efficacy of LK and its clinical outcome in pediatric leukemia patients.

Methods (b):
After obtaining institutional IRB approval, a retrospective chart review was conducted on 20 pediatric leukemia patients (14 ALL, 5 AML, and 1 CML) who underwent LK at Cook Children’s Medical Center from 2000 to 2014. Data on white blood cell count (WBC), platelets, chemistry, complications due to leukostasis at presentation, complete remission (CR), and overall survival rate were collected.

Results (c):
At presentation, 15% children had CNS symptoms, 15% had respiratory symptoms, and 5% had both. First round of LK showed 61.6% reduction in WBC from median value of 474.2 (233 – 910 x 10^9/L) to 182.5 (99.2 – 845 x 10^9/L). Six patients underwent second LK that reduced WBC by another 28.9% with a final median WBC of 139.35 (27.1 – 725 x 10^9/L). Overall, 19 out of 20 patients were alive immediately post LK, and 15 patients achieved complete remission.

Conclusions (d):
LK significantly reduces WBC in pediatric leukemia in patients as young as 22 day old presenting with WBC > 250 x 10^9/L and leukastasis-related complications. LK procedure itself has no significant complications and is concluded to be a safe adjunctive procedure in pediatric leukemia prior to initiation of induction chemotherapy.
Cardiovascular (Abstracts in the 300s)

301 Poster Classification: GSBS Student
Presenter: Katelynn Faulk
Department: Cardiovascular Research Institute
Authors: Katelynn Faulk, University of North Texas Health Science Center at Fort Worth; Tom Cunningham, University of North Texas Health Science Center at Fort Worth;

Angiotensin Converting Enzyme 1 (ACE1) Knockdown in the Median Preoptic Nucleus (MnPO) Attenuates Downstream Neural Activation following Chronic Intermittent Hypoxia
Sleep apnea is associated with a sustained increase in diurnal blood pressure. Chronic Intermittent Hypoxia (CIH), which simulates the arterial hypoxemia of sleep apnea, also produces a sustained increase in diurnal blood pressure. Several CNS regions that contribute to CIH hypertension have been identified including the MnPO and paraventricular nucleus (PVN). We have shown that viral-mediated shRNA knockdown of ACE1 within MnPO selectively decreases CIH hypertension during normoxia. Our hypothesis is that ACE1 knockdown in the MnPO will decrease FosB, a neuronal activation marker, positive neurons in the PVN which is a downstream target of the MnPO. We tested this hypothesis using a viral vector containing shRNA to ACE1 within the MnPO. Isoflurane anesthetized adult male rats were microinjected in the MnPO with 500nl of an adeno-associated virus containing GFP and either shRNA against ACE1 (shACE1) or scrambled shRNA (shSCM). Mean arterial blood pressure was recorded using radio telemetry. Rats were then exposed to 7 days of CIH (3 minute periods of hypoxia (10% oxygen) and 3 minute periods of normoxia (21% oxygen) for 8 hours/day) or normoxia (room air). Immunohistochemistry was used to assess FosB stained neurons within the MnPO and PVN. FosB positive neurons increased in the MnPO and PVN following CIH in both shSCM and shACE1 groups. However, shACE1 significantly decreased the FosB positive neurons in both MnPO and PVN following CIH. The shACE1 had no effects on FosB staining in normoxic controls. These results suggest that FosB activation within the MnPO and the PVN following CIH is at least partially dependent on MnPO ACE1.

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302 Poster Classification: TCOM DO Student
Presenter: Daniel Dietemann
Department: Biomedical Sciences
Authors: Daniel Dietemann, University of North Texas Health Science Center at Fort Worth; Anh Nguyen, University of North Texas Health Science Center at Fort Worth; Albert Olivencis-Yurvati, University of North Texas Health Science Center at Fort Worth; Robert Mallet, University of North Texas Health Science Center at Fort Worth;

Cardiac Arrest Induces Lung Inflammation 3 days after Cardiac Arrest in Domestic Pigs
Introduction: Cardiac arrest, a leading cause of death in the United States, is associated with detrimental damages, which includes the lungs. Reperfusion of ischemic tissue following cardiac arrest leads to systemic inflammation inflicted by free radical production. Pyruvate, a cellular metabolite and an antioxidant, has a demonstrated protective anti-oxidative effect on the heart through enhancement of the natural anti-oxidative glutathione system.
Purpose: Using Myeloperoxidase activity as a marker for neutrophilic inflammation, we sought to quantify the extent of the inflammation in lung tissue, and to determine pyruvate’s protective effect against ischemia/reperfusion injury in the lung.
Methods: Fourteen juvenile male Yorkshire swine were divided into three groups, a sham group(n=3) which underwent no cardiac arrest or CPR protocol, a CPR group(n=5) which received an intravenous infusion of sodium chloride solution, and a CPR + Pyruvate group which instead received an infusion of pyruvate solution(n=6). The CPR groups were placed in cardiac arrest via ventricular fibrillation for six minutes, followed by four minutes of cardiopulmonary compression and subsequent defibrillating counter shocks. The respective infusions were delivered at a rate of 0.1 mmol/kg/min throughout CPR and for 60 minutes following cardioversion. After three days, left lung samples were collected and assayed for protein content and myeloperoxidase activity.
Results: Three days following the procedure, Myeloperoxidase (MPO) activity was elevated in animals subjected to cardiac arrest compared to sham, although the result was not statistically significant (P=0.15). Pyruvate did not dampen MPO activity in the left lung.

Sponsor N/A
IRB/IACUC# 2012/13-29-A10
Cardiomyopathy due to Treatment with Anthracyclines

This case study illustrates the importance of cardiac monitoring in survivors who have received high dose anthracycline therapy for childhood malignancies. A single case medical file and personal interview were used in obtaining information for the study. MG, a 45 year old woman, was diagnosed with Ewing’s sarcoma of the right femur at 9 years of age, and received over 400 mg/m2 of Doxorubicin. An ECHO performed four weeks into her pregnancy demonstrated a decreased left ventricular ejection fraction (LVEF) of 35.4%, and MG was started on aggressive treatment. Despite appropriate treatment, she was not able to sleep while reclining during the last trimester of pregnancy and progressed to lethargy and shortness of breath on postpartum day 1. She was found to have congestive heart failure with cardiomyopathy; MG was hospitalized and given IV diuretics. Her LVEF has gradually improved since then and is stable at 60%. MG’s cardiomyopathy became evident due to a stressful trigger 22 years after her treatment ended. Without an ECHO performed early in her pregnancy, the cardiomyopathy may not have been diagnosed until she developed symptoms. At that stage in her pregnancy, her condition would have likely progressed significantly endangering her life and possibly resulting in the demise of her child. This case study demonstrates that cardiotoxicity can develop at any time after the completion of treatment. Further, this case study establishes the importance of annual cardiac monitoring for childhood cancer survivors who have been treated with high-dose anthracyclines especially.

Sponsor N/A
IRB/IACUC# 2015-051

Cardiovascular Screening in Youth

The objective of this project is to understand general providers’ screening and treatment processes and treatment options in children with a variety of cardiovascular disease risk factors. Currently, the national standard is to screen for hyperlipidemia and hypercholesterolemia every child within the ranges of 9 to 11 years old. Studies have shown this age to be a critical time that could possibly prevent the development of coronary artery disease as adults.

With our study, we aimed to understand current knowledge and the practice patterns of practicing providers for cholesterol screening and treatment in children. Our study created opportunities to understand the knowledge gaps and barriers for universal screening in children ages 9-11 in order to develop improved screening processes and treatment interventions in children with cardiovascular disease risk factors to prevent the future escalation of atherosclerotic heart disease.

We created an electronic questionnaire, which was advertised both through the NIH website and through NIH members’ emails, asking what current physicians are doing for cardiovascular screening and follow-up. Results showed that about 80% of providers agreed to screen all children ages 9-11, but there are still barriers to improve screening and treatment, including poor reimbursement and families’ opposition.

Sponsor N/A
IRB/IACUC# CCHMS 7266314
Central nuclei activated during long-term facilitation of blood pressure following acute exposures to intermittent hypoxia

INTRODUCTION: Acute intermittent hypoxia (AIH) is a protocol used to mimic the arterial hypoxemia that occurs during sleep apnea. AIH involves brief (1 min) exposures to systemic hypoxia (10% FIO2) repeated at 6 min intervals for an hour. Such exposures to AIH induce a phenomenon termed long-term facilitation (LTF). LTF is a long-lasting (at least 3 hr) increase in mean arterial pressure (MAP), heart rate (HR), sympathetic nerve discharge (SND) and phrenic nerve discharge (PND). As LTF represents a form of neuronal plasticity, we were interested in determining what sites within the CNS might be involved in the generation of LTF induced by AIH. Our hypothesis is that AIH will induce activity in central sites typically associated with cardiovascular regulation in the brain.

METHODS: After rats underwent tracheal intubation and were artificially ventilated, they had femoral artery and venous catheters implanted for measurement of arterial pressure and administration of drugs, respectively. AIH was induced as previously described (Yamamoto et al., 2015). The test rats (n=3) were maintained for 1 hour after the last hypoxic exposure. The control group (n=2) was surgically prepared exactly as the experimental group but was not exposed to hypoxia during the 2-hour experimental period. Following the AIH protocol, rats were sacrificed, transcardially perfused with paraformaldehyde and their brains sectioned on a cryostat and processed for immunohistochemical detection of c-Fos in alternate sections. Cardiovascular parameters were statistically analyzed using 2-way ANOVA. Brain sections containing the central nuclei of interest were examined for the presence of c-Fos.

RESULTS: Our protocol of AIH induced a significant increase in all measured cardiovascular parameters (MAP, HR, renal SND and PND) measured 1 hr after cessation of exposure to AIH. This LTF was associated with c-Fos immunoreactivity in neurons located with the NTS and the RVLM but not within the hypothalamic PVN.

CONCLUSIONS & FUTURE STUDIES: The generation of LTF appears to be dependent upon medullary sites involved in cardiorespiratory regulation (NTS) and sympathetic outflow (RVLM) but not within hypothalamic cardiorespiratory and sympathetic regulatory nuclei such as the PVN. Future experiments can also use neuronal inhibitors to determine the specific role of each area in AIH-induced LTF, and further clarify the statistical significance of this result. This could provide insights into central areas involved in the persistent sympatho-excitation and hypertension observed in sleep apnea patients.
**Cerebral Blood Flow Regulation Following Inhalation of Nicotine via Electronic Cigarettes**

**Background:** The use of electronic cigarettes (e-cigarettes) is growing rapidly but the physiologic effects of vaporized nicotine are relatively unknown. We hypothesized that acute inhalation of vaporized nicotine via e-cigarettes would impair regulation of cerebral blood flow (CBF) in response to variations in arterial pressure (cerebral autoregulation, CA). Methods: 13 subjects (6 F; 7 M) inhaled vapor from an 18 mg nicotine (nicotine) or a 0 mg nicotine (placebo) e-cigarette on separate days (randomized). Heart rate (HR), mean arterial pressure (MAP), mean middle cerebral artery velocity (MCAv), and cerebral oxygen saturation (ScO2) were measured non-invasively. Oscillatory lower body negative pressure (OLBNP) between 0 and -60 mmHg was applied for 20 cycles at 0.05 Hz and 0.10 Hz. Results: Between placebo and nicotine conditions, baseline frequency (LF; 0.07-0.2 Hz) power with 0.1 Hz OLBNP were higher under the placebo condition (P≤0.03). Cerebral blood flow (CBF) in response to oscillation in lower body negative pressure (OLBNP) between 0 and -60 mmHg was applied for 20 cycles at 0.05 Hz and 0.10 Hz. Results: Between placebo and nicotine conditions, baseline frequency (LF; 0.07-0.2 Hz) power with 0.1 Hz OLBNP were higher under the placebo condition (P≤0.03). Cross-spectral analysis in the LF (0.2 Hz) power with 0.1 Hz OLBNP and VLF (0.04-0.07 Hz) power with 0.05 Hz OLBNP revealed that gain between MAP-MCAv was similar between conditions (P>0.128). MCAv-ScO2 and MAP-ScO2 coherences were:

**Conclusion:** These data suggest that nicotine, when acutely inhaled via e-cigarettes, does not impair the cerebral pressure-flow relationship.

**Sponsor** University of Texas at San Antonio (UTSA) Collaborative Seed Grant.

**IRB/IACUC#** 2013-160

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**Effects of Music Therapy on Functional Mobility in Patients with Stroke**

**Abstract**

**Effects of Music Therapy on Functional Mobility in Patients with Stroke**

**Introduction and Purpose:** Normally human gait activity is a rhythmic movement of left and right lower extremities, but among patients with stroke, such a movement is often significantly affected or disturbed by the hemiparesis. In last 10-20 years, music therapy (MT) has been introduced to treat patients with stroke for improving mood as well as improving gait pattern. However, no consensus has been reached yet among clinicians on how to best utilize music therapy for patients with stroke. Therefore, the purpose of this review was to evaluate of effectiveness of the music therapy by focusing on: type of music, type of patients with stroke, outcome assessments on functional mobility, and intervention parameters for using music therapy.

**Methods.** PubMed and Scopus were used to search literature in last 15 years. Key words to search were stroke rehab, music rehab, cardiovascular accident, hemiparesis, music, rhythmic, auditory stimulation, metronome, and gait. Longitudinal studies included randomized control trial, single group study or case study with music therapy as one of the interventions.

**Results.** Five articles qualified for our literature analysis. It was found that listening to rhythmic auditory stimulus (3) was the most favored intervention, followed by listening to a patient’s familiar music (1), and utilizing a metronome synchronizing que in gait training. (1) All of these studies indicated that patients with sub-acute and chronic stroke could benefit more; no acute patients were reported. It revealed that combined use of MT with regular gait training could provide better results than MT alone. The most notable used intervention parameters were: 30 minutes each time, 5 times a week, for a minimum of 3 weeks. In these studies patients demonstrated improvement in gait velocity, stride length, cadence, symmetry, and standing balance as measured by GaitRite. Also it showed that after MT, patients with stroke could improve their balance and functional mobility as measured by Biodex, and 10 meter walking test respectively.

**Conclusions.** Music therapy is an effective and economical intervention for patients with stroke. Patients whom are more likely to benefit are those: with sub-acute stroke and have a lesion supplied by the middle cerebral artery. The MT intervention should be provided at least 5 times a week for minimal 3 weeks and used with functional gait training. Both temporal and spatial gait parameters, balance, mobility, and could be improved with MT.
Effects of pyruvate fortified cardiopulmonary resuscitation on myocardial injury after cardiac arrest

Effects of pyruvate fortified cardiopulmonary resuscitation on myocardial injury after cardiac arrest

BACKGROUND: Cardiac arrest kills 400,000 Americans annually. Over 90% of victims outside the hospital and 76% of those inside the hospital succumb to the destructive effects of cardiac arrest on the vital organs. To save the victims, forceful precordial chest compressions and trans-thoracic countershocks are applied, but the use of metabolic substrates as adjuvant treatments for cardiac arrest has not been tested clinically. Pyruvate, a natural intermediary metabolite, energy substrate and antioxidant, has been found to be cardioprotective during ischemia. Pyruvate accomplishes this cardioprotection through several mechanisms including enhancement of myocardial energy reserves and antioxidant defenses, and reduction of reactive oxygen species. Pyruvate-fortified cardioplegic solution administered during cardiopulmonary bypass hastened recovery of cardiac function and shortened hospitalization in patients undergoing coronary revascularization. Despite these discoveries, pyruvate’s effects on myocardial structural damage and inflammation after cardiopulmonary resuscitation and defibrillatory countershocks treated cardiac arrest have not been reported. This study tested the hypothesis that intravenous pyruvate administration minimizes left ventricular structural damage and inflammation that result from myocardial ischemia-reperfusion, precordial chest compressions, and trans-thoracic countershocks.

METHODS: Isoflurane-anesthetized Yorkshire swine, 25-40 kg of both genders were studied. The heart was arrested by rapid pacing. After 6 minutes of arrest, precordial compressions were applied at a rate of 100/min for 4 minutes while sodium pyruvate or NaCl control was infused iv to a concentration of 4 mM. Transthoracic countershocks (200-300 J) were administered until spontaneous cardiac rhythm was restored, and infusions maintained until 60 min recovery. The pigs were recovered for 72 hours, and then transmural biopsies of left ventricular free wall were collected, formalin-fixed and paraffin-embedded. Non-arrested sham experiments also were performed and compared with pyruvate- and NaCl-treated cardiac arrest-resuscitation. Sections were cut, stained with hematoxylin and eosin, and 20 random high power (100x) fields were examined and scored by an investigator blinded to the protocol. Structural endpoints included extracellular expansion, neutrophil invasion and trans-thoracic countershocks.

RESULTS: Sections of left ventricular myocardium are currently being analyzed from the 6 sham, 6 cardiac arrest, and 6 pyruvate treated cardiac hypercontracted tissue. Examined and scored by an investigator blinded to the protocol. Structural endpoints included extracellular expansion, neutrophil invasion and trans-thoracic countershocks.

CONCLUSIONS: Evidence of decreased neutrophil count, extracellular volume and cardiomyocyte hypercontraction in pyruvate-treated vs. control myocardium 72 h after cardiac arrest will be taken as evidence supporting the hypothesis. Such outcomes would argue for the acute use of pyruvate based interventions during initial treatment to promote post-cardiac arrest myocardial structural integrity.

Sponsor TCOM Honors Research Practicum
IRB/IACUC# 2012/13-29-A10
Intermittent hypoxic conditioning (IHC) modulates delta opioid receptor (DOR) phenotypes

IHC mediated cardioprotection is dependent on the DOR in dogs. It is predominantly expressed on cholinergic fibers and recruits both vagotonic and vagolytic pathways. Ganglioside GM-1 treatment decreases recruitment vagolytic DOR pathways. Vagal stimulation is cardioprotective, therefore we tested the hypothesis that IHC modulates the receptor phenotype in favor of the vagotonic receptor subtype by changing expression and DOR and GM-1. Dogs were assigned to 3 groups: non-hypoxic sham, IHC, or IHC + N. Atrial tissue was collected for biochemical analysis. Immunoblot densitometry was used to measure DOR protein content and immunocytochemistry followed by line scan intensity analysis of photomicrographs was used to evaluate GM-1. There was an increase in DOR following IHC+N relative to sham ($p$)

Sponsor: N/A
IRB/IACUC#: 2008/09-14

Median Preoptic AT1a Receptor Increase Responsible for Sustained Component of Hypertension from Chronic Intermittent Hypoxia

Sleep apnea sufferers experience repeated bouts of hypoxemia that result in a sustained increase in blood pressure. This hypertension persists despite the cessation of the hypoxic stimulus. Our lab focuses on a model for the hypoxemia experienced during sleep apnea by exposing rodents to chronic intermittent hypoxia (CIH). Previous studies have shown that there is an increase in neuronal activity in regions of the brain associated with sympathetic nerve activity after CIH, but little is known about the specific maladaptive neural changes that occur to drive this pathophysiology. Work from our lab has shown that the Angiotensin II Type 1a Receptor (AT1aR) is up regulated after CIH in the Median Preoptic Nucleus (MnPO). The MnPO receives inputs from circumventricular organs outside the blood brain barrier and synapses on regions controlling sympathetic outflow. This critical location between peripheral sensation neurons and downstream effector neurons makes the MnPO an attractive target for intervention. We hypothesize that CIH results in up-regulation of AT1aRs in the MnPO and results in excessive activation of downstream neurons responsible for sympathetic activation and sustained hypertension.

Sprague-Dawley rats receive microinjections of a virus with a short hairpin RNA that binds to the AT1a receptor (AT1ashRNA) RNA or a scramble sequence (SCRshRNA) in the MnPO. After recovery, radio telemetry is implanted for continuous monitoring of cardiovascular variables. Rats proceed through a CIH protocol consisting of a 5 day baseline followed by a 7 days of CIH. On the morning of the 8th day animals are perfused for FosB immunohistochemistry (IHC) or snap frozen for qRT-PCR.

Exposure to CIH resulted in a significant increase in AT1aR mRNA in the MnPO which was prevented by of AT1ashRNA (P)

The ability of AT1ashRNA to eliminate the sustained component of hypertension by preventing the increase in AT1aR RNA demonstrates the importance of Ang II MnPO in this type of neurogenic hypertension. The ability of this signaling to influence downstream sympathetic outflow as shown by a lack of FosB IHC in the RVLM provides insight into the mechanism of this disease. These experiments can help us to optimize our current sleep apnea treatment regimen by focusing on blood brain barrier permeable angiotensin receptor blockers as well as provide new therapies for neurogenically derived hypertension.

Sponsor: P01 HL-88052 & T32 AG020494
IRB/IACUC#: 2011/12-36
N-Acetyl Cysteine Attenuates Hypoxia Induced Sympathoexcitation in Human Subjects

This investigation tested the hypothesis that central and peripheral reactive oxygen species (ROS) mediate hypoxia induced sympathoexcitation, which is a central feature of the Obstructive Sleep Apnea-Hypopnea Syndrome (OSAS). 10 healthy human subjects were recruited. One hour prior to experimentation, each subject randomly ingested either 70 mg.kg⁻¹ of N-Acetyl Cysteine (NAC, n=5) or vehicle placebo (n=5). ECG, BP, muscle sympathetic nerve activity (MSNA) and plasma ROS and catecholamines were measured. Subjects underwent a 20 minute intermittent hypoxia training (IHT) protocol consisting of cyclical end-expiratory apneas with 100% N₂. Venous blood was analyzed pre/post IHT for ROS by electron paramagnetic spectroscopy and for catecholamines by ELISA. In the placebo group, MSNA was increased between pre vs. post IHT (P=0.01). In the NAC group, however, MSNA was unchanged (P=0.26). NAC reduced the percent change (% Δ) of ROS observed from pre- vs. post-IHT compared to placebo (P=0.02). The % Δ of ROS was directly related to increasing MSNA (R²=0.83, p=0.01). The % Δ of norepinephrine was lower in the NAC vs. placebo group after IHT (P=0.05), whereas the % Δ of epinephrine was unchanged (P=0.40). These data indicate that NAC reduces central sympathetic outflow in response to IHT, and thereby could reduce cardiovascular risk in OSAS patients.

Sponsor
IRB/IACUC#  2011-079

Neuronal injury from cardiac arrest: aging years in minutes

Cardiac arrest is a leading cause of death and permanent disability. Most victims succumb to the oxidative and inflammatory damage sustained during arrest/resuscitation, but even survivors typically battle long-term neurocognitive impairment. Although extensive research has delineated the complex mechanisms that culminate in neuronal damage and death, no effective treatments have been developed to interrupt these mechanisms. Of importance, many of these injury cascades are also active in the aging brain. In the aged brain, neurons and other cells are under persistent oxidative and inflammatory stress which eventually damages or kills the cells. With respect to these similarities, it is reasonable to propose that the brain essentially ages the equivalent of several years within the few minutes taken to resuscitate a patient from cardiac arrest. Accordingly, cardiac arrest-resuscitation models may afford an opportunity to study the deleterious mechanisms underlying the aging process, on an accelerated time course. The purpose of this presentation is to highlight parallel mechanisms of brain damage and neuronal death that ensue following cardiac arrest and in the aging brain. Despite their different time courses, mechanistic information gained from studying the two conditions could be harnessed to synergistically advance both fields. Ultimately this could lead to the development of treatments targeting specific components in these neurodegenerative pathways, in order to provide more robust protection of patients from neurocognitive impairment and/or death.

Sponsor
R01 NS076975 from the U.S. National Institute of Neurological Disorders and Stroke and P01 AG22550 from the National Institute on Aging

IRB/IACUC#  2012/13-29-A10
Pyruvate Stabilizes electrocardiographic and hemodynamic function in pigs recovering from cardiac arrest

Purpose: Cardiac electromechanical dysfunction may compromise recovery of patients who are initially resuscitated from cardiac arrest, and effective treatments for this post-arrest cardiac dysfunction remain elusive. Pyruvate, a natural intermediary metabolite, energy substrate and antioxidant, has been found to protect the heart from ischemia-reperfusion injury. This study tested the hypothesis that pyruvate-enriched resuscitation restores hemodynamic, metabolic, and electrolyte homeostasis following cardiac arrest.

Methods: Yorkshire swine (30 ± 0.7 kg; 23 male, 19 female) underwent pacing-induced ventricular fibrillation and, after 6 min pre-intervention arrest, 4 min precordial compressions followed by transthoracic countershocks. After 4 min CPR, direct current countershocks were administered with external paddles to restore cardiac rhythm. Up to three 6-7 J/kg countershocks were applied, followed by up to three 8-12 J/kg countershocks, at 30 s intervals with intervening CPR, until spontaneous cardiac rhythm was restored. After defibrillation and recovery of spontaneous circulation, the pigs were monitored for another 4 h. Sodium pyruvate (n=11) or NaCl control (n=12) were infused iv (0.1 mmol/kg min⁻¹) throughout precordial compressions and the first 60 min recovery. Sham control pigs (n=7; 3 male, 4 female) were instrumented, anesthetized, and mechanically ventilated, but not subjected to cardiac arrest, CPR or defibrillation. The sham protocol was the same duration as the cardiac arrest-resuscitation protocol, and these pigs received intravenous NaCl infusion for a period corresponding to that of treatment infusions in the cardiac arrest experiments.

Results: In 8 of the 24 NaCl-infused cardiac arrests, the first countershock converted ventricular fibrillation to pulseless electrical activity unresponsive to subsequent countershocks, but only 1 of 18 pyruvate-treated arrests developed pulseless electrical activity (relative risk 0.17; 95% confidence interval 0.13-0.22). Pyruvate treatment also lowered the dosage of vasoconstrictor phenylephrine required to maintain systemic arterial pressure, hastened clearance of excess glucose, elevated arterial bicarbonate, and raised arterial pH; these effects persisted up to 3h after pyruvate infusion.

Conclusion: Pyruvate-enriched resuscitation fosters electrocardiographic and hemodynamic stability in swine recovering from cardiac arrest.

Sponsor R01 NS076975 from the U.S. National Institute of Neurological Disorders and Stroke and P01 AG22550 from the National Institute on Aging

IRB/IACUC# 2012/13-29-A10

Pyruvate’s Neuroprotection in the Brain Following Cardiac Arrest-Resuscitation

Introduction: Ischemia and reperfusion as a result of cardiac arrest (CA) imposes detrimental injuries to the brain. Previous studies showed that pyruvate, an antioxidant and a cellular metabolite, was associated with upregulation of cellular defense pathways such as hypoxia induced factor 1α (HIF-1α), erythropoietin (EPO), nuclear factor erythroid 2-related factor (Nrf-2) and downregulation of proteins directly involved with apoptosis. Hypothesis: Pyruvate iv infusion during resuscitation preserves neurons and its supportive cells, and thus fosters post-CA neurocognitive recovery in swine.

Methods: Yorkshire swine (25-35 kg; n = 18) were subjected to pacing-induced CA, cardiopulmonary resuscitation (CPR) at approximately 100/min at 10-14 min CA, and transthoracic countershocks to restore sinus rhythm. NaCl or Na-pyruvate was infused iv (0.1 mmol/kg/min) during compressions and the first 60 min recovery. At 4 h reperfusion, brain biopsies were freeze-clamped for biochemical analysis and fixed in 10% formalin for immunohistochemistry.

Results: At 4h recovery, pyruvate treatment was correlated with an increase trend in hippocampal and cerebellar HIF-1α, EPO, and heme oxygenase-1 (HO-1), a key player in Nrf-2/HO-1 antioxidant pathway. Pyruvate did not affect brain Nrf-2 content among animals subjected to cardiac arrest.

Conclusions: Many cellular pathways may contribute to initial brain injury and protection after CA. Further analyses are being conducted to elucidate pyruvate’s neuroprotection effect on the brain after ischemia-reperfusion by CA. NINDS support: R01 NS076975
R21C Mutation in Cardiac Troponin I Imposes Differences in the Degree of Order and Kinetics of Myosin Cross-bridges of Left and Right Ventricles

The effect of the TnI R21C mutation in the human cardiac troponin I, the mutation that is linked to hypertrophic cardiomyopathy, on muscles of the left (LV) and right (RV) ventricles was examined in knock-in mice. Experiments probed 3-4 actin molecules in ex-vivo myofibrils prepared from LV and RV muscles. Control anisotropy experiments revealed that the orientation of actin reflected orientation of cross-bridges (XBs). It was found that the mutation imposed significant difference on the XB kinetics cycle of the LV and RV: XBs from RV displayed a 3-fold decrease in the rate of power stroke and a 2-fold decrease in the rate of dissociation from thin filaments as compared to LV. The mutation also imposed significant differences in the distribution of angles that actin makes with thin filament axis: during contraction, actin angles from LV were more tightly distributed compared to actin angles from RV. We speculate that molecular differences between ventricles are caused by inability of XBs to dissociate promptly from thin filaments. This work reveals phenotypic differences of the R21C mutation in the left versus right mouse ventricles even though both ventricles express the same isoform of the cardiac TnI and highlights the importance of functional differences between the two ventricles of cardiac disease.

Reproducibility of Near Infrared Spectroscopy (NIRS)-Derived Peripheral Muscle Oxygenation Measurements at Rest and During Central Hypovolemia

Background: Noninvasive muscle oxygen saturation (SmO₂) measurements from near-infrared spectroscopy (NIRS) sensors have been demonstrated to track the severity of central hypovolemia. The reproducibility of these devices in detecting and tracking reductions in SmO₂ during central hypovolemia, however, has not been quantified. Methods: 27 healthy human subjects (11 F, 16 M) were instrumented with a CareGuide 1100 muscle NIRS sensor (Reflectance Medical Inc.) on their right flexor carpi ulnaris muscle for assessment of SmO₂, tissue pH, and the microcirculatory index (MCI, an estimate of peripheral resistance). Subjects were exposed to two trials (≥ 4 weeks intervening) of lower body negative pressure (LBNP) applied at a rate of 3 mmHg/min until presyncope or voluntary termination. SmO₂, pH, and MCI were compared to stroke volume (SV) responses derived from a non-invasive arterial pressure waveform. Results: SV decreased by ~50% for both trials (p=0.94), and time to LBNP termination was similar (p=0.36). Both baseline and maximal SmO₂, pH, and MCI were statistically indistinguishable between the two trials (p≥0.17). Responses of SmO₂, pH, and MCI were highly correlated between trials (r=0.91; ps0.004; slopes=0.77), and each parameter tracked the reduction in SV (table). Conclusions: NIRS-derived measurements of SmO₂, pH, and MCI were reproducible during central hypovolemia elicited by continuous application of LBNP. These findings support the use of SmO₂ to monitor blood loss.
Spatial Distribution of Actin and Mechanical Cycle of Myosin are Different in Right and Left Ventricles of Healthy Mouse Hearts

The contraction of the right ventricle (RV) expels blood into the pulmonary circulation, and the contraction of the left ventricle (LV) pumps blood into the systemic circulation through the aorta. The respective afterloads imposed on the LV and RV by aortic and pulmonary artery pressures create very different mechanical requirements for the two ventricles. In spite of these functional differences, it is commonly believed that the right and left ventricular muscles are identical because there were no differences in stress development, twitch duration, work performance and power among the RV and LV. This report shows that the two ventricles in rigor differ in the degree of orientational disorder of actin within thin filaments, and during contraction they differ in the kinetics of the cross-bridge cycle. Mouse ventricle muscle is the source of sample for experiments in this project. Glycerinated muscle bundles were homogenized and myofibrils were extracted. Myofibrils were labeled with 1 nM rhodamine-phalloidin (RP) + 10 nM unlabeled-phalloidin (UP) in Ca²⁺-rigor solution in the ratio of 1:1000 fluorescent to non-fluorescent phalloidin to ensure 1 in ~10⁵ actin monomers carry a fluorophore. Labeled myofibrils were analyzed for error of the mean of polarized fluorescence to determine kinetic rate constants in the ATPase cycle and distribution of orientations emanating from myosin cross-bridges. Histograms were plotted from the polarized fluorescence data and the Full Width at Half Maximum (FWHM) of the mean was calculated. The mean polarization of a contracting WT LV myofibril power stroke 0.159±0.086 was higher as compared to 0.085±0.035 for RV. Similarly, dissociation of myosin from actin was significantly faster in LV compared to RV. The FWHM of actins of RVs were significantly narrower (better ordered) than those of LVs which shows that the LV and RV of the heart are different.

The study suggest that the differences in the rate constants during contraction and orientation of cross bridges during rigor signify the functional differences between left and right ventricles of the healthy mouse heart.

Sponsor: N/A
IRB/IACUC#: 2013/14-31-T04

Structural impact of cardiac arrest and resuscitation on right vs. left ventricular myocardium

BACKGROUND: Cardiac arrest imposes ischemia on the entire body including the heart itself. Although cardio-cerebral resuscitation and defibrillation are essential to save the cardiac arrest victim, these interventions can damage the heart by initiating reperfusion injury culminating in oxidative stress, inflammation and edema. However, the literature contains a paucity of information on the effects of cardiac arrest, precordial compressions and trans-thoracic countershocks on myocardium structure and the degree of acute inflammation that occurs following cardiac arrest-resuscitation-induced ischemia-reperfusion. Moreover, the specific post-resuscitation structural differences in left vs. right ventricular myocardium have never been reported. The right ventricle is positioned directly beneath the anterior chest wall and receives the initial impact of the forceful precordial chest compressions; furthermore, the right ventricular wall is thinner and less robust than the left ventricular free wall and interventricular septum. Therefore, structural damage resulting from resuscitation efforts may differ in the right vs. left ventricles. Accordingly, this study tested the hypothesis that cardiac arrest, closed-chest cardio-cerebral resuscitation and transthoracic countershocks produce structural injury that is more severe in the right than left ventricular myocardium.

METHODS: Isoflurane-anesthetized Yorkshire swine, 25-40 kg of both genders were studied. The heart was arrested by a rapid train of impulses administered with an intravascular pacing wire. After 6 minutes of arrest, precordial compressions were applied at a rate of 100/min for 4 minutes. Transthoracic countershocks (200-300 J) were administered until spontaneous cardiac rhythm was restored. At 72 hours recovery, the heart was excised, and 1 x 1 cm, transmural biopsies of left and right ventricular free wall were collected, formalin-fixed and paraffin-embedded. Non-arrested sham experiments were also performed for comparison with cardiac arrest-resuscitation. Sections were cut, stained with hematoxylin and eosin, and 20 random high power (125 x) fields were examined and scored by an investigator blinded to the protocol. Specific structural endpoints included extracellular expansion, neutrophil invasion and hypercontracted tissue.

RESULTS: Sections of left and right ventricular myocardium are currently being analyzed in 6 cardiac arrest and 6 sham experiments for neutrophilic damage and infiltration. It is anticipated that tissue injury will be evident in both ventricles.

CONCLUSIONS: The finding of greater extracellular volume, neutrophil count and cardiomyocyte hypercontracture in right vs. left ventricular myocardium will be taken as evidence supporting the hypothesis. Such an outcome would argue for development of interventions to promote post-resuscitation myocardial structural recovery.

Sponsor: UNTHSC Honors Research Practicum
IRB/IACUC#: 2012/13-29-A10
The Effect of Continuous Positive Airway Pressure Treatment on Cardiovascular Reactivity in Patients with Obstructive Sleep Apnea

ABSTRACT

INTRODUCTION

Obstructive sleep apnea (OSA) is commonly associated with significantly elevated sympathetic activity throughout the day and during sleep (a time when sympathetic activity normally decreases). It is also well-known that chronically elevated sympathetic activity profoundly increases risk of cardiovascular disease and contributes to disease progression. Nevertheless, it is not clear whether OSA patients tend to have exaggerated stress responses similar to other patient populations. Despite documented improvements on blood pressure with use of continuous positive airway treatment (CPAP), it is unknown whether CPAP also improves the stress response in these patients. We tested the hypothesis that effective treatment of OSA (with CPAP) would reduce the autonomic-mediated stress response to voluntary apneas. We assessed cardiovascular reactivity as the pressor response to apnea and also assessed baseline blood pressure and heart rate variability.

METHODS

22 OSA patients were recruited including 14 who were untreated and 8 who were effectively treated with CPAP for at least 3 months and had demonstrated treatment compliance and efficacy as determined by a high treatment success index. Subjects were fitted with a three lead electrocardiogram to measure the electrical activity of the heart, a pulse oximeter to observe continuous blood oxygen saturation and a Finometer to measure beat to beat arterial pressure through the duration of the study. Following a baseline period, subjects were then instructed to initiate a voluntary apnea (breathhold) lasting 20 sec. Data were collected electronically on to data acquisition system for subsequent analyses.

RESULTS

The CPAP-treated OSA subjects exhibited a lower BP response to apnea than treated subjects (p

CONCLUSION

These data demonstrate that CPAP decreases the pressor response to voluntary breathholds which is a form of stress. Previous studies in our lab have shown that these responses are primarily mediated by the sympathetic nervous system, thus these data suggest that the sympathetic response to stress is reduced in well-treated OSA patients. Finally, the decrease in sympathetic activity appears to be independent of any alterations of vagal outflow as no significant differences in the heart rate variability was observed.

Sponsor: N/A

IRB/IACUC#: 2013152

The effect of hospital factors on mortality rates after abdominal aortic aneurysm repair

Purpose: Patient factors that contribute to mortality from abdominal aortic aneurysm (AAA) repair have been previously described, but few studies have delineated the hospital factors that may be associated with an increase in patient mortality after AAA. This study used a large national database, the Nationwide Inpatient Sample (NIS), to identify hospital factors that affect mortality rates after open repair (OAR) and endovascular AAA repair (EVAR) of elective and ruptured AAA. Methods: A retrospective analysis was completed using NIS from 1998 to 2011. International Classification of Disease, Ninth Revision codes were used to identify patients who underwent elective or ruptured AAA repair by OAR or EVAR. The association between mortality and hospital covariates, including ownership, bed size, region, and individual hospital volume for these patients was statistically delineated by analysis of variance, \( \chi^2 \), and Mann-Kendall trend analysis. Results: A total of 128,232 patients were identified over the 14-year period, of which 88.5% were elective procedures and 11.5% were performed acutely for rupture. Most hospitals that complete elective OAR do between one and 50 cases, with mortality between 0% and 40%. Hospitals with mortality >40% uniformly complete fewer than five elective OAR cases annually and fall in the bottom 2.5% of all hospitals for mortality. Most hospitals that complete elective EVAR do between one and 70 cases, with mortality between 0% and 13%. Hospitals with mortality >13% uniformly complete fewer than eight elective EVAR cases annually and fall in the bottom 2.5% of all hospitals for mortality. The majority of hospitals that complete OAR or EVAR for ruptured AAA have between 0% to 100% for mortality, indicative of the high mortality risk associated with rupture. Conclusions: Hospitals that complete fewer than five OARs or eight EVARs annually have significantly greater mortality compared with their counterparts. Improved implementation of best practices, more detailed informed consent to include hospital mortality data, and better regional access to health care may improve survival after elective AAA repair.

Sponsor: N/A

IRB/IACUC#: N/A
The Role of Regional Cerebral Blood Flow on Tolerance to Central Hypovolemia

Tolerance to central hypovolemia is highly variable, and accumulating evidence suggests that protection of anterior cerebral blood flow (CBF) may not be the underlying mechanism. The posterior cerebral circulation supplies blood to the autonomic and respiratory control centers in the medulla, so may be associated with tolerance to central hypovolemia. We hypothesized that individuals with high tolerance to central hypovolemia would exhibit prolonged preservation of CBF in the posterior versus anterior cerebral circulation. 20 subjects (8M/12F) completed a presyncopal-limited lower body negative pressure (LBNP) protocol (3 mmHg/min onset rate) simulating hemorrhage. Middle cerebral artery velocity (MCAv), posterior cerebral artery (PCAv) (both via transcranial Doppler ultrasound), and arterial pressure (via finger photoplethysmography) were measured continuously. Subjects who completed ≥70 mmHg LBNP were classified as high tolerant (HT; N=9), and low tolerant (LT; N=11) if they completed ≤60 mmHg LBNP. The minimum difference in LBNP tolerance between groups was 214 s. Mean MCAv decreased by a similar magnitude in both groups throughout LBNP (P=0.15 between groups), but HT subjects exhibited greater decreases at presyncope (P=0.02). In comparison, mean PCAv decreased below baseline from -30 mmHg LBNP in LT subjects (P=0.01), but remained unchanged in HT subjects until -60 mmHg (P=0.89). We conclude that individuals with higher tolerance to central hypovolemia exhibit prolonged preservation of CBF in the posterior cerebral circulation, but not in the anterior circulation, thus delaying the onset of presyncope.

Sponsor U.S. Army MRMC Combat Casualty Care Research Program
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Universal Cholesterol Screening of all 9 - 11 year old Children in Community Based Ambulatory Pediatric Clinics

Introduction: In the U.S. and in most Western countries, coronary artery disease (CAD) is the leading cause of death, linked to hypercholesterolemia, especially in familial hypercholesterolemia (FH). Early identification and treatment of children with hypercholesterolemia has been shown to be effective and safe in reducing morbidity and mortality, especially in those with FH. However, few children with FH are currently being identified. Thus, the National Heart, Blood and Lung Institute (NHLBI) issued a guideline recommending universal cholesterol screening (UCS) of all 9 - 11 year old children in November 2011. We report a comparison of the number of 9 - 11 year old children screened for hypercholesterolemia 1 year prior to and 1 year following publication of the NHLBI’s screening guidelines in 5 community-based ambulatory pediatric clinics.

Methods
Five (5) community-based ambulatory pediatric clinics (4 hospital affiliated and 1 university affiliated) were recruited for this study, with retrospectively obtained data that was de-identified. Cholesterol screening results 1 year prior to publication of the NHLBI’s screening guidelines acted as the baseline for each clinic. Rates and results of lipid screening performed by each clinic in all 9-11 year old children at the time of scheduled or unscheduled clinic visits was measured.

Results
Of all eligible 9–11 year-old children, 489 (17.1%) were screened 1 year prior to publication of recommendations, and 686 (20.1%) were screened 1 year following publication of recommendations for universal cholesterol screening. Specifically, Clinic 1 increased screening from 24.2% to 32.3%, Clinic 2 decreased screening from 19% to 16.1%, Clinic 3 decreased screening from 14.7% to 11.9%, Clinic 4 increased screening from 23.1% to 28.5%, and Clinic 5 increased screening from 8.8% to 14.3% of target population.

Conclusion
There was a significant increase in the rates of lipid screening for the five clinics in our study following publication of the NHLBI’s recommendations for universal cholesterol screening compared to the year previous to recommendations. Given the high prevalence of premature CVD associated with familial hypercholesterolemia, additional strategies are needed to improve screening rates. The ability to identify this vulnerable population creates the opportunity for prevention of future cardiovascular disease by encouraging healthy lifestyles and the use of lipid lowering medication.

Sponsor N/A
IRB/IACUC# 2013-141
Case Presentation (Abstracts in the 400s)

400  Poster  Classification:  Faculty (Not for Competition)
Presenter: Thomas Diver PA-C  Department:  Family Medicine
Authors: Thomas Diver, University North Texas Health Science Center; Long Wong, University North Texas Health Science Center;

22 year old male trisomy 21 with Syncope and intermittent hyper-production of C-peptide: A Case Report

Purpose: There are multiple causes of syncope, which is a short loss of consciousness and muscle strength, characterized by a fast onset, short duration, and spontaneous recovery. Most of time, it is difficult to figure out the exact reason for syncope in a young adult. Ruling out cardiac, non-cardiac or neurological life-threatening conditions is important. We offer a case report that manifests as syncope in a young adult with multiple intermittent high C-peptide levels upon testing.

Methods: A 22-year old white male with Down’s syndrome presented to a family medicine clinic with increased intermittent episodes of syncope. These episodes lasted approximately 3-5 minutes and the patient awoke without recall. The patient presented with two main complaints, seizures and syncope frequently over the last two years. The seizures were consistent with epilepsy and he was given standard anti-convulsants which controlled these symptoms. However, the syncope remained. Further testing was conducted including workups for neurology, cardiology, emergency room evaluation and endocrinology.

Results: Neurological causes were ruled out because of a normal brain MRI. Cardiogenic causes were ruled out because of normal results for EKG and echocardiogram. Meanwhile, he went to the emergency room for loss of conscious symptoms and his medication Keppra was increased from 500 milligrams to 750 milligrams controlling his seizures. Repeated blood chemistries indicated that blood glucose levels were normal but C-peptide levels were elevated with each episode of syncope, which could indicate Insulin Hypersecretion Syndrome or a cellular insulinoma. Future testing needs to be conducted at the cellular level, including repeated MRI’s of the pancreas; however, insurance issues are barriers to this process.

Conclusions: No other case reports for young adults with a primary complaint of syncope and similar test results have surfaced in the literature thus far. Without further testing, a definitive cause cannot be determined.

Sponsor  N/A
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401  Poster  Classification:  TCOM DO Student
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A Case Presentation of Acute CHF Exacerbation in the Presence of Several Co-morbidities

Purpose: To highlight clinical features and management of congestive heart failure (CHF) exacerbation in a patient with several co-morbidities such as chronic kidney disease (CKD), hypertension (HTN), and diabetes (DM).

Methods: A 66 year old African American male with a history of systolic CHF, CKD with anemia, DM, HTN, hyperlipidemia, and tobacco abuse presented to his primary care physician with complaints of fatigue, a cough productive of pink sputum, and intermittent chest pain. For 9 months, he had worsening dyspnea with exertion, cough with chest pain, and orthopnea. On physical exam, lung auscultation revealed 50% rales with diminished breath sounds. 2+ edema was present on the lower extremities bilaterally. An EKG in clinic showed left ventricular hypertrophy. The patient was sent to Plaza Medical for evaluation of CHF exacerbation due to fluid overload while on high dose Lasix and a history of CKD.

Results: Labs showed an elevated BUN, creatinine, and BNP. He was anemic with a Hgb of 10.3. Troponins were negative. Initial CXR showed interstitial edema with cardiomegaly and pleural effusions. IV Lasix was started. During his hospital stay, his Hgb dropped to 8.3 and he was started on procrit. Cardiology and nephrology consults were ordered. An echocardiogram showed a dilated left ventricle with an ejection fraction of 25-30% with diffuse hypokinesia. The cardiologist began him on nitrates and digoxin. The nephrologist diagnosed end stage renal disease. A permcath was placed for dialysis. He received 3 treatments of inpatient dialysis. After 6 days, the patient was discharged home and put on outpatient dialysis. Procrit, isosorbide mononitrate, digoxin, hydralazine, and lisinopril were prescribed. The doses of furosemide and simvastatin were increased.

Conclusions: Community based studies show that 30-40% of patients die within 1 year of diagnosis of CHF, 60-70% die within 5 years. NYHA class IV patients have a 30-70% annual mortality rate, while NYHA class II patients have an annual mortality rate of 5-10%. Thus, functional status is an important predictor of patient outcome. In our case, the functional status of the patient had deteriorated to the point of hospitalization. In addition, the patient had co-morbidities that affected the functionality of the heart. HTN, CKD, and DM can all play a role in the functional and morphological changes in the heart resulting in CHF. Management of all co-morbidities is imperative to improve patient outcomes.

Sponsor  N/A
IRB/IACUC#  2015-030
African Tick-Bite Fever: A Case Report

Purpose:
In this report we review the clinical features of African tick bite fever (ATBF) and compare them to domestic rickettsial infections.

Methods:
Information and records were obtained on a 70 year old female diagnosed with ATBF who initially presented with febrile illness, eschars and a history of recent travel to South Africa. She had been misdiagnosed with a staphylococcus infection and treated with Bactrim prior to presentation. Review of the literature was also conducted to research the presentation of rickettsial spotted fever group (RSFG) infections.

Results:
Clinical features and history lead to the diagnosis of ATBF and administration of appropriate treatment with doxycycline.

Conclusion:
African tick bite fever is an acute febrile illness commonly seen in travelers to sub-Saharan Africa and the West Indies. It is a mild illness characterized by fever, lymphadenopathy and multiple eschars. Physicians should consider the diagnosis of ATBF in febrile patients and skin lesions in the appropriate epidemiologic setting.

An Unusual Second Malignant Neoplasm following Treatment for Childhood Non-Hodgkin Lymphoma

Purpose: This case study aims to describe a patient with a secondary malignant diagnosis of Ewing sarcoma following initial diagnosis of childhood non-Hodgkin lymphoma, to discuss the clinical features based on this case study, and to highlight the steps in the patient’s medical care that led to discovery of his diagnosis.

Methods: Information and records were obtained on a 19 year old man who presented to Cook Children’s Medical Center 3 years following his initial diagnosis of childhood non-Hodgkin lymphoma with progressive back pain. Patient was noncompliant with follow-up childhood cancer survivorship program and discovery of a 4 centimeter spinal mass was delayed over six months due to radiology error by an outside institution. Failure to identify the mass early in the course of the disease led to increasing size of the tumor and impingement of the spinal nerves, causing extreme pain, weakness, and paresthesia of the legs.

Results: After review of spinal imaging by a Cook Children's Medical Center radiologist, a progressively enlarging spinal tumor was discovered. Biopsy of the lesion was not wanted by the family and medically risky due to the tumor’s location within the vertebral canal. Although a diagnosis of recurrent non-Hodgkin lymphoma was assumed, biopsy showed a different malignant, small, round, blue cell tumor. A diagnosis of Ewing sarcoma was made, and patient was started on appropriate chemotherapy protocol.

Conclusions: Compliance with cancer survivorship programs is extremely important, especially for patients diagnosed with cancer in childhood. These programs maximize the probability of early discovery of recurrences of the original cancer or of second malignancies. It is also important for physicians to realize the importance of biopsies of new tumors in patients with previous cancer diagnoses so that patients will receive appropriate and effective therapy.
Brain Cyst in a Pediatric Patient: Early Diagnosis and Outcome

Purpose (a):
Pediatric macrocephaly can be caused by a variety of medical conditions such as tumors and cysts, as well as hydrocephaly. Because of the pliability of the infant skull, macrocephaly patients rarely exhibit focal neurological deficits or other obvious symptoms. Infants can often times compensate to changes in brain anatomy until the very late stages of the disease before deteriorating rapidly. As a result, early detection, diagnosis and treatment are essential to prevent permanent damage to the brain tissue and subsequent consequences such as disability or even death.

Methods (b):
An infant presented to the UNT Health Pediatric Clinic for the first time for sick visit due to cough and congestion. She was diagnosed to have a brain cyst. Management, outcome, literature review, as well as educational point are discussed.

Results (c):
We present the case of a 4 month old female infant who originally presented to UNT Health Pediatric Clinic for the first time for sick visit due to cough and congestion. She had virtually no other symptoms except mild macrocephaly. She was first diagnosed by x-ray and CT scan with a huge intra-ventricular or porencephalic cyst, and then subsequently treated by endoscopic fenestration of the cyst. The patient had a period of post-operative seizures, but has now made an impressive recovery.

Conclusions (d):
Brain cyst in pediatric patient is a rare but potentially dangerous situation if early diagnosis and treatment is not provided. The case we presented outlined a success recovery of a pediatric patient with brain cyst. Such case provided excellent educational point for medical students and clinicians regarding early detection, diagnosis and treatment of pediatric brain cyst.

Sponsor
N/A
IRB/IACUC# 2015-053

Eastern Equine Encephalitis: A Case Report

Purpose:
The purpose of this case report is to discuss a rare case of rapid neurological recovery from eastern equine encephalitis (EEE).

Methods:
Information and records were obtained on a 53 year old white male diagnosed with eastern equine encephalitis who initially presented to a Fort Worth, Texas emergency department with new onset slurred speech, confusion and weakness upon waking. The patient had a one week history of worsening headaches, waxing and waning fevers, upper back pain, nausea and vomiting. He had been diagnosed with a non-life-threatening viral illness two days prior to presentation. A thorough literature review on EEE was also conducted.

Results:
Within a few hours of arrival the patient experienced acute flaccid paralysis and a decline in respiratory status requiring emergent intubation. After three days of supportive care in the ICU he was extubated and began rehabilitation therapy. Physical therapy helped to rapidly improve his muscle strength, gait and fine motor skills over the course of one week. At follow-up five weeks later he was able to drive and start working again. He was still in speech therapy twice weekly, but noted improvement.

Conclusion:
Only 2% of adults infected with the EEE virus develop encephalitis. Of those 2%, 90% become comatose or stuporous. The mortality rate is at least 30%, making it the most severe arboviral encephalitis. Complete recovery among survivors is rare, with the most common sequelae being convulsions, paralysis and mental retardation. This patient was one of the unlucky few to develop encephalitis from the virus. He managed to survive and recover rapidly with no major sequelae.

Sponsor
N/A
IRB/IACUC# 2015-048
Ectopic Pregnancy with Unusually High beta-HCG

Purpose (a):
Ectopic pregnancy is a potentially life-threatening emergency and is usually diagnosed using a combination of clinical symptoms, biochemical markers, and ultrasound studies. However, atypical cases will often present without the classic triad of abdominal pain, amenorrhea, and vaginal spotting. Laboratory and ultrasound studies can also be non-conclusive. Such atypical presentation of ectopic pregnancy is illustrated in this case report.

Methods (b):
A 32-year-old female, gravida 4, para 2, abortus 1, presented to the obstetrics department with a chief complaint of vaginal bleeding daily for the past two months. She was diagnosed with an ectopic pregnancy, but had an unusual presentation. Management, outcome, literature review, as well as educational point are discussed.

Results (c):
We report the case of an atypical ectopic pregnancy with initial workup more consistent with an adnexal mass and possible germ cell tumor. The patient denied any lower abdominal pain, had serial beta-hCG levels approaching 60,000 mIU/mL, and a mass of unknown etiology was found on ultrasound. This mass was later discovered to be an intact fetus upon laparoscopy.

Conclusions (d):
This case illustrates the importance of recognizing ectopic pregnancy in the absence of hemoperitoneum, abdominal pain, confirmatory laboratory or ultrasound studies. Even with extremely high beta-hCG levels, keeping the differential of ectopic pregnancy in mind is crucial and can save the life of the mother.

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Life-Threatening Nocardia Empyema: A Case Report

Purpose (a):
To highlight a rare presentation of empyema and osteomyelitis of the ribs caused by Nocardia species bacteria. This case discusses the clinical features, imaging, and treatment of this unusual infection.

Methods (b):
A chart and literature review were performed with emphasis on disease presentation, imaging, cultures obtained, and treatment regimen involved in the management of osteomyelitis of the rib caused by Nocardia infection. The infection initially began as a pneumonia which was untreated due to the patient's lack of health insurance coverage. The pneumonia then transformed into an empyema and eventually infiltrated the chest wall. This allowed bacteria to colonize in the rib causing an osteomyelitis that presented as a large subcutaneous mass of the chest.

Results (c):
The unusual clinical presentation of a large, painful, subcutaneous mass prompted a CT scan at the emergency department which identified an empyema in the lung and a rib fracture suggestive of osteomyelitis. Infectious etiology was confirmed with culture of both the rib and empyema aspirate, showing colonization with Nocardia. The patient was treated with aggressive IV Bactrim for 6 weeks followed by 4 weeks of oral Bactrim. At follow up he had complete resolution of symptoms.

Conclusions (d):
Adults with a history of untreated pneumonia who present weeks later with a large, subcutaneous mass on the thorax should be worked up for possible empyema and osteomyelitis of the ribs. In addition, it is important to obtain cultures and identify the correct infectious organism in order to ensure complete eradication of the infection.

Sponsor N/A
IRB/IACUC# 2015-054
Lung Mass in a Patient with Rheumatoid Arthritis: A Case Report

Purpose: We present a case of a patient who smokes and has a past medical history of rheumatoid arthritis who presented to clinic with a chief complaint of symptomatic rheumatoid exacerbation. Given the patient’s status as a smoker, we investigated whether the patient was presenting with atypical symptoms of lung cancer.

Methods: We performed a physical exam on the patient and ordered appropriate labs and imaging. For the purposes of this report, we performed a literature review investigating the correlation between smoking, rheumatoid arthritis, and lung cancer.

Results: The patient presented with fatigue and diffuse, symmetrical joint and bone pain. Chest x-ray and CT revealed a lingual lung mass. Smoking is a well-established risk factor for the development of lung cancer. Recent studies have shown smoking also increases the risk for the development of rheumatoid arthritis, while rheumatoid arthritis is correlated with increased risk for the development of lung cancer.

Conclusions: Lung cancer typically presents with symptoms of shortness of breath and cough with or without hemoptysis, but non-specific extrapulmonary symptoms such as fatigue may also be present. This patient presented with symptoms of acute rheumatoid exacerbation, but could also have been presenting atypically for lung cancer. Imaging confirmed the presence of a lung mass, but imaging by itself is inappropriate for making the diagnosis of lung cancer. Still, the presence of a lung mass on imaging in a patient with a history of smoking is highly suspicious for malignancy. Rheumatoid arthritis is correlated with increased incidence of lung cancer, but this correlation is small.

Mycobacterium Abscessus Infection Post Gastric Band Surgery: A Case Report

Purpose: To describe a patient with resistant Mycobacterium abscessus infection, discuss the clinical features and review treatment.

Methods: Information and records were obtained on a 39 year old Hispanic male diagnosed with an abdominal abscess who initially presented to the emergency department with a two week history of fever and chills. He had been prescribed ciprofloxacin and flagyl two days prior to presentation. The patient had a significant past surgical history of laparoscopic adjustable gastric band surgery.

Results: The gastric band had eroded through the stomach wall causing an intra-abdominal abscess. The band was completely removed and the abscess was drained. Cultures grew Mycobacterium abscessus. Antibiotic susceptibility testing revealed that it was only sensitive to clarithromycin.

Conclusion: Patients that present with fever and chills not responsive to routine antibiotics should be tested for resistant bacteria, such as Mycobacterium abscessus. This is especially important in patients that have foreign bodies in their abdomen. Currently, there are no guidelines on treatment for resistant intra-abdominal infections. The plan is to have this patient on clarithromycin for at least one and a half years to prevent additional resistance.
Nerve Hydrodissection for Impingement of the Suprascapular Nerve

Nerve compressions are common clinical presentations. In this case study, the ability for nerve hydrodissection, a non-surgical technique for the release of a compressed nerve, is established. This patient had a compression of the suprascapular nerve in the posterior shoulder. The patient failed traditional non-operative therapies such as physical therapy and corticosteroid injections prior to this procedure. Immediately after the procedure, the patient noticed a significant decrease in pain with an increase in ROM, and was able to complete physical therapy to maintain a pain free ROM. Therefore, this case study demonstrates that nerve hydrodissection can be a viable non-surgical option for compressed nerves refractory to traditional options.

Sponsor
IRB/IACUC# 2015-042

Primary Pigmented Nodular Adrenocortical Disease: A Rare Condition of Cushing’s Syndrome

Purpose (a): Cushing’s syndrome (CS) is uncommon in children and may be either ACTH dependent or independent. The most common cause of CS is exogenous administration of glucocorticoids. We present an unusual case of ACTH-independent CS in a 14-1/2 year old Caucasian male.

Methods (b): A 14-1/2 year old Caucasian male was referred for accelerated weight gain, which first became apparent at 8 years of age. In the past 2 years he gained ~50 pounds, during which time he reported intermittent fatigue, vague abdominal pain, and pain in his lower back. There was no history of muscle weakness, hypertension or diabetes. Diurnal cortisol and ACTH levels, 24-hour urinary free cortisol, and overnight 0.5 mg dexamethasone suppression studies were performed. To further determine the etiology of Cushing’s syndrome and localize the source of excess glucocorticoids production, additional studies were performed.

Results (c): There was no suppression of adrenal steroids following 2 days of high dose dexamethasone. CT scan showed a slight nodular adrenal contour bilaterally. Further workup was consistent with primary pigmented nodular adrenal disease (PPNAD) without evidence of Carney Complex. A bilateral adrenalectomy was performed and the patient maintained on oral adrenal hormone replacement therapy.

Conclusions (d): PPNAD accounts for only 2% of ACTH-independent CS. Absence of adrenal suppression following high dose dexamethasone and nodular changes of the adrenal with CT scanning aid in the clinical suspicion of PPNAD. Bilateral adrenalectomy is the treatment of choice and, in the absence of Carney complex, should be curative.

Sponsor  N/A
IRB/IACUC#
Severe Insulin Resistance and Recurrent Pancreatitis in an 18 year old with Alström Syndrome

Background: Alström syndrome (AS) is a rare autosomal recessive disorder caused by a mutation of ALMS1 gene. ALMS1 is located in primary cilia, which serve important sensory roles for the extracellular environment in virtually every organ. Insulin resistance is one of the earliest metabolic changes seen in individuals with AS; and progression of the disease tends to be accelerated.

Case report: We describe an 18-year-old female with AS who experienced severe insulin resistance and recurrent pancreatitis. Despite good compliance and multiple combinations and dosing of insulin, including insulin pump therapy, her glycemic control remained inadequate. Over the past 5 years, she has been hospitalized 12 times for treatment of acute pancreatitis. Pancreatitis in AS seems to be related to severe hypertriglyceridemia, the latter caused by hyperphagia and insulin resistance.

Discussion: Early onset of obesity with the multi-organ involvement characteristic of ALMS1 may explain the accelerated development and increased severity of insulin resistance. Defective function of ALMS1 also results in reduced numbers of GLUT4 receptors mobilized to adipose cell membranes when stimulated by insulin. Diet modifications and increased physical activity may be beneficial. Recurrent pancreatitis in AS seems to be related to hypertriglyceridemia.

Conclusion: Early onset insulin resistance is characteristic of AS and can be severe. The expression of the ALMS1 mutation in the hypothalamus may contribute to hyperphagia, resulting in obesity. An elevated BMI is a significant risk factor for developing diabetes at a young age. A better understanding of the pathophysiology in this disease may help improve glycemic control and offer more effective treatment of multisystem disease in affected individuals.

Sponsor N/A

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Squamous Cell Carcinoma of the Neck with Second Primary Malignancy vs. Metastasis: A Case Study

Although head and neck squamous cell carcinoma (HNSCC) with a second primary malignancy (SPM) are considered rare, 25-33% of deaths in patients with HNSCC are due to SPMs. This statistic underscores the significance of diagnosing SPMs accurately in the management and treatment of HNSCC.

A 56 year old male presents with a large neck mass, dysphagia, and a raspy voice. A magnetic resonance imaging (MRI) of the head and neck displayed a 9x7 cm right neck mass. Therefore, a laryngoscopy with biopsy was performed to assess the severity of the neoplasm. The patient underwent a panendoscopy to exclude any evidence of additional primary malignancies in the neck, larynx, and esophagus. A staging computed tomography (CT) scan of the chest, abdomen, and pelvis revealed two hepatic lesions. These results were inconclusive in defining the lesions as metastases or SPMs, so a triple-phase CT scan of the abdomen was utilized to help explain the origin of the lesions. A liver biopsy was indicated following imaging results of the triple-phase CT. An alpha-fetoprotein level was also measured.

The laryngoscopy with biopsy showed evidence of translaryngeal extension and moderately differentiated squamous cell carcinoma (SCC) at the base of the tongue. The CT scan revealed two hepatic lesions: a heterogeneous irregular 6.2x7.1 cm mass within the superomedial right and left hepatic lobes and an ill-defined 4.2x5.4 cm mass at the porta hepatis, which was incompletely visualized. The triple-phase CT scan showed the 6.2x7.1 cm mass as an arterially enhancing lesion with imaging characteristics consistent of hepatocellular carcinoma (HCC) while the 4.2x5.4 cm mass was evaluated as a large necrotic lymph node at the porta hepatis. The liver biopsy’s findings of the 6.2x7.1 cm mass showed a high grade undifferentiated carcinoma favoring HCC and the alpha-fetoprotein was also abnormally high. The patient has undergone induction chemotherapy with cisplatin and 5-fluorouracil followed by concurrent chemoradiotherapy for the HNSCC, while the HCC is stable and remains untreated until the HNSCC is fully addressed.

This report provides valuable insight of an uncommon case of HNSCC with a SPM in the liver while illustrating the systematic approach towards a diagnosis based on the results of lab studies to distinguish SPMs from metastases. These types of precise diagnoses are necessary for appropriate treatment of the patient and additional work up is necessary to identify SPMs from metastases.

Sponsor N/A

IRB/IACUC#
Surgical Management of a Complex Enterocutaneous Fistula with Small Bowel and Gluteal Cleft Involvement Post-Resection of Rectal Adenocarcinoma

Purpose: The purpose of this case report is to discuss the importance of recognizing the presentation of an enterocutaneous fistula (ECF) as well as its management.

Methods: This case report describes a 51 year old African-American male with a past medical history of status post rectal cancer resection performed 9 months ago presented to clinic for follow-up of a persistent perirectal wound with constant drainage. The patient had no complications during the initial hospital stay for the surgery, but later returned to the emergency department 2 weeks later with symptoms of fever and abdominal pain. The patient was found to have a presacral abscess which was drained by interventional radiology. The patient continued to receive wound care, but the perianal wound failed to heal with persistent mucopurulent drainage over many months. Five months later, the patient underwent a fistulogram to visualize the extent of the wound. The fistulogram revealed 2 draining gluteal cleft wounds that converged into 1 tract extending cephalad with small bowel communication. The patient followed up 2 months later, and due to failure of the fistula to heal, it was determined that surgical repair of the ECF was necessary.

Results: The patient was taken to the operating room to undergo open repair of the ECF. Due to potential bladder involvement, a urologist performed a cystoscopy but was not able to visualize any obvious fistula involvement. Ureteral stents were placed bilaterally. Afterwards, an open laparotomy was performed and bowel was carefully dissected in order to visualize bowel involvement of the fistula. Once loops of small bowel were freed from the fascia, an obvious opening along the dorsal aspect of bowel was found. There was no obvious visual evidence of an enterovesical fistula. At this point, about 12-14 cm of small bowel was resected with primary anastomosis of the small bowel. Afterwards, 180 cc of methylene blue was injected into the bladder to assess for a leaking fistula, but no leakage was found. The peritoneal cavity was irrigated and the abdominal fascia and skin was closed. The patient tolerated the procedure well. The patient’s postoperative stay was non-eventful and the patient was discharged postoperative day 6 and was instructed to follow-up in clinic.

Conclusions: An ECF is a potentially catastrophic complication of surgery, and it continues to remain a significant challenge in its management. While definitive surgical repair is often purposefully delayed for months, it is imperative to recognize the signs of an ECF, as uncontrolled sepsis as well as electrolyte imbalances will result in very poor outcomes. However, this case reveals that it may be rather difficult in definitively diagnosing an ECF, especially when it develops postoperatively outside of the hospital stay. This case hopes to illustrate a presentation of an ECF as well as clinical considerations of its management.

Sponsor: N/A
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Type I Choledochal Cyst a Case Presentation

Choledochal cysts are cysts of the biliary tree of varying location and quantity with the majority being categorized as Type I showing a fusiform dilation of the common bile duct. They affect 1:100,000 to 1:150,000 individuals in the Western world and are usually diagnosed on abdominal CT or US when looking for a source of right upper quadrant pain. Types I and IV choledochal cysts have an increased likelihood of transforming into cholangiocarcinoma and because of this must be caught early to allow total cyst excision followed by a Roux-en-Y hepatojejunostomy. Following total cyst removal, malignancy is seen in 0.7-6% of patients and for this reason they must be followed up annually for liver enzyme monitoring. The case described here is that of a 43 year old Hispanic male who presented with epigastric pain and was found to have a Type I choledochal cyst on abdominal CT. A brief discussion of presentation, management, and treatment for choledochal cysts will follow.

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A comparison of photophysical characteristics of rHDL encapsulated anti-cancer drug valrubicin and free valrubicin.

Nanotechnology as a channel for drug delivery is one of the rapidly developing fields in cancer therapeutics. Targeted drug delivery has the advantage of having minimal interaction with healthy tissue, thereby reducing the toxicity of the drug to the rest of the body. rHDL nanoparticles have been found to be an efficient delivery system for highly lipophilic anti-cancer drugs. This is achieved through the interaction of scavenger receptors class B type I (SR-BI), which are highly expressed on cancer cells interact with rHDL nanoparticles for effective drug delivery to the cancer cell and tumor. The drug under investigation is Valrubicin, which, apart from being an effective anti-cancer drug, also has intrinsic fluorescence. This allowed for the comparison of photophysical properties of free Valrubicin and rHDL Valrubicin via steady state and time resolved fluorescence measurements. The steady-state anisotropy of rHDL Valrubicin is higher as compared to free Valrubicin, suggesting its encapsulation in rHDL nanoparticles. A longer rotational correlation time was observed for rHDL Valrubicin in time resolved anisotropy measurements compared to free Valrubicin, further supporting steady state anisotropy data.. We also studied the cellular internalization of free Valrubicin and rHDL Valrubicin using confocal microscopy. This could help track the movement of rHDL nanoparticles within the cancer cells.

Sponsor
IRB/IACUC#
Inhibition of the Glutaredoxin System Increases Doxorubicin Sensitivity in Hepatocellular Carcinoma by Impairing the Nrf2-dependent Antioxidant Response

Purpose: Hepatocellular carcinoma (HepG2) is the most common type of liver cancer, causing approximately 1.25 million deaths annually. Even with premier anti-cancer drugs like doxorubicin, the lethality of hepatocellular carcinoma has increased and is mainly attributed to growing drug resistance. Specifically, overexpression of key antioxidant enzymes such as the glutaredoxin system (Grxs) may enable drug resistance. Glutaredoxin is a powerful protective thiol repair enzyme that increases cancer cell survival. In this study, we explored a new anti-cancer strategy, the inhibition of Grxs, as a way to both increase doxorubicin sensitivity and reverse resistance in HepG2 by impairing the Nrf2-dependent antioxidant response.

Methods: HepG2 cells (Sigma) were transfected with Grxs or scramble shRNA vector. HepG2 was treated with doxorubicin in a dose and time-dependent manner. Cell viability was measured by the WST-8 colorimetric assay. Western blot was performed to test expression levels of pro- and anti-apoptotic proteins like Bax, Bcl2, and cleaved caspase-3. The level of protein glutathionylation (PSSG) was measured by immunoblotting using anti-PSSG antibody. Western blot was used to also examine the expression levels of Nrf2 and its downstream genes in Grxs-inhibited cells before and after doxorubicin treatment. Nrf2 translocation assay and co-immunoprecipitation with Grxs and PSSG was also performed. Antioxidant gene screening for 91 Nrf2-pathway related genes for scramble and Grxs shRNA after doxorubicin treatment was analyzed. Results: shRNA transfection gave a 50-70% Grxs knockdown. Grxs inhibition caused increased doxorubicin sensitivity with lower cell viabilities, higher pro-apoptotic protein expression levels, and increased glutathionylation than control. Grxs inhibition also decreased the expression of antioxidant enzyme transcription factor regulator, Nrf2, and its downstream antioxidant genes like HO-1, catalase, thioredoxin, and NQO1 especially after doxorubicin treatment. Nrf2’s presence in the nucleus and cytoplasm decreased with glutaredoxin knockdown. Glutaredoxin inhibition also significantly increased Nrf2 glutathionylation. Gene screening also showed significant decrease in mRNA levels of Nrf2-pathway related genes with Grxs inhibition after doxorubicin treatment.

Conclusions: Grxs inhibition causes increased doxorubicin sensitivity and apoptosis of hepatocellular carcinoma by attenuating Nrf2 and its downstream antioxidant genes activation.

Sponsor: UNTHSC Institute for Cancer Research

IRB/IACUC#
Omega-3 Content of Fish Oil Supplements as Monitored by Benchtop Time-domain NMR

Benchtop time-domain nuclear magnetic resonance (TD-NMR) is well suited for probing the visco-elastic and phase properties of samples of biological and industrial interest. Unlike conventional NMR spectroscopy, TD-NMR relaxometry does not require homogeneous magnetic fields and can be performed using relatively simple low-field instruments. Using TD-NMR, we observed that the T2 values of hydrocarbon chains in non-esterified fatty acids were linearly correlated with fluidity and dependent on cis-double bond content (Robinson, M.D, & Cistola, D.P., 2014, Biochemistry 53, 7515-7522. DOI:10.1021/bi5011859). Here we apply this method to analyze the omega-3 fatty acid content of triglyceride-based fish-oil supplements. The standard chemical methods for assessing the purity and potency of commercial fish oil products are expensive and tedious. Therefore, there is a need for simpler, non-invasive methods for quality control during manufacturing and for consumer safety monitoring. Using TD-NMR, the T2 profiles for pure triglycerides and mixtures reveal four resolved domains, corresponding to different segments of the hydrocarbon chain as well as the glycerol backbone. The T2 value for each resolved domain increases with the number of cis-double bonds. Across a wide series of pure triglycerides, mixtures and commercial fish-oil supplements, the T2 values are linearly correlated with percent ω-3 content, as quantified by gas-liquid chromatography. These results provide a framework for developing a quick, non-invasive benchtop TD-NMR method for analyzing the quality and potency of fish oil products.

Post-Transcriptional Regulation of Astrocyte-Tissue Inhibitor Metalloproteinase-1 (TIMP-1) in HAND

Purpose (a): HIV-1 can lead to several central nervous system impairments collectively termed HIV-1-associated neurocognitive disorders (HAND). In acute versus chronic neuroinflammation, differential regulation of Tissue Inhibitor of Metalloproteinase-1 (TIMP-1) is relevant to HAND neuropathogenesis. However, the underlying mechanisms are still being uncovered. In our study, we investigated the post-transcriptional regulation of TIMP-1 3’UTR via miRNAs.

Method (b): Microarray analysis was used to analyze miRNA changes in IL-1β-activated astrocytes. To investigate miRNA-mediated TIMP-1 3’UTR post-transcriptional regulation, TIMP-1 3’UTR and specific miRNA overexpression constructs were used. Primary human astrocytes were nucleofected with TIMP-1 3’UTR and Pmir 146b/Pmir 155, and treated with IL-1b 24 h post-transfection. Firefly luciferase activity and astrocyte TIMP-1 levels were analyzed in parallel experiments 24 and 72 hours after IL-1β treatment.

Result (c): Microarray analysis showed an increase in 12 miRNAs and decrease in 4 miRNAs. Seven of those were further confirmed by RT-PCR. The most consistent increase was observed in miRNA 155 and miRNA 146b.

Overexpression of miRNA 155 and miRNA 146b in IL-1β-activated astrocytes decreased both luciferase activity and endogenous TIMP-1 levels.

Conclusion (d): In summary, our preliminary studies suggest that astrocyte-TIMP-1 may be regulated post-transcriptionally by miRNAs (146b and 155) during HAND.
Depression and Perception of Exercise as Treatment in Rural Texas

Purpose: There is a lack of research about depression treatment specific to rural communities. There have been positive correlations with physical activity and mood disorders. The purpose of this study was to assess rural community patient’s views on validity of exercise as a treatment in depression.

Methods: A survey collected patient information about demographics, participation in exercise, and perception about exercise as a valid depression treatment. Questions pertaining to exercise included how many days a week engaged in exercise, minutes per session, and type of exercise. Logistic regression was used to analyze data obtained from the survey.

Results: Group 1 (18-39 years) was 0.570 times [0.117-2.767] less likely and Group 2 (40-59 years) was 1.6 times [0.257-10.662] more likely than Group 3 (60+ years) to perceive exercise as valid treatment for depression. Based on ethnicity, Whites were 0.945 times [0.210 – 4.264] less likely and Blacks are 0.179 times [0.008-3.809] less likely than Hispanics to perceive exercise as valid treatment. We identified a correlation between exercise performed (independent variable) and perception of exercise as a valid or adjunct treatment approach for depression (dependent variable). Results indicate that participants who exercised for 0-30 minutes on an average day are 1.683 times [0.3-9.425] more likely and participants who exercised for 30-60 minutes are 2.347 times [0.339-22.748] more likely to perceive exercise as valid treatment for depression than participants who exercised for more than 60 minutes.

Conclusions: Participants between age group of 40-59 years and participants of Hispanic ethnicity independently are most likely to perceive exercise as a valid treatment for depression. This is important because these findings can help healthcare providers tailor treatment of depression to specific age and ethnic groups. No correlation was observed between exercise time on a typical average day and their perception of exercise as a valid or adjunct treatment approach for depression.

Sponsor: N/A
IRB #: 2014-070

Exploring how Age of Mothers Influence Maternal Practices among NICU Infants

Purpose: Infants placed in the neonatal intensive care unit (NICU) after births have a greater risk of Sudden Infant Death Syndrome (SIDS), infections, and impaired cognitive skills compared to fully term infants. In the NICU, mothers are encouraged to practice safe sleep environments and breastfeeding. Mother’s choice in adopting breastfeeding and safer sleep positions may be influenced by their level of brain maturity and infant’s health. At the age of 25, the brain fully matures, which promotes less risky behavior and more timely decisions. We are interested in learning how maternal practices such as breastfeeding and baby’s sleep positions are influenced in two age groups of mothers (18-24 and 25-40) among NICU infants.

Methods: In-person surveys were administered by research personnel to mothers 18 years or older with infants aged 2 weeks to 3 months during their UNTHSC-Pediatric Outpatient Clinic visits. The surveys asked questions about demographics, perinatal history, breastfeeding and other feeding practices, sleep position, and sleep locations, and exposure to smoking. IBM SPSS Statistics 21 software was used for double-data entry and statistical reporting.

Results: Selected results reported here include factors related to breastfeeding and sleep position. Of all mothers (103) surveyed, 21 had infants placed in a NICU after birth. Among all NICU infants, 10 infants had younger mothers (18-24 years) and 11 had middle-aged (25-40) mothers. All of the mothers had breastfed or pumped breast milk for a short period of time, but currently only 60% of younger mothers and 64% of middle-aged mothers were breastfeeding. Among all, 7 out of 10 younger mothers and 9 out of 11 middle-aged mothers placed baby on back position to sleep.

Conclusions: Compared to those under age 25, middle-aged mothers with a NICU infant did not show a significant increase in adopting healthy maternal practices such as breastfeeding and safe sleep position. The lower incidence of breastfeeding might related to the challenges that parents with preterm infants face such as milk productions, latching problems, etc. Understanding the reasons why mothers are not choosing to adopt more healthy maternal practices is very important. Clinicians and researchers need to examine the reasons mothers are discontinuing breastfeeding and implement new strategies to promote longer breastfeeding.

Sponsor
IRB/IACUC# 2013-232
Hypertension and Obstructive Sleep Apnea are Associated with Abnormal Pressor Responses to Apnea

Background: Cardiovascular diseases are commonly associated with elevated sympathetic nerve activity (SNA). Previously, we have shown that the blood pressure response to a voluntary apnea is closely correlated with the SNA response in patients with sleep disordered breathing (SDB) and thus may serve as an index of SNA responsiveness. In the current study, we hypothesized that the pressor response to apnea is 1) reduced with effective treatment of SDB in SDB patients, and 2) that it is exaggerated in hypertensive patients (HTN) when compared to healthy control subjects.

Methods: 22 OSA patients (14 treated and 8 untreated), 19 treated hypertensive patients and 23 healthy normotensive control subjects were recruited from the UNTHC Primary Care Center and Sleep Consultants of Texas. Subjects completed a medical history questionnaire and Epworth Sleepiness survey. Blood pressure was measured by standard auscultatory assessment in the seated position. Baseline blood pressure was obtained in triplicate during quiet rest. Then after practicing a voluntary breath hold, subjects repeated three voluntary 20-second breath holds each beginning at end-expiration. Comparisons were made 1) between treated and untreated SDB patients, and 2) between HTN patients and healthy control subjects using a Student t test.

Results: Importantly, as in prior studies the pressor response to apnea was not different from zero in the healthy control subjects (-1.0 ± 4.2 mmHg, p>0.05). In the SDB patients, the pressor response was significantly greater than zero in both treated (11.4 ± 3.9 mm Hg) and untreated (24.5 ± 9.8 mm Hg) SDB patients (p

Conclusions: These data support our hypotheses that the pressor response to voluntary apnea is exaggerated in both untreated SDB and treated HTN patients and that effective treatment of SDB reduces this response, but does not normalize the response. These data suggest that the pressor response to apnea may be a simple physiologic index of exaggerated sympathetic responsiveness.

Sponsor: N/A
IRB/IACUC#: 2013-152
Purpose of the research: The purpose of this investigation was to analyze the historical development of Medicare and the progression to its current state with the intention of better understanding the problems that Medicare is facing today. With this, we hoped to draw current solutions from national and local perspectives. Our goal was to examine the basics of Medicare and identify national and community resources that assist Medicare enrollees and their families.

Material/Methods: Our methodology consisted of examining reports produced from non-profit and governmental organizations like Kaiser Family Foundation, Centers for Medicare & Medicaid Services and Center for Disease Control and Prevention to elicit insight on cost, demographics, and trends. We also gathered information from the National Hospital Discharge Survey published by the Center for Disease Control.

Summary: Medicare costs are increasing rapidly and the program is entering a period of growth faster than ever recorded before. As of 2010, Medicare accounts for $453 billion. To reduce future costs and help close loopholes, the Affordable Care Act (ACA) was introduced in 2010. ACA extended the Medicare budget by 12 years. In addition to these federal initiatives various local level organizations also help reduce the financial burden by preventing medical conditions in enrollees which lead to post acute care and hospice care which are two of the major burdens on the Medicare system.

Conclusion: The rising costs of the Medicare system will be financially taxing in the future as enrollment increases over the next few decades. However, the ACA policies will lead to significant reductions in Medicare cost. Additionally, there are a variety of local community resources in Tarrant County that can help families and enrollees learn more about Medicare, mitigate their healthcare costs and participate in preventative care.

Sponsor
N/A
IRB/IACUC#
but did not find an association between breastfeeding and sleeping in mother's bed at night. Although Hispanic mothers were slightly less likely
rates vary by ethnicity with Caucasians having the highest rate followed by Hispanics and Blacks3. Subsequently, death rates are highest for high mortality rate of ovarian cancer is due to its deep location within the pelvis, often leading to no symptoms until an advanced stage. Risk factors include women of middle age or older, family history, BRCA1/2 mutation, endometriosis, taking estrogen supplements alone and having never given birth3. To reduce risk, women are advised to use birth control pills, have ovaries removed, giving birth and breastfeeding3. Incidence of ovarian cancer, and 303 women died with a mortality rate of 63%, the third highest of all cancers in the county2. Our research focuses on identifying community resources within Tarrant County that can guide and assist patients in coping with this difficult illness. Epidemiology The high mortality rate of ovarian cancer is due to its deep location within the pelvis, often leading to no symptoms until an advanced stage. Risk factors include women of middle age or older, family history, BRCA1/2 mutation, endometriosis, taking estrogen supplements alone and having never given birth4. To reduce risk, women are advised to use birth control pills, have ovaries removed, giving birth and breastfeeding5. Incidence rates vary by ethnicity with Caucasians having the highest rate followed by Hispanics and Blacks5. Subsequently, death rates are highest for Caucasians3. Tarrant County Resources The level of care available in Tarrant County can vary greatly depending on the patient's ability to pay and health insurance status. While health insurance enrollment numbers have grown since the passage of the Affordable Care Act, many still do not have insurance. Community centers such as JPS help those with low income or lack of insurance find the guidance and support that they need. Additional resources include Texas Oncology, the Gynecological Cancer Navigational Program, Moncrief Cancer Resources from UT Southwestern, and the University of North Texas Health Science Center. With early detection and aggressive treatment, the 5 year survival rates of women with invasive stage I ovarian cancer can be as high as 90% compared to only 17% in stage IV. Thus, it is imperative that women gain access to the care that they need as early as possible to ensure the best possible outcome.

Prevalence of Infant Bed-sharing in Breastfeeding Mothers

Purpose: Research has shown that bed-sharing is a risk factor for SIDS and infant suffocation, two of the leading causes of infant mortality. Several studies have shown a strong relationship between breastfeeding and bed-sharing. Almost all mothers who continue to breastfeed for more than eight weeks incorporate bed-sharing into their nocturnal feeding and sleep routine early in infant’s life for minimal disruption of night-time breastfeeding. The intent of the research is to analyze infant care practices and parent beliefs. The information gained will help identify trends in breastfeeding, infant sleep location, and parents’ reasoning behind these practices. We are interested in finding out if breastfeeding is associated with a mother’s reasoning behind choosing her infant’s sleep location among Hispanic mothers.

Methods: Study design consisted of surveying mothers ≥ 18 years who had an infant between ages of 2 weeks and 3 months visiting UNTCH Pediatric Outpatient Clinic. Survey questionnaire inquired about demographics, breastfeeding and infant sleep routine.

Results: Out of 103 mothers surveyed, 45% were of Hispanic origin. Among Hispanic mothers, 50% were currently breastfeeding or feeding pumped milk. Out of all Hispanic mothers responded, 44% reported baby sleeps in mother’s bed at some point in the night. When all breastfeeding mothers (55) were asked to select reason for choosing infant’s sleep location, 17 mothers selected that it was easier to feed their baby and 32 mothers selected it seems safer for baby.

Conclusion: Results showed a significant association between breastfeeding and selecting sleep location due to ease of feeding (P-value < 0.05), but did not find an association between breastfeeding and sleeping in mother’s bed at night. Although Hispanic mothers were slightly less likely to breastfeed and slightly more likely to bed-share at night than non-Hispanic mothers, these relationships did not prove significant.

Sponsor: IRB/IACUC# 2013-232

Tarrant County Community Resources for Ovarian Cancer Treatment

Background Ovarian cancer accounts for 3% of reproductive system cancers among women, but it causes more deaths than any other form of reproductive cancer1. An analysis of 5 year cancer data revealed that between 2008 and 2012, 484 women in Tarrant County were diagnosed with ovarian cancer, and 303 women died with a mortality rate of 63%, the third highest of all cancers in the county2. Our research focuses on identifying community resources within Tarrant County that can guide and assist patients in coping with this difficult illness. Epidemiology The high mortality rate of ovarian cancer is due to its deep location within the pelvis, often leading to no symptoms until an advanced stage. Risk factors include women of middle age or older, family history, BRCA1/2 mutation, endometriosis, taking estrogen supplements alone and having never given birth3. To reduce risk, women are advised to use birth control pills, have ovaries removed, giving birth and breastfeeding4. Incidence rates vary by ethnicity with Caucasians having the highest rate followed by Hispanics and Blacks5. Subsequently, death rates are highest for Caucasians3. Tarrant County Resources The level of care available in Tarrant County can vary greatly depending on the patient’s ability to pay and health insurance status. While health insurance enrollment numbers have grown since the passage of the Affordable Care Act, many still do not have insurance. Community centers such as JPS help those with low income or lack of insurance find the guidance and support that they need. Additional resources include Texas Oncology, the Gynecological Cancer Navigational Program, Moncrief Cancer Resources from UT Southwestern, and the University of North Texas Health Science Center. With early detection and aggressive treatment, the 5 year survival rates of women with invasive stage I ovarian cancer can be as high as 90% compared to only 17% in stage IV. Thus, it is imperative that women gain access to the care that they need as early as possible to ensure the best possible outcome.
Texas, Medicaid and the Coverage Gap

Title: Texas, Medicaid and the Coverage Gap
Purpose: Medicaid provides medical coverage to millions of Americans, and makes up a large part of the Texas state budget. Many medical students do not know what exactly Medicaid provides, who can register for it, and where indigent patients can go to register. Our presentation helps define the what, how, and who of Medicaid insurance
Methods: We searched local, state, and federal government resources for Medicaid signup and what services are offered to whom. To improve relevance, we also searched popular and public websites for the impact of the Affordable Care Act (ACA)
Results: There are a number of ways to sign up in the Tarrant county area, both directly and through connecting organizations. The ACA has affected Medicaid coverage in other areas more than Texas, but the number of uninsured has nonetheless declined. We found that the main population of Medicaid beneficiaries comprises children in impoverished families.
Conclusions: Medicaid is a large part of many doctors' practices, and there is little reason to believe this will change in the near future. We hope that resources listed here will encourage students and physicians to help connect their uninsured patients with coverage, and will enlighten students of the role government insurance plays in the modern medical environment.

Sponsor: N/A

IRB/IACUC#: N/A
Association Between Peak Plantar Shear Stresses and Physical Body Measures

PURPOSE
Peak pressure has been long considered a risk factor for diabetic foot ulceration. Recent studies also indicated shear as a significant pathological factor. Cavanaugh et al (1991) demonstrated a significant correlation between body mass and peak pressures in diabetic patients. However, Ahroni et al (1987) claimed that peak pressure values of heavier individuals may not necessarily be abnormally high. Another physical body attribute, body height, has been associated with step length which depends on anteroposterior ground reaction forces.

To our knowledge the literature does not contain any reports that discuss a potential correlation between peak plantar shear stress and pressure and body measures such as body mass, height or presence of neuropathy. The purpose of this study was to explore these relationships using a custom-built pressure-shear plate.

METHODS
The study was approved by the Institutional Review Board. Subjects gave informed consent before participation. There are three groups: first - (DN) consisted of 14 diabetic neuropathic patients, second - (DC) comprised 14 diabetic patients without neuropathy and third - (HC) healthy control group, which included 11 subjects. Peripheral neuropathy was tested with a biothesiometer. Each subject walked multiple times at self-selected speeds on the stress plate, which was installed on a 12-ft walkway and set flush. Data from three trials were averaged and used in statistical analysis. Two shear stress and pressure variables were identified in each subject; peak shear (PS), peak shear-time integral (STI), peak pressure (PP) and peak pressure-time integral (PTI). These were correlated against the patients’ body mass, height and vibration.

RESULTS
Normality assumption was satisfied. Pearson correlation analysis was carried out for each group and each stress and pressure variable. No correlation was statistically significant. Body mass and body height could not account for any degree of variance in PS, STI, PP and PTI. In addition, plantar shear and pressure magnitudes do not correlate with vibration perception in DN group.

CONCLUSION
Thus, plantar shear stresses do not depend on body weight and body height and they need to be measured rather than calculated.

Sponsor NIH grant 1R15DK082962
IRB/IACUC# 2014-028
Hospital Admission Rates for Children with Diabetic Ketoacidosis (DKA)

**Background and Objective**
Diabetic Ketoacidosis (DKA) is a potentially life threatening complication of diabetes mellitus. Emergency Departments (ED) are usually the first point of contact. Following stabilization in the ED, patients are generally discharged home for outpatient management or hospitalized for continued care. Our objective is to gain a better understanding of the patient characteristics and treatment/disposition strategies used by ED physicians to improve care of children with DKA.

**Methods**
A retrospective chart review was performed of children seen in the Cook Children’s Medical Center ED from September 2011 – Aug 2014. No attempt was made to classify patients as T1 vs T2. APR-DRG 420 (diabetic ketoacidosis) was used for subject selection.

**Results**
During the study, 401 children were seen in the ED with a diagnosis of DKA. Ten percent (40) of patients were transferred from an outside facility to the ED for assessment and treatment; 90% (361) were not transferred. Of the total patients seen in the ED, 16.2% (65) were discharged for home management after initial assessment and treatment (1 transfer; 64 non-transferred); 83.8% (336) were admitted to the hospital (transfer 39; non-transfer 297). Of the patients who were admitted, the majority (66.9%) were admitted to the inpatient unit (inpatient 225 vs. PICU 111).

**Conclusion**
A large number of children with DKA are evaluated and treated in Emergency Departments. Continuing research on the characteristics of these children and the treatment strategies used by ED physicians can help improve care of children with DKA.

**Sponsor**  N/A
**IRB/IACUC#**  CCHMS 2014-076
Link between Diabetic Treatment Modalities (Oral medication, Insulin) and Global Cognitive Functioning Among Mexican Americans: An HABLE Study

Background: Diabetes is a significant health concern for the Hispanic population as it occurs, on average 10 years earlier than among non-Hispanic Whites and at a higher frequency. The link between diabetes and cognitive impairment has been supported though this link is not well understood. Recent empirical findings have suggested the use of insulin as a potential means for improving cognitive functioning; however, only one study to date has examined the implications of diabetes medication treatment on cognitive functioning among a sample of non-Hispanic whites. The aim of this study was to examine the implications of diabetes treatment modalities (oral medication, insulin) on cognitive functioning among a sample of Hispanic adults and elders.

Methods: Data was analyzed from 201 Hispanic Mexican American participants with a diagnosis of diabetes and who endorsed diabetic treatment (oral medication n=172; insulin n=54) from the Health and Aging Brain Study among Latino Elders (HABLE). Each participant underwent an interview (i.e. medical history, medications, and health behaviors), neuropsychological testing, blood draw, medical examination, and informant interviews. Diagnosis of MCI was assigned according to published criteria and was designated based on weekly consensus reviews. Global cognitive functioning was assessed utilizing the Mini Mental Status Examination (MMSE). HbA1c levels were categorized based on diabetic control status with values below 8% being considered controlled. Linear regressions were utilized with the dependent variable being global cognitive functioning and the independent variable being diabetic treatment modality. Age, gender and education were entered into the models as covariates.

Results: Among the total sample, use of oral medication as a treatment for diabetes was associated with higher global cognitive functioning (B[SE]=1.43[0.66], t-test=2.14, p-value = 0.033). When split by diabetic control status, those with uncontrolled diabetes (HbA1c level ≥ 8) and who were taking oral medications also demonstrated higher global cognitive functioning as measured by the MMSE (B[SE]= 2.28 [0.76], t-test=3.03, p-value = 0.003). Insulin treatment was not found to be significantly associated with global cognitive functioning within the total sample or when split by diabetic control status.

Conclusions: The results of our study suggest that diabetic treatment modalities differentially impact cognitive functioning among a sample of Hispanic Mexican Americans with oral medication showing to be significantly impactful. Future studies should further examine the link between specific oral diabetic medications and cognitive functioning.

Poster

Sponsor

IRB/IACUC# 2012-083

Parental Ideology of Diet and Exercise and Associated Risk of T2DM in Children

Background: Type 2 diabetes mellitus (T2DM) in children is a major public health issue. This study examined parental ideology of diet and exercise and the associated risk of T2DM in children.

Methods: Data were obtained from 10-14 year old children in North Central Texas participating in a study examining risk for T2DM. Questions on parental ideology were measured using three questions, including “Making my child eat a healthy diet and exercise regularly would be pleasant,” “I intend to make my child eat a healthy diet and exercise regularly” and “Making my child eat healthy and exercise will reduce their risk of developing diabetes”. Associations were assessed using logistic regression models controlled for race, gender, SES, neighborhood safety and age.

Results: Among 290 subjects, 5.7% were Caucasian, 15.4% were African-American, and 78.9% were Hispanic. Mean age was 11.87±1.4, while 50.3% of subjects were female. Increased pleasant perception of exercise and diet had decreased odds of being high risk for T2DM (0.916 OR, 95% CI: 0.591-0.997). Increased intention to make their child eat healthily and exercise had slightly increased odds of being high risk for T2DM (1.01 OR, 95% CI: 1.007-1.631). Finally, belief in healthy diet and exercise reducing risk for T2DM had decreased odds of being high risk for T2DM (0.969 OR, 95% CI: 0.591-0.997).

Conclusion: Results from this study suggest that parental ideology of diet and exercise is associated with a child’s risk for T2DM. Improving parents’ positive ideology of exercise and diet may reduce children’s risk of T2DM.

Poster

Sponsor

IRB/IACUC# 2011-136
Prolonged High Glucose Treatment Increased Orai1 Protein Expression through Inhibition of Lysosomal Pathway in Human Mesangial Cells

The Orai1-mediated store operated calcium entry (SOCE) is associated with many physiological and pathological processes in a variety of cells, including glomerular mesangial cells (MCs). We have previously demonstrated that prolonged treatment of MCs with high glucose (HG) significantly increased Orai1 expression at protein level, but not at mRNA level. These findings suggest that a post-transcriptional mechanism(s) contributes to the HG effect. The aim of the present study was to identify if proteosomal and/or lysosomal pathways were involved in the increased abundance of Orai1 protein in response to HG. Cultured human MCs were with and without treatment with 10 μM MG132 (an inhibitor of proteosomal pathway) or 10 mM ammonium chloride (an inhibitor of lysosomal pathway) in the presence of normal glucose (NG, 5.6 mM) or HG (25 mM) for 6 days. Western blots of the whole cell lysates were conducted to evaluate Orai1 expression level. Fura-2 fluorescence ratiometry was performed to study the intracellular calcium changes in the human MCs. We found that both MG132 and ammonium chloride increased abundance of Orai1 protein in MCs incubated with NG. The MG132 response was further increased by HG treatment. However, HG failed to cause additional increase in Orai1 protein expression in ammonium chloride-treated cells. Furthermore, fura-2 fluorescence ratiometry study showed that both MG132 and ammonium chloride increased the cyclopiazonic acid (25 μM)-stimulated SOCE. Simultaneous treatment with HG only enhanced the MG132 response, but not the ammonium chloride response. Taken together, our results indicate that HG increased expression of Orai1 protein by inhibiting its degradation through the lysosomal pathway.
The association of individual, interpersonal, and physiological factors on obesity in African American women.

Objective(s): This study evaluated individual, interpersonal, and physiological factors related to obesity. By determining the various underlying factors associated with weight, potential protective factors against obesity can be identified. Background: 34.9% of adults are obese with African Americans (AA) demonstrating the highest rates of obesity (47.8%). Obesity is associated with a variety of chronic health conditions, and has been strongly linked to type II diabetes. In fact, nearly 90% of overweight or obese individuals have a concurrent diagnosis of type II diabetes.

Methods: Associations between individual, interpersonal and physiological variables and Body Mass Index (BMI) were evaluated in 62 AA women (mean age 45.8 years [SD 12.4], mean BMI 37.4 [SD 8.3]). Individual and interpersonal variables including social support, self-efficacy for diet and physical activity, and weight management self-efficacy were evaluated with reliable and valid self-report surveys. Physiological variables including LDL cholesterol and Hemoglobin A1C were collected by trained measurement staff. BMI was calculated with objectively collected height and weight data.

Results: Of the 62 participants, 21% were overweight (BMI 25-29.9), 24.3% were Class I Obese (BMI 30-34.9), 25.8% were Class II Obese (BMI 35-39.9), and 29.0% were Class III Obese (BMI≥40, extreme obesity). The only individual level variable associated with BMI was motivation for physical activity (r=-0.32; p=.01). The interpersonal variable of support for weight management was negatively associated with BMI (r=-0.23; p=.08). LDL cholesterol was not associated with BMI, however hemoglobin A1C was significantly associated with BMI (r=0.29; p<.05).

Conclusion: In this sample, greater motivation for physical activity and social support for weight management were associated with lower BMI. Hemoglobin A1C was associated with greater BMI, demonstrating increased risk for diabetes based on weight. Future research should evaluate the role of motivation for physical activity and social support to improve weight management efforts in AA women.

Sponsor NIH
IRB/IACUC# 2011-164
The effect of sensory reintegration training with virtual reality and vibratory noise on gait in patients with diabetic peripheral neuropathy

Purpose: The purpose of this study was to assess the effectiveness of a training program designed to improve gait function and decrease fall risk through sensory reweighting based on the principles of stochastic resonance and using virtual reality (VR) in subjects with diabetic peripheral neuropathy.

Methods: This study was conducted using a V-Gait CAREN system. Subjects had 6, one hour long training sessions in which they walked on the treadmill at self-selected speed while practicing increasingly more challenging mobility tasks while their visual attention was engaged by the VR. During training, subjects were fitted with vibratory devices placed above the level of sensory loss (around the ankles) delivering constant sub-threshold white noise. At visits 1 and 8, assessments of gait function and fall risk were conducted using self-selected gait speed, Timed Up and Go (TUG) and Dynamic Gait Index (DGI). Data was analyzed with paired t-tests.

Results: Comparisons of pre- and post-training data revealed a significant change in TUG (p=0.02) and a significant change in DGI (p=0.02). At the end of the training subjects were able to maintain a straight walking trajectory even in the presence of visual inputs entraining lateral movements.

Conclusions: Preliminary results suggest support for the stochastic resonance theory and show that sensory retraining with VR and the vibratory device is feasible in diabetic subjects, holding promise for improvement of function due to an increased ability to integrate all sensory inputs available and a decreased reliance on visual inputs.

Sponsor Texas Medical Research Consortium RI 6026
IRB/IACUC# 2012-007

The effect of social support on outcomes of disease management for type II diabetic patients in a rural community

PURPOSE: The Texas Diabetes Prevention and Control program reported a 23% prevalence of Texas residents above the age of 65 who have diabetes. Factors such as health literacy, education, socioeconomic resources, and social support play an important role in compliance to diabetes treatment and medical outcomes. The objective of this study is to explore the relationship between support and outcomes of disease management, such as hemoglobin A1C (HbA1C), in diabetic patients over the age of 65 in rural Fredericksburg, Texas.

MATERIALS AND METHODS: Diabetic patients from the Fredericksburg Clinic who were 65 years or older were administered a 16 question survey. The survey consisted of questions about demographics, previous therapy received for diabetes, and the modified Medical Outcomes Study Social Support Survey. Patient charts were reviewed to obtain the most current HbA1C and fasting blood glucose levels. The survey was completed by 52 patients from July 7, 2014 to September 26, 2014. Pearson’s correlation coefficient was used to analyze the relationship between social support and HbA1C.

RESULTS: A total of 29 males and 23 females were surveyed. The average patient had an education of 1-3 years of college or technical school. The majority of surveyed patients were Caucasian (48 of 52). The average income was $36,000-$45,000. The average age was 74 years. The average age of diagnosis was 60 years old. Patients had an average of 3 diabetes-focused doctor visits per year. The average social support score was 4.1 and the standard deviation was 1.04. The average HbA1C and fasting blood glucose were 6.7 and 130.9, respectively. The standard deviation of HbA1C and fasting blood glucose were 0.94 and 46.61, respectively. The Pearson’s correlation coefficient between average social support score and HbA1C was 0.11. The Pearson’s correlation coefficient between average social support score and fasting blood glucose was 0.04. Therefore, no correlation exists between HbA1C and fasting blood glucose with average social support score.

CONCLUSION: Due to a relatively small sample size, no correlation between social support and diabetes management was found. However, further research is still needed to explore the impact of social factors on diabetes management in larger group studies.

Sponsor N/A
IRB/IACUC# 2014-083
Purpose: Type 2 Diabetes Mellitus, also known as adult onset diabetes, is a disease in which there is development of insulin insensitivity within the body. Recently, rises in obesity and metabolic syndrome have caused increased prevalence of type 2 diabetes in the US population, with 9.3% of the US having the disease, and about 1.7 million new cases per year. As a health consequence, diabetes has become the 7th leading cause of death in the United States. The purpose of this research was to analyze the barriers in prevention and treatment of type 2 diabetes mellitus, as well as propose solutions to addressing this growing problem.

Methods and Materials: To examine diabetes prevalence dependent on different social factors, information was collected from the CDC's National Diabetes Statistics Report and the American Diabetes Association. For Texas, statistics from the Texas Department of State Health Services were examined. From this information, significant barriers towards prevention and treatment were identified. Solutions to these barriers were analyzed to find the most efficacious methods of prevention and treatment of type 2 diabetes.

Results: The prevalence of diabetes has risen in recent years, due in part to lack of diet, exercise, and education in the community. Dietary factors that are responsible for increased prevalence dealt with the lack of access to healthier foods and ease of access to foods that are cheaper but lack nutritional substance (so called 'empty calories'), mainly seen in low socioeconomic locations. A decrease in time spent exercising was also noted; exercise results in a higher caloric consumption by the body, as well as being linked to prevention and mild reversal of insulin insensitivity. Lack of information was seen as a major contributor, especially for people of lower socioeconomic standing.

Conclusions: These barriers provide a great deal of resistance in the treatment and in the prevention of type 2 diabetes, thus they must be brought down if there is to be effective containment of diabetes development. Programs and support groups have shown significant increases in the development of knowledge of the patient on not only treating their own diabetes, but in also helping people make more informed decisions. Early childhood intervention was shown to be a major benefit to disease prevention, with plans such as school lunch remodeling and nutrition education helping inform and direct children towards healthier lifestyles.

Sponsor N/A
IRB/IACUC#
A Biopsychosocial Analysis of Professional Undergraduate Medical Education in the United States

The biopsychosocial model of illness asserts that treating patients is a holistic process, thus emphasizing the importance of holistic medical training. In this light, I have conducted a novel biopsychosocial analysis of three (3) key components (basic sciences, psychology, and sociology) of 21st-century professional medical education in the United States. I conducted a literature review of empirical research, news articles, and medical school curriculum web pages. I found a strong emphasis on the hard sciences in the basic sciences component of (primarily) allopathic medical education. The present analysis is thus limited in scope, due to limited data available for osteopathic, homeopathic, and naturopathic modalities, which are utilized by many patients. Research in these areas is highly recommended. Moreover, the analysis of the psychological component of medical education concludes that professional medical education should teach patient-desired skills and qualities, such as communication and empathy, to their students via practice with simulated and virtual patients, as well exposure to theatre and the humanities. Likewise, medical schools should encourage students to enter primary care and also train their students in sociology to tackle the problems of health inequalities in the United States healthcare system. The final conclusion of this study is that, in order to deliver the most holistic health care possible, it is necessary to expose medical students to the vast array of topics that affect medicine.

Sponsor N/A
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Empowerment Evaluation: A Learning Model

Purpose:
To demonstrate the use of empower evaluation as a teaching/learning and it's role in promoting inter professional Education.

Background:
A successful community program must include a continuous quality improvement system that increases its likelihood of accomplishing the set goals (Fetterman & Wandersman, 2005). In order to build this continuous system, stakeholders must have the tools to plan, implement and evaluate their program. Often community organizations lack these tools, thus, creating a barrier in achieving their specified goals. Empowerment evaluation aims to provide such tools to the developers and stakeholders. Driven by the idea of improvement, in empowerment evaluation participants have full control and ownership of their decisions (Fetterman & Wandersman, 2005). Additionally, empowerment evaluation recognizes inequalities and thrives to bridge the gap through social justice, inclusion, community involvement and democratic participation. Hence, it is a necessary approach to a successful program.

Method:
In a graduate level evaluation course offered by Behavioral and Community Health Department at University of North Texas Health Science Center, a group of students conduct empowerment evaluation with partner organizations as a part of their service learning project each semester. The group initiates this process through dialogue with the organization; helping stakeholders reflect on their work, goals, achievements, existing data collection and management methods, and a vision for the future. Hence, this course provides empowerment evaluation as a teaching as well as a learning model.

Results:
Through this course two successful empowerment evaluations were completed during spring and fall semesters of 2014. Two community organizations were involved in this process in the respective semesters. The partner organizations shared their anxiety attached to large data management and interpretations and identified it to be one of their major barriers in developing full ownership of their respective programs. They expressed their desire to learn to effectively manage their data which would better equip them in keeping track of their progress. The class, in turn, helped these organizations understand and learn the simple ways in which data can be managed and presented these ideas to the organizations as the final project. Both partners are now implementing these ideas in various capacities. Hence, both organizations have increased their sense of ownership of their respective programs.

Conclusion:
This poster aims to highlight this unique approach to empowerment evaluation as a teaching/learning model. Moreover, the poster hopes to shed light on the importance of inter-professional learning; collaborating with organizations that work parallel to the fields of public health and appreciating co-learning in its truest sense.
Helping students beat the odds: Large scale Freshman Research Initiative improves student performance and persistence in the sciences

Purpose: The U.S. is not producing enough graduates in STEM (science-technology-engineering-math) fields to meet current and projected needs. The Freshmen Research Initiative (FRI) is a large-scale undergraduate research program that involves students at the University of Texas at Austin (UT) in authentic research in the areas of biology, chemistry, physics, computer science, astronomy, and math beginning early in their undergraduate career. The purpose of this study was to assess the efficacy of FRI in improving undergraduate student persistence and success in the sciences.

Methods: Using data from 2006 to 2012, we assessed whether participation in FRI showed differences in passing gateway courses, accumulating credit, remaining in academic track, maintaining adequate GPAs, and obtaining a degree. Multiple logistic regression analyses with adjusted odds ratios (AORs) were conducted to determine any significant differences in outcomes between FRI participants and all other students in their CNS entering freshman cohort after adjusting for demographic characteristics, college preparedness, and participation in other college programs.

Results: Differences in demographic characteristics, college preparedness, and participation in other college programs were found between FRI participants and non-FRI participants. However, after adjusting for all factors related to demographic characteristics, college preparedness, and participation in other college programs, FRI participants were significantly more likely to have desired outcomes such as having a GPA ≥ 3.0 and graduating with a science degree within four years and were significantly less likely to have undesired outcomes such as having a GPA < 2.0 and failing science classes.

Conclusions: The results indicate that FRI participation was related to improved undergraduate student persistence and success in the sciences. Programs like FRI may help students overcome risk factors such as lack of college preparedness and underrepresented status, and, thus, address our national shortage of STEM graduates.

Sponsor: N/A
IRB/IACUC#: UT Austin IRB protocol number 2011-12-0001

Integrating Medical Research into the Undergraduate Medical Education Curriculum

Purpose: Medical research is an important, yet often under represented, component of undergraduate medical education (UME). Though acknowledged, the fundamentals of biomedical research and its application to clinical medicine are infrequently part of the UME curriculum. To address this need, in 2013 – 2014 University of North Texas Health Science Center (UNTHSC) faculty and Cook Children’s Medical Center (CCMC) medical staff came together to formalize a mentored research program for medical students. A collaborative Pediatric Research Program (PRP) was established, with the goal of providing a mentored research experience for medical students designed to enhance research awareness and knowledge through systematic investigation, including research development, testing and evaluation.

Methods: Medical Students completing the first year of UME who expressed an interest in pediatric research were eligible to participate in the PRP. Students were given options in various areas of Pediatrics. All of the students were able to participate in their first or second preferred research area in Pediatrics. All administrative procedures and requirements were completed before the program started, including Collaborative Institutional Training Initiative (CITI) and Best Clinical Practices certification. A four week didactic course, which included- i) Research Design and Protocol Development; ii) Literature Review / Copyright and Plagiarism Issues; iii) Data Collection and analysis; and iv) Presentation and Publication Guidelines and Tips, took place during the students’ summer break of 2014.

Results: 25 students joined PRP with mentorship of 19 faculty mentors. The faculty mentors were either General/Specialist in Pediatrics (MD/DO) or Doctor of Philosophy (PhD) with research-focused in Pediatrics. Out of 25 students, only 3 chose not to continue their research project in Year II of medical school. The students, who continued research during Year II of medical school, presented status reports of their projects to group of research mentors, administrative staff and fellow students in fall 2014.

Conclusions: Majority of students were very satisfied with their mentors’ contributions in helping them achieve their research goals. Most of the students were very satisfied with accessibility to their faculty mentors and research coordinators. Almost all of the students were satisfied with clarity and practicality of program requirements and found the didactic course beneficial.

Sponsor: N/A
IRB/IACUC#: UT Austin IRB protocol number 2011-12-0001
Peerwise Study for Assessment of Higher Order Thinking in Students

This study investigates the impact of PeerWise software system (Denny et al., 2008) as an instructional strategy to increase the quality of student's ability to construct a multiple-choice question (MCQ's) that tests Higher-Order Thinking (HOT). Today's education system goes beyond recalling and understanding facts, and assessing learning outcomes. Promoting students' HOT skills should be considered as an important educational goal. According to Bloom's (1956) taxonomy, HOT is about engaging students at the highest levels of thinking to foster stimulating learning environments where students become creators of new ideas, analyzers of problems, generators, and evaluators of knowledge. PeerWise is a web-based system that supports the creation of MCQ's by students, allowing them to provide an explanation for their question. It enables students to answer questions generated by other students, and helps them evaluate the quality of each question using a HOT rubric. We conducted statistical analysis on the number of questions created by students, number of questions answered, number of substantial comments, and average question rating. Additionally, students were given a pretest and posttest before and after the use of Peerwise to assess the improvement in HOT skills. We test the benefits of providing PeerWise support and conclude that PeerWise works efficiently to improve HOT skills in students.

Pre-Clinical Medical Student Attitudes Toward Interprofessional Practice

Hypothesis: (1) Brief exposure to Interprofessional Practice (IP) curriculum will improve student attitudes about working within a medical team model of care.

Objectives: The IP curriculum was created to capitalize on the expertise from multiple healthcare professionals working together to enhance patients' quality of care, resolve safety issues, and improve prognostic outcomes [1]. The integrated model of care is especially relevant to the osteopathic philosophy of holistic medical practice. Thus, students who are exposed to IP curriculum should have a better understanding about the importance of providing patient care within an interdisciplinary team of healthcare professionals. First, a longitudinal, paired comparison study of pre-clinical medical students who matriculated in July, 2012 and had received at least one formal course of IP education was designed to measure pre- and post-course attitudes about interprofessional healthcare. A larger cross-sectional study was conducted to examine potential relationships among attitude response items from pre-clinical medical students who matriculated in 2010 - 2014.

Materials and Methods: Pre- and post-course attitudes were measured with the Attitudes Toward Health Care Teams (ATHCT) Scale, a 21-item validated tool [2]. Comparisons were analyzed using a one-way ANOVA with semester entered as a grouping variable. A correlation matrix was used to examine attitude response item relationships in the cross-sectional analyses. A 95% confidence interval and a probability of >0.05 was considered statistically significant.

Results: 190 students completed the ATHCT in both the pre- and post-course conditions. Out of 21 response items, 10 showed no significant improvement in attitudes such as team care results in more complications (item #1, p = 0.29), team care results in holistic patient care (item #5, p = 0.44), increased satisfaction (item #8, p = 0.28), or patient needs are better met (item #20, p = 0.15).

Conclusions: Although pre-clinical medical students were exposed to various interprofessional team experiences (community service, preceptorship) and at least one formal IP class session, these data show some resistance and misunderstanding about the importance of the team model of care. More IP coursework exposure and clinical faculty teaching by example in the clinic may help strengthen the team model of care.
Psychomotor Videos for Osteopathic Manipulative Medicine (OMM) Instruction

Hypothesis: Osteopathic Manipulative Medicine (OMM) lab often consists of demonstration from the stage by a professor accompanied by small group practice with faculty table trainers. However, given a low faculty to student ratio, class demonstrations do not optimize student’s time with table trainers. We hypothesize that our instructional videos will improve student satisfaction by limiting need for class demonstration, thus increasing one on one instruction with table trainers.

Research Design: Prospective Experimental – IRB approved.

Materials and Methods: We designed videos with written instructions that incorporate psychomotor learning principles for year 2 osteopathic medical students. Instructional videos for Still and Facilitated Positional Release techniques were used in lieu of faculty demonstration during lab. Three surveys were administered to the second year Texas College of Osteopathic Medicine class to assess their satisfaction with the current teaching method compared to the new instructional videos. Clinical competency scores were also compared to the previous year’s class who did not have the videos.

Results: The instructional videos improved student confidence and satisfaction when compared to the traditional method. However, no clear statistical significance was found between exam scores when compared to the previous years’ students.

Conclusion: The new instructional videos showed improvements in student satisfaction and confidence compared to traditional methods. Use of the videos could allow more time for feedback from faculty table trainers. Exam scores did not improve, however factors involving small sample size and varying faculty graders could account for this finding. Videos could serve a valuable role in the education of osteopathic students in OMM.

Sponsor: UNTHSC Innovations in Teaching Using Technology Seed Grant

IRB/IACUC# 2014-098

Seniors Assisting in Geriatric Education (SAGE): Reynolds Program addresses the lack of training in geriatrics and provides a model for interprofessional education.

Seniors Assisting in Geriatric Education (SAGE) is a program that helps healthcare students develop competency with older adults and strengthen their clinical applications of medical education through an interprofessional team experience. Two objectives for this study: 1) To increase development of competency in attitudes, knowledge, and skills in the care of older adults; and, 2) To provide an interprofessional experience where students learn about, with, and from collaborating as a team member in the context of working with an older adult.

Senior volunteers 60 years and older are mentors in the program. Student teams meet with senior mentors in their homes for a series of home visits over the course of a two year period. SAGE curriculum guides program content and is delivered through an online learning system. Student teams conduct eight home visits which include conducting environmental home safety and nutritional assessments; medical history, physiology of aging, bio-psychosocial interviews; medication reconciliation, review of community resources, and end of life issues. A survey was administered to students to evaluate perceptions of learning after participating in the SAGE Program; this is a self-report model.

A quantitative survey using a five-point Likert Scale evaluates student perceptions of learning. Findings (n=332) revealed modest levels of student confidence and attitudes toward geriatric patients (3.6), and comfort in performing physical examinations (3.5). Higher levels were found in recognizing unique medical and psycho-social issues (3.8); competency in interviewing, physical assessment and examination skills (3.8); and practice using ADLs and IADLs (3.8). Highest overall scores were found in environmental home safety and falls risk (3.9); use of Mini-Mental Status Exam (3.9); and real world experience (4.0).

The SAGE experiential learning program provides insight into medical student perceptions toward older adults using a senior mentoring and home visit model. Medical education in geriatrics combined with experiential learning in student teams resulted in modest improvement in student perceptions of confidence and patient interaction.

Sponsor: Donald W Reynolds Foundation

IRB/IACUC# 2009-074
Purpose: The purpose of this research was to evaluate the effects of student to student peer interactions during service learning (SL) activities on the overall learning experience.

Materials/Methods: Sixty eight Doctorate of Physical Therapy (DPT) students were randomly assigned to one of two SL activities. SL 1 was a fall prevention program called Seniors in Action, in which each pair of DPT students had to assess fall risk and implement exercise programs working directly with senior participants. Activity 2 was an in-class case study based on the assessment derived from SL 1, including plan of care development without exercise implementation. All students spent 5 hours involved in one of the two SL activities and were supervised by a licensed DPT. Outcomes were assessed by the student responses to pre- and post- surveys using a Likert-like scale and self-reflection comments. Questions on pre- and post- surveys evaluated the anxiety level on working with seniors, confidence level in ability to communicate, screen for risk for falls, interpret results, as well as the effect of peer interaction on facilitating the learning activities. Data was analyzed with paired t-tests.

Results: Pre- SL students in Year 2 had significant lower anxiety and higher confidence compared to Year 1 students (p=0.02 and p<0.01 respectively). However students from both years increased their confidence level in PT skills both after the SL 1 and SL 2 (p<0.001 and p=0.01). Anxiety levels decreased in Year 1 students (p=0.03) but did not changed for students in year 2 (p=0.1) post-SL. Students in year 1 reported that peer interaction during SL facilitated their learning more than year 2 student (p= 0.02).

Conclusion: The SL activities were effective in meeting a community need, decreasing student anxiety toward geriatric population, improving confidence of professional skills and positive learning experience from peer interaction. Overall reflection comments expressed student satisfaction and affirmed benefits of learning from peers during SL. SL combined with peer pairing provides excellent opportunity for active learning while employing practical application which in turn strengthens a PT program curriculum.

Sponsor n/a
IRB/IACUC# 2013-190
Results: BMP4 (10ng/ml) significantly induced ID1 and ID3 mRNA and protein expression, starting 30 minutes after treatment (p

expression of IDs in TM cells and determine the role of BMP4 induced ID1 and ID3 in regulating TGFb2 induction of ECM proteins

BMP4 pathway are inhibitor of DNA binding proteins (IDs). There are four family members of IDs (ID1-4). In this study, we determine the

is to determine the mechanism by which BMP4 inhibits the TGFb2 induction of ECM proteins in the TM. Prominent downstream targets of the

Due to the small samples size, further experiments are required. We will also try to determine possible genetic components such as the ratio between GC receptor isoforms GRα and GRβ in the TM cells.

Sponsor
N/A

IRB/IACUC#

A Study of Consistency of Dexamethasone Responsiveness between Paired Bovine Eyes

Purpose: Glucocorticoid (GC) therapy can lead to elevated intraocular pressure (IOP) and GC-induced glaucoma. IOP elevation is also a major risk factor for the development and progression of primary open angle glaucoma (POAG). Glaucomaticus and GC-induced IOP elevation is due to increased aqueous outflow resistance in the trabecular meshwork (TM). Because the pathological findings and clinical presentations of the two types of glaucoma are similar, GC-induce ocular hypertension often used as a model to study POAG. Although the bovine eye perfusion culture model has been established, the consistency of paired bovine eyes to GC treatment has not been determined. Therefore, this study is to determine if Dexamethasone (DEX) changes IOP similarly in paired bovine eyes.

Methods: Fresh bovine eyes were obtained from local abattoir, transferred to the lab and carefully dissected. The vitreous, uveal tract, retina, retinal pigment epithelium, and lens were removed. The remaining anterior segment, which contained the cornea, sclera, and TM, was mounted and sealed on a custom-made acrylic dish with an O-ring. Perfusion medium was infused by a syringe pump at a constant infusion rate of 5 µL/min. After IOP was stable, bovine eyes were perfused with medium containing 0.1% dexamethasone for 6-7 days. Bovine eyes with IOP elevation of more than 2.82mmHg was defined as a responder eye according to our published results.

Results: Of the seven pairs of bovine eyes tested, one pair of eyes were DEX responders and the other six pairs were non-responders. The responder pair had IOP elevation of greater than 2.82mm Hg in both eyes. The other six pairs of non-responder eyes showed IOP change between -0.6 and 1.7 mm Hg.

Conclusion: Our study showed that the DEX-responsiveness in paired bovine eyes are highly consistent. As suggested by early studies, it is very likely that induced IOP elevation and glaucoma are highly associated with genetic background. These results further validate the use of paired bovine eyes in glaucoma research. Due to the small samples size, further experiments are required. We will also try to determine possible genetic components such as the ratio between GC receptor isoforms GRα and GRβ in the TM cells.

Sponsor
N/A

IRB/IACUC#

BMP4 Induced ID Protein Protects TM From Glaucomatous Effects of TGFβ-2

Purpose: Elevated levels of pro-fibrotic growth factor transforming growth factor b2 (TGFb2) are have been reported in the aqueous humor and trabecular meshwork (TM) of primary open angle glaucoma (POAG) patients. TGFb2 treatment results in accumulation of extracellular matrix (ECM) molecules in the TM, which are associated with increased outflow resistance. Expression of TGFb2 in rodent eyes and ex-vivo anterior segment perfusion models elevate intraocular pressure, suggesting that TGFb2 plays a role in the development and progression of glaucoma. Interestingly, bone morphogenetic protein 4 (BMP4) inhibits ECM proteins that are up-regulated in TM cells by TGFb2. The purpose of our study is to determine the mechanism by which BMP4 inhibits the TGFb2 induction of ECM proteins in the TM. Prominent downstream targets of the BMP4 pathway are inhibitor of DNA binding proteins (IDs). There are four family members of IDs (ID1-4). In this study, we determine the expression of IDs in TM cells and determine the role of BMP4 induced ID1 and ID3 in regulating TGFb2 induction of ECM proteins

Methods: Time and dose dependent BMP4 induction of ID1 and ID3 were studied in cultured human TM cells by Q-PCR and western blot analysis. GTM3 cells were transfected with pCMV-ID1 and pCMV-ID3 plasmids to determine their effect on TGFb2 induced ECM proteins

Results: BMP4 (10ng/ml) significantly induced ID1 and ID3 mRNA and protein expression, starting 30 minutes after treatment (p

Conclusions: BMP4 induced ID1 and ID3 expression in TM cells, and ID1/ID3 suppressed the profibrotic ECM effects of TGFb2. Therefore, the BMP4 suppression of TGFb2 effects in TM cells may be mediated by ID1 and ID3. Further this study suggests ID1 and ID3 to be potential therapeutic targets for POAG.

Sponsor
NIH grant EY-017374 (N/A)

IRB/IACUC#
Characterization of Novel Sigma-1 Receptor (σ1-r) Ligands

Purpose: Sigma-1 receptors (σ1-rs) are non-opioid ligand receptors that are associated with the endoplasmic reticulum. Upon agonist stimulation during stress, these receptors have the ability to translocate to the plasma membrane. σ1-rs are known to mediate ion channels such as L-type Voltage Gated Calcium Channels (VGCCs), thus facilitating neuroprotective effects in neurons such as retinal ganglion cells (RGCs). The purpose of this study was to determine if novel σ1-r agonist (PB190) and novel σ1-r antagonist (PB212) in purified RGCs have similar actions to that of known σ1-r agonists and antagonists, such as Pentazocine and BD1063, respectively.

Methods: Purification and the culture of RGCs were performed by a double immunopanning technique using an antibody to Thy1.1 from P3-P7 Sprague-Dawley rats. RGCs were cultured for 5-7 days in vitro prior to experiments. Purified RGCs were incubated for 30 minutes with 1µM treatments of either Pentazocine, PB190, BD1063, PB212, or PB212 + PB190 combined. FURA-2 AM fluorescent dye was used to determine calcium concentration within RGCs. Immunoblot and immunocytochemistry were used to determine purity of RGCs and expression of σ1-r.

Results: Immunocytochemistry determined 98% purity of isolated RGC cultures following 7 days in vitro. σ1-r expression was identified in purified RGCs through immunocytochemistry and immunoblot (MW~26 kDa). Intracellular calcium concentration [Ca2+]i was determined in RGCs where control (no treatment) group calcium levels were equal to 265 ± 104 nM. Pentazocine [Ca2+]i levels were equal to 115 ± 13 nM. PB190 [Ca2+]i levels were equal to 102 ± 9 nM. BD1063 [Ca2+]i levels were equal to 119 ± 13 nM. PB212 [Ca2+]i levels were equal to 118 ± 14 nM. PB190 and PB 212 co-treatment [Ca2+]i levels were equal 135 ± 15 nM. At the concentrations used (1µM), all of these σ1-r ligands significantly [Ca2+]i levels compared to control group.

Conclusion: All σ1-r ligands utilized in this study modulated basal intracellular calcium levels. The new compounds PB190 and PB212 have similar effects in decreasing basal calcium levels as those seen in the known compounds Pentazocine and BD1063. Activation or inhibiting σ1-r could be modulating calcium channels involved in homeostasis such as the VGCCs. Future studies are needed to determine if these new ligands are more efficacious than that of known σ1-r ligands, and what other calcium channels they may modulate.

Sponsor: N/A

IRB/IACUC#: 2012/13-17-A05
Crosstalk of transforming growth factor beta-2 and toll-like receptor 4 in the trabecular meshwork

Purpose: Glaucoma is characterized by progressive optic neuropathy that is associated with elevated intraocular pressure (IOP) and extracellular matrix (ECM) remodeling. The trabecular meshwork (TM) is involved in the outflow of aqueous humor and IOP regulation. Glaucomatous eyes show elevated levels of transforming growth factor-β 2 (TGF-β2) and its signaling pathways in the ECM of the TM have been extensively studied. Recent evidence has implicated toll-like receptor 4 (TLR4) in the regulation of ECM and fibrogenesis in the liver, kidney, lung and skin. Based on the potential for shared signaling pathways, we hypothesize that endogenous TLR4 ligands activate TLR4 and augment TGF-β2 signaling sensitivity by downregulating BAMBI, leading to increased ECM production in the TM and increase IOP.

Methods: Cross-sections of human donor eyes and dissected mouse TM rings were used to determine TLR4 expression in the TM. Primary human TM cells were used to test for the expression of BAMBI. To study the role of TGF-β2 and TLR4 crosstalk in the expression of ECM proteins, four primary human TM cell strains were treated with a selective TLR4 inhibitor (TAK-242, 15µM), TGFβ2 (5ng/ml), and a TLR4 ligand (Fibronectin-EDA isoform). In-vivo studies were carried out to examine the induction of ocular hypertension in wild-type (A/J, AKR/J, BALBc/J, and C3H/HeOuJ) or Tlr4 mutant strains of mice (C3H/HeJ) by intravitreally injecting Ad5.hTGFβ2242, 15µM and TGFβ2 (2.5x10^7 pfu) in one eye while the contralateral uninjected eye was used as negative controls.

Results: Our studies reveal the expression of TLR4 in the human and mouse TM. BAMBI is expressed in human TM cells and its expression is significantly decreased in the presence of TGF-β2. Inhibition of TLR4 in the presence of TGF-β2 decreases fibronectin and collagen-1 expression. Activation of TLR4 in the presence of TGF-β2 increases fibronectin and collagen-1 expression and TLR4 inhibition blocks this effect. Our in-vivo studies show that Ad5.hTGFβ-2 induces ocular hypertension in wild-type mice but has no effect in Tlr4 mutant mice.

Conclusions: These studies identify TGFβ2 – TLR4 crosstalk as a novel pathway involved in ECM regulation in the TM and ocular hypertension. These data provide potential new targets to lower IOP and further explain the mechanisms involved in the development of glaucomatous TM damage.

Histone Acetylation as an Epigenetic Regulator of Glaucoma-Associated Growth Factors in the Trabecular Meshwork

Glaucoma is a leading cause of blindness in the U.S. and worldwide. This disease leads to progressive, irreversible damage to the optic nerve and visual function. The primary risk factor of primary open angle glaucoma (POAG), the major type of glaucoma, is elevated intraocular pressure (IOP). IOP elevation in glaucoma patients is due to glaucomatous insults to the trabecular meshwork (TM) and compromised TM function, which increase aqueous humor outflow resistance. In the glaucomatous TM (GTM), there is excessive extracellular matrix (ECM) protein deposition. Many studies have suggested that cell signaling pathways, such as the transforming growth factor beta (TGF-β) and Wnt signaling pathways, play key roles in TM homeostasis. The growth factors that are associated with these pathways, including TGFβ1 and sFRP1, are increased in the GTM cells compared to normal TM cells. Little is known about the role of epigenetics in regulating glaucoma-associated growth factors in the TM. We hypothesize that histone acetylation is responsible for the increased expression of glaucoma associated factors in the TM. Primary human TM cell cultures were treated with 10nM Thalidomide (TDP-A), a histone deacetylase inhibitor (HDACi), or 1% DMSO as vehicle control for 3 - 4 days. TM cells were a kind gift from Novartis. RNA was extracted for qPCR to compare gene expression. We also treated paired perfusion cultured bovine anterior segments with DMSO or TDP-A for 7 to 10 days. Additionally, we treated paired perfused anterior segments with TDP-A or TDP-A plus sFRP-1 or TGFβ receptor 1 inhibitors. The IOPs of the bovine eyes were continuously monitored. Data were analyzed by using Student’s t-test. P values less than 0.05 were considered significant. We found that TDP-A elevated the expression of sFRP-1 and TGFβ1 in TM cell cultures. Our bovine eye perfusion culture study also showed that TDP-A treatment increased the expression of sFRP-1 and TGFβ1, as well as significantly elevated IOP (n=9, p less than 0.05). Furthermore, use of sFRP-1 or TGFβ receptor 1 inhibitors decreased IOP. Histone acetylation may play an important role in the dysregulation of growth factors in the GTM. This mechanism provides a unique opportunity to elucidate the etiology of POAG. Also, TDP-A is a potent HDACi that can be used as a powerful research tool in glaucoma research.
**In Vivo Detection and Modulation of Reactive Oxygen Species in a Mouse Model of Retinal Ischemia/Reperfusion**

Purpose: Ischemia results in deprivation of oxygen and metabolic substrates, energy depletion, and ultimately cell death. As a result, there is a significant and detrimental increase in free radical formation, mediators of oxidative stress. Our study aims to establish a novel method for noninvasive in vivo detection of reactive oxygen species (ROS).

Methods: Retinal ischemia/reperfusion (I/R) was induced in left eyes of C57BL/6J mice. They were cannulated in their anterior chamber, and intraocular pressure (IOP) was raised to 120 mmHg for 60 minutes. Right eyes served as internal controls. Detection of ROS was conducted by a chemiluminescent compound L-012. At indicated days after I/R, L-012 (75mg/kg) was injected intraperitoneally. Pupils were dilated using phenylephrine HCl 2.5% and mice were placed in the small animal In Vivo Imaging System Lumina XR 15 minutes after L-012 administration. In some studies, ROS scavenger TEMPOL (100mg/kg) or NADPH oxidase inhibitor apocynin (50mg/kg) was injected 30 minutes prior to L-012 treatment. At day 14, eyes were harvested and paraffin embedded for H&E staining. Retinal morphological changes were evaluated. All measurements were conducted in Living Image software (Caliper Life Sciences) and statistical analysis was performed using SigmaPlot (Systat).

Results: L-012 chemilluminescent signals were successfully detected in the I/R-injured eyes following systemic L-012 administration. Over a 14-day time course, only 24 and 48 hours post I/R were statistically significant (p<0.05) signals detected for greater than 1 hour after L-012 injection. No toxicity or gross inflammation was observed throughout the eye. Treatment with both TEMPOL and apocynin caused a statistically significant (p<0.01) reduction of L-012 radiance at both 24 and 48-hour time points.

Conclusions: Our studies indicate retinal I/R causes a transient and significant induction in ROS production. L-012 appears to be a reliable and nontoxic tool for noninvasive detection of ROS in mice. Furthermore, we showed TEMPOL and apocynin successfully reduce chemiluminescent signal through the removal of excess ROS. Previous detection of ROS was possible only in post mortem samples; however, our method does not require euthanasia of animals fulfilling a largely unmet need in the study of oxidative stress.

**Mechanisms Underlying AMPA-Mediated Excitotoxicity of Retinal Ganglion Cells Under Hypoxic Conditions**

Purpose: Excessive AMPA receptor (AMPAR) stimulation has been implicated in producing excitotoxicity in many neurodegenerative diseases such as glaucoma. The purpose of this study was to investigate if AMPAR desensitization attenuates excitotoxicity in purified retinal ganglion cells (RGCs) under normoxic and hypoxic conditions.

Methods: Purified RGCs were treated with AMPAR agonists (100μM s-AMPA (desensitizing), 100μM kainic acid (non-desensitizing)), an AMPAR modulator (100μM cyclothiazide), AMPAR antagonist (50μM C FM-2), and kainate receptor antagonist (50μM UBP301) for 72h in RGC defined medium. To determine if excitotoxicity occurs following hypoxic injury, RGCs were subjected to oxygen-glucose deprivation (OGD) for 4h, followed by s-AMPA treatment under OGD for an additional 4h. Live-Dead Assays were carried out to assess cell viability. AMPA receptor mediated calcium influxes in RGCs were determined by imaging with fura-2 AM following 4h either normoxic-glucose-free or OGD treatments.

Results: Significantly enhanced viability was found in RGCs treated with 100μM s-AMPA (84 ± 1% viable) compared to vehicle (0.1% DMSO) group (71 ± 4% viable) alone (ps-AMPA in combination with cyclothiazide or kainic acid significantly reduced cell viability to 50 ± 3% and 54 ± 2%, respectively (ps-AMPA (22 ± 5% viable) following OGD injury compared to those under normoxic-glucose-free conditions (67 ± 4% viable). Additionally, no significant decrease in RGC survival was observed when OGD was carried out for 8h in the presence of s-AMPA in the cell culture medium (85 ± 2% viable). Increased calcium influx was observed when RGCs were maintained in OGD (1085 ± 97 nM) compared to control (764 ± 72 nM). However, there was no difference between treatments of normoxic-glucose-free and RGC medium with RGC defined medium.

Conclusions: Desensitization of AMPAR is a key determinant of s-AMPA-mediated excitotoxicity, whereby blocking the desensitization of AMPAR induces cell death. Future studies will determine if AMPAR subunits with greater ion current influx possibly mediate increased sensitivity to excitotoxicity following injury.
Novel Strategy for RPE Protection: Glutaredoxin-Targeting Natural Products

Purpose: Oxidative stress-induced retinal pigment epithelial (RPE) cell damage is known as an important factor in the pathogenesis of retinopathies, such as age-related macular degeneration (AMD). In our previous study, we identified glutaredoxin 1 (Grx1), a thiol-disulfide oxidoreductase, as a new cytoprotective enzyme in RPE cells. In this study, we searched for small molecule Grx1 inducers from natural products to protect RPE cells from oxidative damage.

Methods: Five natural antioxidant phenolics, including Salvianolic acid A (Sal A), Salvianolic acid B (Sal B), total salvianolic acid, curcumin, and epigallocatechin gallate (EGCG) were screened for their Grx1-inducing activities and cytoprotective effects in primary human RPE cells. Grx1 expression was examined by Western blot. Cell viability was evaluated with the WST8 assay. The level of protein glutathionylation (PSSG) was measured by using anti-PSSG antibody.

Results: Among all the tested compounds, Sal B was found to be the most potent Grx1 inducer, which upregulated Grx1 by ~3 fold at 50 µM after 24 h. In both a time and dose-dependent manner, Sal B protected cells from H2O2-induced cell viability loss. Sal B also reduced annexin V positive cells, decreased Bax/Bcl-2 ratio, prevented caspase-3 cleavage, and inhibited ROS production. Additionally, H2O2-induced PSSG accumulation was markedly decreased by Sal B treatment. Moreover, knockdown of Grx1 by siRNA significantly reduced the cytoprotective effects of Sal B.

Conclusions: Sal B protects primary human RPE cells from oxidative stress-induced damage by upregulating Grx1. Naturally occurring Grx1 inducers may be used as new therapeutic strategies to treat oxidative stress-related retinopathies like AMD.

Sponsor: UNTHSC faculty Startup Fund to Hongli Wu

IRB/IACUC#: 2011/12-58
Retina ganglion cell subtype specific cell death following optic nerve crush in mice

Purpose: Glaucoma is an optic neuropathy that causes cupping of the optic disc, retina ganglion cell (RGC) loss, and characteristic visual field defects. Published literature suggests differential RGC susceptibility to damage. However, the mechanisms by which the optic nerve and RGCs become more susceptible to injury and damage are largely unknown. We investigated individual RGC subtypes’ susceptibility to damage after optic nerve crush (ONC).

Methods: We utilized two mouse strains that selectively express GFP in individual RGC subtypes: CB2-GFP strain (selectively expresses GFP in transient OFF-alpha RGCs) and TRHR-GFP strain (selectively expresses GFP in On-Off direction selective RGCs). ONC was performed unilaterally, with the contralateral eye serving as a control. RGC subtype specific damage was evaluated at 0, 1, 3, 7, and 14 days post ONC. RGC damage was assessed by immunofluorescence of labeled retinal flat mounts using the GFP biomarker for the specific RGC subtypes and NeuN for total RGCs.

Results: Throughout the 14 day time course, GFP positive RGCs in the CB2-GFP strain died faster than the GFP positive RGCs in the TRHR-GFP strain, with similar rates of total RGC death in each strain. The half-life (T1/2) of GFP positive cells in the TRHR-GFP strain was T1/2=7.11 days with total RGC death T1/2=9.65 days. There was a significant difference in percent cell survival of each individual RGC subtype at 3 days (TRHR-GFP, 61.3 +/- 7.4%; CB2-GFP, 38.2 +/- 14.3%; n=4, p=0.029), 7 days (TRHR-GFP, 63.1 +/- 26.4%; CB2-GFP, 22.2 +/- 5.3%; n=4-5, p=0.011) and 10 days (TRHR-GFP, 38.0 +/- 2.9%; CB2-GFP, 3.5 +/- 3.5%; n=4-5, p<0.001) post-crush. There was no significant difference in percent cell survival of each individual RGC subtype at 1 day (TRHR-GFP, 76.2 +/- 20.9%; CB2-GFP, 70.3 +/- 10.0%; n=4-5, p=0.621) and 14 days (TRHR-GFP, 5.0 +/- 6.5%; CB2-GFP, 2.6 +/- 3.3%; n=3-4, p=0.556) post-crush.

Conclusions: These studies demonstrate differences in individual RGC subtype susceptibilities to ONC. These data provide valuable information to develop new targets to slow and/or prevent the progression of RGC damage and new methods to detect early damage in diseases such as glaucoma.

Sponsor
IRB/IACUC# 2011/12-58

Role of Extracellular Matrix Crosslinking Enzymes in the Trabecular Meshwork

Purpose - Transforming Growth Factor - B2 (TGFβ2) increases deposition of extracellular matrix (ECM) in the trabecular meshwork (TM), which could be responsible for increased aqueous humor (AH) outflow resistance in primary open angle glaucoma (POAG). TGFβ2 induces expression of extracellular matrix (ECM) crosslinking enzymes tissue transglutaminase (TGM2), Lysyl oxidase (LOX) and Lysyl-oxidase like 2 (LOXL2) in the TM. These enzymes covalently crosslink ECM proteins leading to resistance to ECM degradation and turnover. In POAG, there is increased expression of TGFβ2, which increases TGM2, LOX and LOXL2 expression. Increased expression and crosslinking activity of these enzymes may enhance ECM deposition in the outflow pathway. This could lead to increased AH outflow resistance and elevated IOP. To determine whether these crosslinking enzymes play a role in regulating IOP, we developed and validated TGM2, LOX and LOXL2 expression vectors in-vitro. Viral vectors expressing these enzymes will be used in ex-vivo and in-vivo models to study the effect of their overexpression on IOP and AH outflow resistance.

Materials and methods – Transformed glaucomatous TM (GTM-3) and primary TM cells were transfected with plasmids expressing TGM2, LOX and LOXL2. Conditioned medium was collected, and overexpression was determined using western immunoblots. TGM2 activity was assessed by exposing cells to biotin-cadaverine followed by incubation with AlexaFluor 488 streptavidin-conjugate followed by fluorescence microscopy. LOX and LOXL2 enzyme activity were evaluated by western blots of the substrate tropoelastin in transfected cells with or without the LOX inhibitor b -aminoproprionitrile (BAPN) for 48 hours.

Results - TM cells transfected with TGM2, LOX and LOXL2 significantly overexpressed the enzymes. The TGM2 activity assay demonstrated increased crosslinking activity in cells transfected with TGM2 expression plasmid. LOX and LOXL2 activity was increased in cells transfected with LOX and LOXL2 expression vectors as exhibited by increased expression of the LOX substrate tropoelastin in western blotting.

Conclusions - Our results indicate that TGM2, LOX and LOXL2 expression vectors significantly over-express these proteins and also show increased enzyme activity. In conclusion, these plasmid constructs will be packaged into adenovirus expression vectors and tested for effects on AH outflow and IOP in ex-vivo and in-vivo models.

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IRB/IACUC#
Transforming Growth Factor-β2 Regulated Expression of Bone Morphogenetic Protein 1 (BMP-1), Tissue Transglutaminase (TGM2), Lysyl Oxidase (LOX), Procollagen C-endopeptidase Enhancer 1 (PCOLCE1), and Periostin (POSTN) in Human Optic Nerve Head Cells

Methods: Primary human ONH cells were obtained from Alcon Laboratories (Fort Worth, Texas). Human ONH cells were isolated and subjected to qPCR (n=3) and Western immunoblotting (WB; n=6) for BMP1, TGM2, LOX, POSTN and PCOLCE1. qPCR was used to determine whether expression of BMP1, TGM2, LOX, POSTN and PCOLCE1 in ONH cells are regulated by TGF-β2 (5ng/ml). WB results were used to determine the effects of TGF-β2 on BMP1, TGM2, LOX, POSTN and PCOLCE1 protein expression in cell lysates of ONH cells treated for 48 hours. TGM2 and LOX activity assays were used to determine differences between non-treated and TGF-β2 treated in ONH cells.

Results: Human ONH cells expressed mRNA and protein for BMP1, TGM2, LOX, POSTN and PCOLCE1. Exogenous TGF-β2 statistically increased BMP1, TGM2, LOX, POSTN mRNA expression at 24 hours compared to their controls. TGF-β2 statistically decreased PCOLCE1 mRNA expression compared to their controls at 24hours. WB analysis showed induced BMP1, TGM2, and POSTN levels in cell lysates after TGF-β2 treatment compared to controls. However, WB analysis showed that TGF-β2 decreased PCOLCE1 levels in cell lysates. TGF-β2 increased both TGM2 and LOX enzyme activity in the ONH.

Conclusions: BMP1, TGM2, LOX, POSTN and PCOLCE1 are expressed in human ONH cells. These molecules may be involved in the normal function of the ONH. Altered expression of BMP1, TGM2, LOX, POSTN and PCOLCE1 by TGF-β2 may lead to functional changes and ECM remodeling within the ONH.

Poster: W81XWH-10-2-003
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Wnt induction of SMAD/TGFβ signaling in the Trabecular Meshwork

Purpose: Primary Open Angle Glaucoma is a progressive, irreversibly blinding disease, the leading risk factor of which is increased intraocular pressure (IOP) thought to be due to an inherent pathological change in the trabecular meshwork (TM) tissue. Canonical Wnt signaling genes are expressed in the TM, the primary site for regulation of aqueous humor outflow and therefore IOP. Canonical Wnt signaling activation has been found to regulate IOP, but the mechanism behind this phenomenon remains unknown. Extracellular matrix deposition in the TM caused by increased activation of the TGF-β pathway by the TGF-β2 ligand has been associated with increased IOP and with primary open angle glaucoma. In other cell types and diseases, evidence exists for crosstalk between the TGF-β and Wnt signaling pathways. Our study aims to pinpoint the affect of Wnt signaling on the glaucoma-associated TGF-β pathway in the TM.

Methods: Lentivirus-based luciferase assays were conducted in normal trabecular meshwork (NTM) and glaucomatous trabecular meshwork (GTM) cells by using TGF-β/SMAD or TCF/LEF (Wnt) signaling reporter vectors. Trabecular meshwork cells were all kind gifts from Novartis. Cell were treated with or without 100ng/ml Wnt3a or 5ng/ml TGF-β2. In some experiments, siRNAs were also used to knock down smads in NTM cells. Western immunoblotting was performed on nuclear and cytosolic fractions of NTM and GTM cells with corresponding primary as well as secondary antibodies.

Results: In NTM cells, Wnt3a treatment increased TGFβ/SMAD pathway reporter activity (n=5 p less than 0.05) but TGF-β2 did not affect and even slightly decreased TCF/LEF (Wnt) signaling activity, although this decrease was not statistically significant (n=5, P greater than 0.05). SiRNA knockdown of SMAD pathway mediator smad3 decreased Wnt3a-induced SMAD/TGFβ signaling activity (n=6 p less than 0.05) in NTM cells. However, nuclear fractions of NTM and GTM cells showed translocation of smad4 (co-smad) into the nucleus upon Wnt3a treatment but not smad2 or smad3. Nuclear fractions also showed translocation of β-catenin by TGFβ2 treatment.

Conclusions: The Wnt pathway ligand Wnt3a is able to activate SMAD/TGFβ transcriptional activity in TM cells, but not vice versa. This activation seems to involve translocation of only smad4. We hypothesize that a protein complex consisting of β-catenin and smad4 can form in the TM. By selectively recruiting other smad proteins into the complex during SMAD activation, the SMAD/TGFβ pathway can be differentially regulated. Defining how Wnt and SMAD signaling pathways crosstalk in the TM is imperative in defining the role of Wnt signaling in IOP regulation, and could lead to discovery of a therapeutic target for regulation of TGF-β pathway and therefore regulation of POAG.

Poster: NEI 5R21EY023048-02
IRB/IACUC#: Hannah Webber, University of North Texas Health Science Center at Fort Worth; Abbot Clark, University of North Texas Health Science Center at Fort Worth; Weiming Mao, University of North Texas Health Science Center at Fort Worth;

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A Variant of Extensor Medii Proprius: A Case Report

Purpose: The extensor medii proprius (EMP), a documented variation of human hand extensor muscles, originates from the distal 1/3 of the ulna and inserts on the dorsal aponeurosis (extensor expansion) of the 3rd manual digit. This case report describes an anomaly in which the EMP originates from the lunate, an origination reported in the medical literature.

Methods: During routine gross anatomy dissection of the left hand of a 67-year old female who died of “stroke,” an unusual EMP muscle was observed and documented.

Results: The flat, fleshy muscle originated from the lunate bone, narrowed into a flat tendon near the 3rd metacarpophalangeal joint, and continued distally to insert on the extensor expansion of the 3rd digit. A branch from the posterior interosseous nerve was traced to the EMP. We propose that this previously unreported variation be termed extensor medii proprius brevis (EMPB).

Conclusions: Several anomalies found here have not been previously reported in the literature. First, the EMP originated at the lunate, which means the muscle does not cross the radiocarpal joint as described in previous reports. Second, the co-existence of the EMP with the extensor indicis or related muscles was not observed in this case. Third, the EMP tendon traveled deep to the intertendinous connection between the 2nd and 3rd tendon slips of the extensor digitorum muscle. Finally, this is the first time that the EMP was found to be innervated by a branch from the posterior interosseous nerve. In functional terms, the EMP/EMPB may act as an accessory MCP extensor. Due to its small size, however, the impact of EMP/EMPB on MCP extension may be negligible. Clinicians should still be aware of this variation, since swelling or tenderness of the muscle may lead to misdiagnoses of ganglion cysts or adipose tumors around this area of the dorsal hand.

Sponsor N/A
IRB/IACUC# Not Needed Not Needed
**GERIATRIC EXERCISE: GET THEM MOVING!**

As we get older, the physiological changes that occur in our body systems begin to limit our ability to perform at the level we once did as young adults. Most people gain weight, and on average there is an increase in blood pressure and cholesterol levels. Limitations in our musculoskeletal system puts a strain on movement and most adults 65 years and above are living with multiple comorbidities either in hospitals or nursing homes. While these changes are inevitable and will eventually catch up with each and every one of us, numerous studies have shown that a healthy lifestyle which includes good nutrition and regular exercise can slow down these changes, prevent some of these diseases and even enable most adults to lead healthy and independent lives into their 80s.

Exercise is especially important, not only because it can prevent high blood pressure and its related comorbidities, it can also strengthen the joints and help with movement and stability. In this poster, we show how to conduct a fall assessment and identify local community resources that are available to help older adults live more active and healthy lives.

**Sponsor**

N/A

**IRB/IACUC#**

N/A N/A
Million Veteran Program

Purpose:
The Million Veteran Program (MVP) is a national, voluntary research study conducted by the Department of Veterans Affairs Office of Research & Development. It is collaboration between the VA and veterans, whose goal is to illuminate potential links between genetic heterogeneity and disease. This is an important step in our scientific understanding about how genetic, as well as epigenetic makeup impinges upon disease characteristics and drug efficacy.

Methods:
Veterans who are treated in Veteran Affairs are eligible to participate. Those who provide consent are contacted by one of the researcher in the group. Veteran fills the survey related to their health and consent to give a blood sample. Central MVP biorepository saves the sample. Each sample is coded and so is their corresponding health information. Neither the person in the lab nor in the analysis knows the identity of the veteran. The key to the code is known to only a few personnel who are highly trained in research ethics thus safeguarding the privacy of the veterans.

Results:
Though the collection of data is ongoing, based on the analysis done so far, the correlation found between genetic and phenotypic pattern is helping to improve current treatment for certain cancers.

Strong links that will very likely be found in this study, due to the large number of participating veterans (1 million), will be used to generate testable hypotheses for future study, such as if a particular gene polymorphism or epigenetic mark leads to a particular disease trait. This will enhance our understanding about how to better prevent and treat various diseases such as heart disease, diabetes, cancer, and post-traumatic stress disorder.

Conclusions:
Our site has contributed actively in the recruitment of veterans for this study by enrolling approximately 5000 veterans till now. With the help of research program, at our institution, we continue to work towards achieving our target. All over US, more than 250,000 patients have been enrolled in MVP. The research on the 250,000 samples has helped us discover a couple of useful drugs for cancer and schizophrenia. MVP aims to establish the largest of its kind database in the United States.
Mighty Care is a community-based geriatric primary care program designed to reach Medicaid eligible adults and elders who are 50 and above, with the purpose of increasing access to care and improve patient quality of life. This is a new initiative for UNTHSC that utilizes mobile teams and clinics to increase access to care by providing appropriate levels of care within the community where the patients live. Generally, research indicates that as people age their quality of life (QOL) declines. The purpose of this study is to do a preliminary analysis of the QOL of the patients seen through this program, and examine age related differences in scores.

Methods

QOL was assessed using the 36-item short form health survey (SF-36). The SF 36 is a widely used tool, and possesses good psychometric properties. The SF 36 consists of eight domains, which make up the physical and mental health composite scales. Descriptive statistics were calculated to compare the scores from our sample to the national means. To examine the impact of age, we split the sample into two groups: those 64 and under and 65 and older. Independent t test were used to examine the impact of the age groups on QOL scores.

Results

The sample consisted of 229 patients (53 males and 176 females) with a mean age of 61. The average of PCS was 34.78 (SD= 9.87) and MCS was 45.075, falling slightly below the national average. For physical health there was a significant difference in the scores between the two groups, t (227)=-2.458, p=.015, with participants 64 and below (M= 33.7, SD=9.27) having lower scores that the 65 and above group (M=37.15, SD=10.84). For the mental health scores, there was a significant difference between the two groups, t (227)=-3.934, p=.000; suggesting that participants 64 and below (M= 42.71, SD= 13.66) had lower scores those over 65 (M=50.18, SD=12.18).

Conclusion

Past research has indicated that age decreases scores on the physical and mental health scales. However, these results indicated that individuals 65 and older reported better QOL than their younger counterparts. One potential explanation for these findings has to do with the fact that at 65 most of these patients are able to apply for Medicare. All participants in this program have Medicaid, however as an individual reaches 65 they are considered dually eligible which means they can have both Medicare and Medicaid. This gives this population access to a wider array of health services and benefits. The data is from baseline QOL measures in the Mighty Care program. This study had a small sample size, therefore more data is needed.
Relationship of Metabolic Syndrome Risk Factors and Reported Depression Among Hispanic Men and Women

Title: Relationship of Metabolic Syndrome Risk Factors and Reported Depression Among Hispanic Men and Women
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Background: Hispanics are disproportionately affected by metabolic syndrome (MetS). The link between depression and MetS has been of increasing clinical interest but has not been well studied among racial/ethnic groups. This study aims to determine relationships between number of MetS risk factors and self- and caregiver-reported depression among Hispanics.

Hypotheses: (1) Hispanic women with increased number of MetS risk factors will have more depression symptoms by self- and caregiver-report. (2) Hispanic men with increased number of MetS risk factors will not have more reported depression symptoms.

Methods: Data were analyzed from Hispanic women (n=589) and men (n=277) in the Texas Alzheimer’s Research and Care Consortium (TARCC) Longitudinal Research Cohort. Participants were given the Geriatric Depression Scale (GDS). Caregivers were given the Neuropsychiatric Inventory Questionnaire (NPI-Q). GDS total score, NPI-Q occurrence and occurrence by severity scores were analyzed in relationship to total number of selected risk factors of MetS (hypercholesterolemia, hypertension, and obesity). Data were analyzed using Chi square, t-test and multivariate analysis of variance.

Results: Men and women did not differ on number of risk factors (X²=.34, p=.560). Women scored higher on GDS (p=.044) but not on NPI-Q. A significant main effect for number of risk factors was found for NPI-Q but not for GDS. Number of risk factors was not related to depression symptoms for men, although the GDS score approached significance when comparing no risk factors to three risk factors (p=.07). Women with three risk factors had significantly higher (p

Conclusion: Hispanic women with three risk factors of MetS have significantly higher rates of depression symptoms when compared to Hispanic women with fewer risk factors. This finding did not hold for men. When examining Hispanic women with increased risk factors of MetS, it is important to evaluate for depression.

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Sponsor N/A
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Variation of Sternalis Muscle: A Case Report

Purpose: The sternalis muscle was first documented in the 19th century and since has been shown to have variations in its origins, insertions, direction, extra muscle slips, and nerve innervations. This case report describes anomalous features not previously reported in the medical literature.

Methods: During routine gross anatomy dissection of the anterior chest wall of an 100-year old woman who died of “natural causes” at UNTHSC, obvious anomalies in the bilateral appearance of the sternalis muscle were observed and documented.

Results: The left sternalis originated from the clavicular origin of the left sternocleidomastoid (SCM) muscle, while the right emerged from the sternal origin of the right SCM muscle. Both the left and right original tendons of the sternalis’ were separated but wrapped in a tight connective tissue band. The fleshy muscle bellies of each sternalis travelled down inferolaterally to insert on the aponeurosis of the left and right external oblique muscles, respectively. The innervation to the muscle could be traced to the 4th, 5th, and 6th anterior intercostal nerves. The fleshy muscle bellies of each sternalis travelled down inferolaterally to insert on the aponeurosis of the left and right external oblique muscles, respectively. The innervation to the muscle could be traced to the 4th, 5th, and 6th anterior intercostal nerves.

Conclusions: Several anomalies found here have not been previously reported in the literature including (1) the sternalis muscles originating from the clavicular head of the SCM muscle, (2) the tendinous band suspended over and slightly left of the sternal angle with only a loose connection to the underlying sternal angle, and (3) the inferolateral and nearly symmetrical 30 degree angle traveled by the sternalis to the sternum. Awareness of the location of the sternalis will help radiologists and reconstructive surgeons avoid misdiagnosis during mammography or misjudgment during breast surgery. Because of its superior attachment to the sternocleidomastoid muscle, therapists may need to be aware that a person with such an anomaly may have an automatic accessory inspiration with head rotation.

Sponsor N/A
IRB/IACUC# Not needed Not Needed
1,2,4-Trimethylbenzene (Pseudocumene) Formation of Photochemical Smog and Contribution to Atmospheric Greenhouse Gases (GHGs)

Objective
To examine 1,2,4-Trimethylbenzene’s contribution to photochemical smog and affect cardiac and pulmonary disease.

Introduction
1,2,4-Trimethylbenzene, a chemical derivative of benzene, is an industrial solvent and easily volatilizes to the atmosphere. In the presence of other VOCs, it was found to contribute to formation of photochemical smog. Photochemical smog is known to exacerbate respiratory conditions, including asthma and may contribute to cardiac and pulmonary disease. This study examined 1,2,4-Trimethylbenzene in hydraulic fracturing fluids and produced water and its ability to contribute to atmospheric levels of GHGs and photochemical smog.

Methods and Materials
A meta-analysis was performed and articles related to 1,2,4-Trimethylbenzene evaluated. Databases searched include PubMed, Scopus, Web of Science, TOXNET and Science direct. Keywords 1,2,4-Trimethylbenzene, pseudocumene, Trimethylbenzene, atmospheric conversion, atmospheric degradation/reaction, hydraulic fracturing, and health effects. Published article dates ranged from 1994 – 2011. Inclusion criteria were chemical properties of 1,2,4-Trimethylbenzene, atmospheric degradation and reaction, and atmospheric sustainability, and health effects. Exclusion criteria were articles related to 1,2,4-Trimethylbenzene and water pollution, and animal toxicology studies. Articles meeting inclusion criteria were retrieved as full-text and examined.

Results
This study confirmed high concentrations of 1,2,4-Trimethylbenzene in hydraulic fracturing fluids and produced water, and ability to aerosolize to the atmosphere from water and soil. Degradation of 1,2,4-TMB in the atmosphere by reactions with hydroxyl radicals are an indirect contributor to atmospheric GHG levels from hydroxyl radical scavenging, and may contribute to local/regional climate change. Slow atmospheric conversion of 1,2,4-TMB in the presence of ozone was found to occur with a half-life of more than 24 years, making it a candidate for long-range transportation.

Conclusion
1,2,4-Trimethylbenzene may be present in tanks and ponds in areas where hydraulic fracturing is occurring. The general public in close contact with these tanks and ponds may be exposed to 1,2,4-Trimethylbenzene in air and may experience adverse health effects.

A Qualitative Analysis on the Effects of Social Support among Women of the Reentry Population

Purpose:
Promotion of positive social support through family reunification and mentorship through the Second Chance Mentoring (SCM) program reduces risk of recidivism among moderate-to-high risk incarcerated women.

Methods:
The SCM program is offered through a collaboration between Family Pathfinders and three partner organizations in Tarrant County. SCM provides assistance to women who have been incarcerated to support their successful reintegration in to the community. Information is collected during incarceration to determine the recidivism risk level using the Ohio Risk Assessment Scale (ORAS) scores. Participants are enrolled in 12 months of mentoring services upon their release from prison or jail. Post-release, Family Pathfinders uses progress notes to monitor SCM service activities and other information which may contribute to reentry success or failure. These progress notes were analyzed by the evaluation team at UNTHSC to code for different types and levels of support which may promote or reduce recidivism among women.

Results:
The initial analysis of a sample size made of 50 women indicates that those who actively engage in a mentoring relationship are more likely to seek assistance elsewhere in order to promote successful reentry. Women who have support of negative influences have more issues becoming self-sufficient and set minimal goals for behavior change by the end of the 12 month program.

Conclusions:
A mentoring relationship with women who pose a high risk of recidivism upon release provides a foundation for building additional supportive relationships. Ensuring a reliable support system to incarcerated women may increase the effectiveness of successful community reintegration.
Adaptation of the CDC Evaluation Framework to Design the Evaluation of Reaching Teens, a Multi-Institutional, Region Wide Teen Resiliency Training Program

Purpose Mental Health Connection of Tarrant County (MHC) is a collaboration of public and private agencies working together to revolutionize the mental health service delivery system in Tarrant County, Texas. MHC is partnering with the American Academy of Pediatrics (AAP) on a multi-institutional region-wide staff training program. This program, Reaching Teens, uses the teen resiliency curricula developed by Dr. Kenneth Ginsburg, a pediatrician specializing in Adolescent Medicine. The goals of Reaching Teens are to develop a trauma-informed workforce, improve system integration and increase the use of evidence-informed practices in youth behavioral care in Tarrant County. Our research purpose was to adopt the Centers for Disease Control and Prevention (CDC) evaluation framework to planning the evaluation of Reaching Teens. The CDC evaluation framework engages stakeholders in the evaluation with the goal of stimulating innovation that leads to improving outcomes and detecting program effects. Methods We engaged agency stakeholders (Step 1), described the program using a logic model (Step 2), and focused the evaluation design on the issues most important to MHC and the organizational partners (Step 3). We conducted a baseline assessment of knowledge, attitudes and beliefs about teen resiliency and approaches for successfully working with adolescents in the mental health system. Results Our results consist of: (1) a logic model and (2) baseline survey findings. The Reaching Teens logic model is a roadmap to guide the ongoing planning, program activities and evaluation. With stakeholders, we prioritized three program components: (1) staff development; (2) organizational capacity building; and (3) system-wide collaboration. We identified key program outcomes: (1) engaging youth; (2) boundary-setting; (3) trauma-informed care; (4) commitment to “care” factor; (5) strengths-focussed; (6) resiliency; (7) job satisfaction; (8) system recognized for effective communication with youth; and (9) decreased turnover. Key baseline survey findings (n=438 staff participants from 15 agencies) are: high levels of job satisfaction (4.2 – 4.5, 5-point scale), congruence of personal and organizational values (3.3 – 4.0, 5-point scale), average teamwork in workplace (3.4 – 4.0, 5-point scale). Conclusion The Reaching Teens logic model is a powerful tool to guide system-wide collaboration toward the goal of more effectively reaching adolescents in mental health care. There are three program components: staff development, building organizational capacity, and strengthening system-wide collaboration. Baseline levels of the outcome measures (job satisfaction, teamwork, and value congruity) are relatively high among participating staff; thus, it may be difficult to demonstrate program impact by increasing these scores post-intervention.

Sponsor Mental Health Connection of Tarrant County

IRB/IACUC# 2014-135

Adverse Child Experiences and Their Effects on Child Behavior and Mental Health

Background: The association between Adverse Child Exposures (ACEs) and risk for child mental health outcomes such as depression, anxiety problems, and behavior/conduct problems has not been thoroughly investigated for three age groups - ages 6 to 10 (elementary school), ages 11 to 13 (middle school), and ages 14 to 17 (high school). We examined the relationship of these three mental health outcomes with a variety of ACEs among children 6 to 17 years old. We also examined the prevalence of ACEs for each mental health outcome in order to better understand the nature of any influential exposures.

Methods: National Survey of Children’s Health 2011-2012 dataset was used to investigate nine ACEs: socioeconomic hardship, divorce/separation of parent, death of a parent, parent served time in jail, witness to domestic violence, victim of neighborhood violence, lived with someone who was mentally ill or suicidal, lived with someone with an alcohol/drug problem, and treated or judged unfairly due to race/ethnicity. Total number of ACE exposures were categorized cumulatively into 5 classes: 0, 1, 2, 3, ≥4. They were then compared with the three child mental health outcomes: depression, anxiety problems, and behavior/conduct problems.

Results: A dose response relationship was observed between each of the child mental health outcomes and the number of ACEs for the full model (where age groups are included as a co-variable). The odds for depression in the full model increases by 2.59, 3.08, 6.24, and 9.66 for those exposed to 1, 2, 3, or 4 or more ACEs respectively, when compared to those who had not been exposed to an ACE. Children with 1, 2, 3, or 4 or more ACEs were 2.01, 2.28, 2.88, and 5.45 times more likely to have anxiety problems, respectively. Children with 1, 2, 3, or 4 or more ACEs were 3.21, 3.80, 6.96, and 10.51 times more likely to have behavior/conduct problems, respectively.

Conclusion: A dose response relationship was observed between the number of ACEs and risk of developing each of the examined child mental health outcomes (depression, anxiety problems, and behavior/conduct problems). Further examination of relationships between specific ACEs and the chosen mental health outcomes may help researchers identify significant or influential combinations of ACE risk factors.

Sponsor N/A

IRB/IACUC# 2015-021
An Analysis of the Second Chance Mentoring Program among Female Offenders

Purpose:
To assess the effectiveness of the Second Chance Mentoring (SCM) program, which works to reduce the rate of recidivism among moderate-to-high risk incarcerated women.

Methods:
The SCM program offered through collaboration between Family Pathfinders and Cornerstone Assistance Network of Tarrant County provides assistance to successfully reintegrate incarcerated women into the community. Information is collected during the incarceration to determine the recidivism risk level using the Ohio Risk Assessment Scale (ORAS) scores. Participants are enrolled in 12 months of mentoring services with a matched mentor upon their release from prison. Post-release, data is submitted to Family Pathfinders on a regular basis by the mentors and agency. The participants are deemed successful if one does not recidivate, meaning the individual is not arrested and incarcerated on new charges within 12 months of their release from their most recent incarceration. Upon successful completion of SCM, data of the participants is collected from the Texas Criminal Justice system to obtain background information in the justice system.

Results:
Complete data profiles for the initial cohort were used. Of the 50 women who expressed some interest in the program, 29 complete profiles were provided between the justice system and community partners. These were then further investigated for successful and unsuccessful completion. Findings indicate that middle-aged women without the equivalent of a high-school diploma were more likely to be unsuccessful than compared to middle-aged women with a diploma/GED. Of those who were unsuccessful, 55% reported not having a place to live upon their release, where 89% of the successful women did have a place to live. Findings also suggest that the mentor relationship does contribute to less recidivism when 30% of those who were unsuccessful were not yet matched with a mentor before recidivating.

Conclusions:
The Second Chance Mentoring program provides sufficient support to reduce the risk of recidivism among moderate-to-high risk women. The promotion of social capital and encouragement to continue education through SCM allows for a successful reentry into the community.
Associations between socioeconomic and demographic characteristics of ZIP codes and the availability of tobacco products

Objective
To examine associations between tobacco product availability and demographic and socioeconomic characteristics in ZIP codes.

Introduction
The awareness of e-cigarette use has been increasing in U.S. population since its introduction in market. Research supports that female gender, less education population, lower income, and racial and ethnic minority status are associated with electronic cigarette use. It is important to understand the strategies employed by the cigarette retailers to attract the users in order to understand these disparities in use.

Methods and Materials
We constructed a database using a variety of data sources. Demographic and economic data were obtained from the U.S. Census Bureau’s 2008-2012 American Community Survey 5-Year Estimates. Data on number of licensed tobacco retailers was identified retrieved from appropriate government agency within each state. Data on electronic cigarette retail availability was gathered from websites maintained by manufacturers.

Results
Regression models were constructed to examine associations between the retail availability of tobacco products and the socioeconomic and demographic characteristics of ZIP codes. A number of socioeconomic and demographic variables were associated with the number of tobacco outlets, after adjusting for population size of ZIP codes.

Conclusion
Understanding the geographic distribution of tobacco and electronic cigarette retailers is important to develop effective policies to control use and reduce/eliminate health disparities. To the investigators’ knowledge, this is the first known study to examine the retail availability of electronic cigarettes by the demographic and socioeconomic characteristics of populations.

Concentration of Volatile Organic Compounds in Urban Cities Compared to Urban Areas Experiencing Natural Gas Extraction and Processing

Objective
The objective is to compare atmospheric concentrations of volatile organic compounds in urban areas of natural gas extraction as compared to areas without natural gas extraction.

Introduction
Expansion of unconventional shale gas extraction and processing over the last decade has progressed significantly across the United States. Environmental concerns for what affect this energy expansion is having on air quality have been of great concern to many communities. Many of the VOCs present in natural gas and present in chemicals used in hydraulic fracturing are contributors to atmospheric greenhouse gas (GHG) levels and hazardous air pollutants (HAPs). Exposure to GHGs and HAPs are known to be a major factor in respiratory illnesses in humans. In this research, atmospheric volatile organic compound concentrations were compared in areas experiencing natural gas extraction and processing with urban area VOC concentrations.

Material and Methods
Relevant articles were identified by a systematic search of reliable databases. Due to lack of literature for comparison of VOCs, all the study designs were included. Having difference in measurement unit, all the readings in different studies were converted to one common unit and compounds were compared.

Results
Methodology of ambient air monitoring varied considerably from locations. Among analysis of over 100 concentrations, only 7 compounds were collected in urban studies which include Acetone, Benzene, Chloroform, 1, 2 dichloroethane, Ethylbenzene, Tetrachloroethane and Styrene. Concentration of VOCs was found to be 70% higher in urban areas experiencing natural gas extraction.

Conclusion
VOCs are found to be higher due to natural gas extraction process in urban areas. Greenhouse and HAPS are pervasive and responsible for adverse health and environmental effects. Our future studies are focused on consistent monitoring of HAPS and other chemicals.
Determining Effective Collection and Identification Measures of Estradiol in African-American Women

Purpose: Estrogen is important for overall health and reproduction, and has been linked to obesity. Currently, estrogen is time and cost intensive to measure. The purpose of this research was to establish a more cost-effective way to measure estradiol in community based settings, and to determine a methodology for collection and identification of peak estradiol levels.

Methods: Four saliva samples, medication information, and previous menstrual cycle history from 61 premenopausal and postmenopausal African-American women were collected over a 4-6 week time period. The saliva samples were analyzed by an independent laboratory to identify levels of estradiol (E2). A primary sample was defined as the sample that was collected on or most closely aligned with day 13 of the menstrual cycle when estradiol peaks. A secondary sample was identified if a primary sample was not aligned with day 13 of the menstrual cycle. The secondary sample was determined by projecting the next menstrual cycle period. A secondary sample and the average of all samples were calculated to determine the best method for identifying peak estradiol levels.

Results: Using this protocol, for the premenopausal subjects, 56.3% of their primary samples were equal to their peak estradiol sample, and 37.5% of their average estradiol samples were equal to their peak sample. Only 6.3% of the participants’ secondary samples were equal to their peak level. For the postmenopausal women, 73.9% of the participants’ average samples were equal to or ≤ .03 of their peak estradiol sample.

Conclusion: This data suggests that this modified protocol demonstrates preliminary ability to identify peak estradiol levels in a community setting in a cost-effective and time efficient manner.

Sponsor: NIH Grant
IRB/IACUC#: 2011-164

Effects of Maternal Health on Child Utilization of Dental Care among Medicaid and CHIP Participants: Results from the 2011-2012 National Survey of Children's Health (NSCH)

Introduction: Understanding the preventive dental health care utilization of children is essential to reducing child dental disease rates in low income families. Previous studies have not examined the relationship between the mother’s health status and the child’s dental care utilization. The aim of this study is to examine the association between maternal health status and use of preventive dental care among children enrolled in Medicaid and CHIP programs.

Methods: We conducted a cross sectional study of children enrolled in Medicaid and CHIP programs. A sample of 88,460 children was obtained from the 2011-2012 National Survey of Children’s Health (NSCH). We used multivariable logistic regression modeling (SAS 9.3) to estimate the adjusted odds ratio for having at least one dental visit in the past 12 months associated with self-reported maternal health. We statistically adjusted for child’s age, sex, maternal education, family structure, and parental satisfaction with the child’s health care provider.

Results: Our key result is that children of mothers with excellent or very good health were 2.48 times more likely (95% CI 1.41-4.38) to have visited the dentist in the last year as compared to children of mothers with poor general health. There was a 45% reduction in access to dental health care when maternal health status decreased from excellent or very good status to good or fair health status.

Conclusion: Our findings suggest that poor maternal health status decreases the likelihood that children will have an annual dental visit. Preventive dental outreach efforts and programs are needed to target these children.

Sponsor: N/A
IRB/IACUC#: 2015-024
RESULTS: Occupational studies of EB exposed workers in natural gas and petrochemical industries confirmed multi-system toxic effects and endocrine impairment. Ambient air monitoring studies confirmed elevated levels of EB in residential communities experiencing urban drilling. Studies supported the findings. Adverse health effects included respiratory, cardiovascular, reproductive, hematologic, digestive/liver, excretory selected and reviewed as full text.

METHODOLOGY: A meta-analysis was performed and articles related to health effects from EB exposure evaluated. Databases searched included: PubMed, Scopus, Science direct and TOXLINE. Keywords were ethyl benzene, health effects, occupational exposure, natural gas and ambient air. Initially, 500 articles on the health effects of EB were selected. Publication dates ranged from 1967 to 2014. Inclusion criteria were occupational exposure, health effects, ambient air and toxicological animal studies. Exclusion criteria were soil and groundwater contamination, and EB exposure from other sources like cigarette smoke. Retrieved abstracts were evaluated for relation to study focus. Fifty articles were included: Pub-Med, Scopus, Science direct and TOXLINE. Keywords were ethyl benzene, health effects, occupational exposure, natural gas and ambient air. Initially, 500 articles on the health effects of EB were selected. Publication dates ranged from 1967 to 2014. Inclusion criteria were occupational exposure, health effects, ambient air and toxicological animal studies. Exclusion criteria were soil and groundwater contamination, and EB exposure from other sources like cigarette smoke. Retrieved abstracts were evaluated for relation to study focus. Fifty articles were included.
**Family History Information in Dallas/Fort Worth: What We’re Not Telling Patients**

**Purpose:** Patients can be empowered to assess their own family health history (FHH) by providing accurate information that: (1) explains the importance of FHH in the context of heritable conditions and (2) outlines how to take an accurate FHH. The aim of this study is to assess the quality of information provided to patients regarding FHH prior to a clinical encounter in the Dallas/Fort Worth area.

**Methods:** FHH information from local health organizations was collected throughout the Dallas/Fort Worth area. Information was included if published by a local health organization (or national organization with local offices) and FHH was discussed in the capacity of health risk assessment.

The information was categorized based on source into the following groups: local electronic, national electronic, print, and health fair. Each source was further assessed for quality of information by a series of questions following the Genetics in Primary Care Institute (GPCI) guidelines for taking FHH and disease-specific questions based on familial risk guidelines. The percentage of positive “Yes” answers is tabulated for each category and assessment question.

**Results:** A search for local information on FHH was conducted between June, 2014 and December, 2014. Information on FHH was provided by 48% (25/52) of outlets searched. 73 sources were included for analysis. 53% came from websites of local health organizations, 16% came from print resources, 11% came from health fairs, and 19% came from national health organizations. Of these sources, 22% were general FHH information and 88% were disease specific.

Information from health fairs had the greatest proportion of guideline components (18.8%) and local electronic sources had the fewest components (12.4%). Printed information had a greater percentage of guideline components (15.5%) than electronic (14.6%). General FHH information was more likely to have guideline components (24.3%) than disease specific information.

**Conclusions:** Difficulty in obtaining information on FHH was noted with less than half of potential resource sites providing FHH information. Few sources provided all components recommended by GPCI guidelines and differences in the quality of information between source categories (electronic vs. print) were found. Sharing FHH with a provider was only recommended 59% of the time. Here we have demonstrated a clear need for health organizations to provide FHH information to patients.

**Sponsor** N/A

**IRB/IACUC#**
Geographic Disparity in Health Insurance

**Purpose**
The purpose of this study is to identify factors associated with having adequate health insurance for children with special health care needs (CSHCN) differ by geographic region.

**Methods**
The proposed analysis was conducted on the 2009-2010 databases of the NS-CSHCN using SAS which accounted for complex survey weighting and sampling design. The analysis included examining the overall distributions of variables using means and frequencies. Distributions of variables were examined for those who had any kind of health insurance and those who did not. Differences in whether having health insurance or not by region were analyzed using chi-square test and logistic regressions were performed. Odds ratios and 95% CIs were examined.

**Results**
Out of total population, 10110 were insured for entire year while 919 were insured at some point during the year. Education level, family structure and financial condition of the family have significant effect on the insurance status of CSHCN. Based on chi square analysis, education level of the household had significant effect on insurance status of CSHCN in northeast and south and west region while family structure, number of missed school days of CSHCN, Family financial burden was significant for all region. Odds ratio obtained from logistic regression where individuals who were uninsured was used as reference. Thus, odds of having insurance were higher in individuals with higher education in all the regions. Odds of CSHCN being insured was significantly lesser in northeast, south for Hispanics while was significantly higher in west for blacks compared to white non- Hispanics. Odds of CSHCN being insured was significantly lesser in midwest, south in family consisted of only mother and was significantly lesser in northeast in family consisted of parent stepfamily when compared to either biological or adopted parents. Odds of CSHCN being insured was significantly higher in midwest if child’s problems never affected ability to do compared to those where their ability was usually affected. Odds of CSHCN being insured was significantly higher in midwest, northeast, south in family with no financial burden compared to who had financial burden.

**Conclusion:**
Policies should be directed to increase the educational awareness, focus on Hispanic groups for insurance, expand the insurance plans that will accommodate the families having financial burden.

**Sponsor**
IRB/IACUC# 2015-031

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**Purpose:** Helicobacter pylori (H. Pylori) bacteria produce a strong inflammatory response in the body. It is hypothesized that strong immune responses to H.pylori can enhance systemic inflammation and produce an autoimmune response against the thyroid. Epidemiologic studies have assessed an association between H. pylori infection and autoimmune thyroid diseases, but with conflicting results and small study populations. Using a large, nationally representative US population, we investigated whether there is an observable association between H. pylori infection and levels of serum thyroid hormones (T4 and TSH) and anti-thyroglobulin antibodies.

**Methods:** We analyzed cross-sectional data from the most recent National Health and Nutrition Examination Survey III (1988-1994) containing serum H. pylori and thyroid hormone levels. H. pylori infection status was determined by detection of antibodies. Chi-square and t-tests were used to assess differences by H. pylori status. Multivariable linear regression models were used to quantify the association between T4, TSH, and anti-thyroglobulin antibodies separately, while adjusting for age, sex, race/ethnicity, and BMI.

**Results:** Among 5848 adults studied, the prevalence of H. Pylori infection was 32.8%. Mean T4, TSH, and anti-thyroglobulin antibodies differed by H.pylori status (p <0.05), but remained within the wide reference values. H. pylori infection was a significant predictor of higher T4 and anti-thyroglobulin antibodies, particularly in younger persons (<40 years of age). Conversely, a significant inverse association was observed for TSH. Similar differences were observed for the higher risk cytotoxin associated gene A H.pylori strain.

**Conclusions:** Our findings suggest that H. pylori eradication may be important before abnormal thyroid levels can return to normal.

**Sponsor**
N/A
**IRB/IACUC#** 2013-245
Health Behavior Changes Among First Year Medical Students: A Pre- and Post-Analysis

Background: Entering medical students begin their journey into medicine with the desire of being a healthcare professional whose healthy habits serve as a model for their patients. In truth, the high stress of the academic environment of medical training makes students vulnerable to poor health behaviors. Research has shown that there is a correlation between high stress environments and poor health behaviors. This study is a follow-up to that research.

Hypothesis: We hypothesized that first year medical students' consumption of energy drinks is associated with less positive health behaviors upon reassessment during medical school.

Methods: The study involved the administration via Qualtrics of two surveys to the Texas College of Osteopathic Medicine Class of 2018. The pre-survey was distributed during the 3rd week of class which was completed by 135 students when there were no impending exams. The participation in the survey was voluntary, and the subjects were recruited by the following methods: announcement in class, announcement on social media, and announcement via email to the Class of 2018. The survey was re-administered during the last 2 weeks of the semester, and it was completed by 99 students. Data analyses of the two surveys only included the students who completed both surveys (n=49). To compare pre- and post-variables of typical hours per sleep in a 24-hour day, days per week exercised (≤2 days or ≥3 days), changes in reported GI symptoms, and whether the subject consumed energy drinks in the past month (yes or no), the nonparametric McNemar's test was used. An alpha level of less than .05 was considered significant. The Perceived Stress Scale between pre- and post-measurement surveys were compared with a dependent sample T-test.

Results: 63% of the students were male and 37% were females ranging from ages 22-41 with a mean age of 25.3±3.6. General trends included an increase in energy drink consumption, reported headaches/palpitations and GI symptoms, and decrease in sleep hours per day. Statistically, there was a significant increase in energy drink consumption (from 26.5% at pre-test to 42.9%, p=0.008), and an increase in gastrointestinal symptoms (from 16.3% at pre-test to 34.7%, p=0.012).

Conclusion: An increase in energy drink consumption and gastrointestinal symptoms supports our hypothesis that first year medical students' consumption of energy drinks is associated with less positive health behaviors.
Health effects from Exposure to Benzene and Benzene Related Compounds in Residential Communities Experiencing Natural Gas Extraction and Processing Operations

Advancement of natural gas extraction into urban areas across the United States has raised concern for a potential increase in exposure to volatile organic compounds, including air toxics, to the public. Benzene is a primary chemical of concern (COC) due to its classification as a known human carcinogen. Ambient air sampling performed in an earlier study found elevated levels of benzene and 17 benzene related compounds in residential areas where natural gas extraction and processing operations were occurring. Benzene is present in geologic rich formations and released during pyrolysis and venting of fuels. Drilling within city limits has increased the potential for human exposure. The evolution of this study began, as the health effects of exposure to natural gas well emissions are increasingly visible in our society.

Study Objective
The main purpose of this study was to determine the health effects that results from exposure to benzene and benzene related compounds in residents of and workers in natural gas extraction sites; To also determine the routes of exposure and the distance that benzene can travel from the point source of generation, and to make recommendations of ways to reduce benzene exposure.

Methods
A meta-analysis was conducted and identified all published articles related to benzene and benzene related compounds, and health effects of benzene in residents of natural gas extraction plants and occupational workers. Databases comprehensively searched included: MEDLINE, TOXLINE, PubMed, Scopus, Web of Knowledge, and the Clinical Trials Registry. Reference lists of reports and reviews were also searched. The authors of this paper determined the suitability of the articles by evaluating all related title/abstracts. Articles found relevant were retrieved as full texts and thoroughly reviewed. Health effects of benzene exposure were analyzed based on organ system.

Results
Results revealed that exposure to benzene can lead to multiple health effects affecting multiple systems. Health effects can be short term and long term. The health effects were prevalent amongst residents of natural gas extraction sites and people with occupational exposure to benzene. Routes of exposure to benzene are; inhalation, ingestion and dermal. It is metabolized extensively in the liver and can be stored for long periods in adipose tissue and bone marrow. It is excreted in the urine via the kidneys as phenols. Residents in communities experiencing natural gas extraction have higher cases of anemia, leukemia (Acute Myeloid Leukemia, Acute Lymphoid Leukemia), and non-Hodgkin’s lymphoma, which is explained by the hematotoxic effect of benzene. Several studies report that benzene affects the reproductive system, Central nervous system and respiratory system.

Recommendations and Conclusion
Use of environmentally friendly hydraulic fracturing chemicals should be encouraged. Residential areas and especially schools should be protected from industrial mining operations. Children exposed to emissions from natural gas extraction/processing should be tested regularly through bio monitoring of urine and blood. Future studies should be done on the effects of benzene exposure to children. Through this study we were able to establish that there is an association between benzene exposure and natural gas drilling in residential communities and the health effects can be debilitating to children, women and workers.

Sponsor N/A
IRB/IACUC#
**Health Literacy Systems Approach: Empowering Healthcare Practitioners Through Education**

**Problem**: Research indicates that limited health literacy can lead to adverse health outcomes due to patients' inability to follow instructions regarding medications, labels and health messages especially in preventative care (Koh et al., 2012).

**Hypothesis**: The Affordable Care Act (ACA) has mandated improved patient understanding of medical diagnoses through effective communication by providers. The purpose of this study was to determine if health literacy trainings can improve healthcare practitioners understanding and use of health literate communications.

**Materials and Methods:**
- **Context**: Trainings were conducted at four healthcare organizations between December 18, 2013 and June 20, 2014. Site selection utilized a purposive convenience sample through community partner networking.
- **Intervention/Instrument**: Trainings engaged participants utilizing a variety of mediums to build capacity towards health-literate practices using the Health Literacy Universal Precautions Toolkit (HLUPT).
- **Study Design**: Knowledge levels of training participants were measured by a pre-test, post-test, and a follow-up survey consisting of closed-ended scaled items and open-ended items. Statistical Analysis: Univariate analyses offered descriptive statistics and bivariate analyses assessed mean score changes between pre- and post-tests both in SAS 12.1 using Wilcoxon Signed-Rank test (p = .001). NVivo software analysis of qualitative data assessed open-ended survey questions through coding and emergence of themes, sub-themes and frequency of response.
- **Outcome Measures**: Eighty-eight providers and staff members were trained at four healthcare entities. Eighty-eight pre- and post-test surveys and 29 follow-up surveys were collected with 37 pending.

**Results**: Health literacy knowledge increased in 100% of participants and 75% increased knowledge in over half of the survey questions. Follow-up survey respondents demonstrated 100% retention of knowledge.

**Conclusions**: The intervention showed that healthcare providers improved health literacy knowledge after a short, evidence-based training. The knowledge is retained at three months post-training.

**Future Implications**: Despite knowledge increases, patient-centered care depends on improved health information and services. Longitudinal follow-up is needed on whether knowledge becomes integrated into clinical systems and improves compliance, patient outcomes and ultimately population health.

**Sponsor**
- United Way, Texas Health Resources

**IRB/IACUC#**
- 2014-118 Health Literacy in Clinical Settings: A Systems Approach

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**Impact of Individual and Parental Determinants on the Development of Attention Deficit Hyperactivity Disorder**

**Methods:**
- The National Survey of Children’s Health (2011-2012) data was used for the analysis of 65,680 children from 6 to 17 years of age. Multivariate logistic regression technique was applied to find the association between low birth weight, time spent for viewing television or playing video games per day, maternal and paternal mental and emotional health status and ADD/ADHD controlling for age, gender and poverty level.

**Results:**
- As compared to female children, male children had 2.5 times higher odds of developing ADD/ADHD. Age was also significantly associated with ADD/ADHD. Children of mothers with fair or poor mental and emotional health status had 1.8 times higher odds of developing ADD/ADHD as compared to children of mothers with excellent or very good mental and emotional health status. In addition, children whose father had fair or poor and good mental and emotional health status had 1.5 times increased odds of having ADD/ADHD as compared to children whose father had excellent or very good mental and emotional status.

**Conclusion:**
- Parental mental and emotional health had significant association with the development of ADHD in their children. Six to seventeen years of age children whose mother or father had poor mental and emotional health conditions were more likely to have ADD/ADHD.

**Sponsor**
- IRB/IACUC# 2015-020
Improving Risk-Adjustment Methods for Cardiac Patients by Using Present-On-Admission(POA) Data

The purpose of this study is to examine whether the predictive power of risk-adjustment models can be improved by incorporating Present-On-Admission (POA) codes for patients with coronary artery disease (CAD).

We studied POA-coded data from 174,909 CAD discharges of the Texas Hospital Inpatient Discharge Public Use Data File for 2012. Conditions could either be complications or comorbidities, depending on whether they were present on admission. Major complications were identified based on both frequency of occurrence and in-hospital mortality. We compared the performance of three logistic regression models in terms of mortality prediction and explanatory power.

We found these: Risk models including POA had greater explanatory power, by approximately 10% (pseudo-R2: 9.2% vs. 10.4%), compared with the baseline model which did not include POA information. Separation of complications and comorbidities revealed additional information for some conditions. When present-on-admission, Peptic Ulcer Disease was not a significant predictor of mortality (OR=1.05; p-value>0.9), but was highly significant when it occurred as a complication (OR=20.55; p-value<0.01).

Overall, we concluded that POA information can greatly improve the utility of administrative data for risk-adjustment for patients with CAD. Report cards of hospitals' risk-adjusted mortality rates for cardiac patients can increase their validity and end-user acceptance by incorporating POA information. However, more standardization and uniformity in POA coding is needed. Some hospitals may still be reluctant to report complications or, alternatively, chronic comorbidities (e.g., depression, alcoholism) may be misreported as complications.

Sponsor
IRB/IACUC# 2015-062

Meeting Healthcare Needs of Children with Autism Spectrum Disorders: Family Centered Medical Home Matters

Purpose: The prevalence of Autism Spectrum Disorders (ASD) has increased over the past decade. Children with ASD have complex healthcare needs that may be best served in a family-centered medical home (FCMH) model. A family-centered medical home provides effective primary health care that is accessible, family-centered, continuous, comprehensive, coordinated, compassionate and culturally competent. We examined whether having a FCMH increased the likelihood that children with ASD receive the therapy, mental health care, preventive services and specialty care they need.

Methods: We conducted a cross-sectional national study of 3025 children (3 to 17 years) with parent-reported ASD. We analyzed data from the 2009-10 National Survey of Children with Special Health Care Needs (NS-CSHCN). We estimated the impact of having a medical home on receiving needed medical and non-medical therapy, mental health care, preventive services and specialty health care. Using the Andersen Model of Health Care Utilization as our conceptual framework, we fit hierarchically well formulated logistic regression models consisting of predisposing (P), enabling (E) and health need (N) variables as predictors of receiving needed healthcare services. We estimated the increased likelihood (odds ratio) of receiving needed services when the child has a FCMH versus no FCMH, adjusting for the P, E and N variables.

Results: Only half of children with autism (51.8%) had healthcare that is considered part of a FCMH. Children with a FCMH were more likely to report receiving needed specialty care (OR=4.068, 95%CI 2.20-7.52), therapy (OR=1.754 95% CI 1.18 – 2.60) and mental health care (OR=2.74 95% CI 1.55 – 4.84). Having a FCMH was not significantly associated with receiving needed preventive health services. Each model was adjusted for predisposing factors (age, gender, race, family structure), enabling factors ( household education, poverty level, adequacy of current insurance, receipt of early intervention services, age at diagnosis) and need ( severity level, difficulty communicating).

Conclusions: Having a FCMH significantly increased the likelihood that the healthcare needs of children with ASD were met, adjusting for relevant predisposing, enabling and need variables.
We analyzed data from 4949 adults participating in the National Health and Nutrition Examination Surveys (NHANES 2011-2012). Decayed, missing, and filled teeth (DMFT) and decayed, missing, and filled surfaces (DMFS) were used as the proxy for oral health. We also collected sociodemographic variables including age, race, gender, smoking status, marital status and diet.

Methods
We performed a cross-sectional analysis using data from 4949 adults aged 18 years and older from the NHANES 2011-2012. We used binary logistic regression to examine the association between poor oral health and depression. We adjusted for age, race, gender, smoking status, marital status and diet.

Results
We found that poor oral health was associated with depression. The adjusted odds ratio for depression in people with poor oral health was 1.01 (95% CI: 1.00, 1.03; p= 0.4).

Conclusion
There is a weak positive association between poor oral health and depression that is independent of age, race, gender, smoking status, marital status and diet.

References

Sponsor
IRB/IACUC# 2015-020
analyses found that NSD was not a significant predictor of MVPA% on weekdays (adjusted R²=-0.15, p=0.944) or weekends (adjusted R²=-0.06, p=0.226).

Results: Teens slept an average of 392.5 min/night (SD=77 min) on weekdays and 506.4 min/night (SD=85 min) on weekends. Multiple regression analyses examined NSD as a predictor of MVPA% with grade, race, BMI, and sex as covariates for weekdays and weekends.

Introduction: While previous research shows increased obesity and obesity markers in children with shortened sleep durations, there is a scarcity of research exploring the effects sleep may have on teens’ physical activity levels. The paucity of research conducted so far is conflicting with some studies showing shorter sleep durations were associated with decreased physical activity while others indicate that longer sleep durations are associated with decreased physical activity. A clear need exists for additional exploration into the connection between sleep and physical activity. The hypothesis of the current analyses was that increased actigraph-measured nighttime sleep duration will predict higher rates of next day moderate-to-vigorous physical activity.

Methods: Participants were 29 normal to obese teens (mean BMI=25.1) in grades 9-12 (mean grade=10th), mean age=15.4 yrs, 73% female, 23% Hispanic) who were relatively healthy and reported sleeping assent, teens’ height(cm) and weight(kg) were assessed with a stadiometer and digital scale, which allowed for the calculation of BMI. During the study week, teens followed a self-selected schedule while wearing an actigraph to record their sleep/wake schedule. Night sleep duration (NSD) was equal to the sleep duration recorded by the actigraph during the night sleep period. Teens also completed 3 Previous Day Physical Activity Recalls (1 weekend, 2 weekdays) assessing activities engaged in the previous afternoon-evening (1500-2300). The % time engaged in moderate-vigorous physical activity (MVPA) was calculated (total time spent engaged in MVPA divided by total time spent not sleeping). These data were from a larger prospective study assessing sleep and health in teens. Multiple regression analyses examined NSD as a predictor of MVPA% with grade, race, BMI, and sex as covariates for weekdays and weekends.

Results: Teens slept an average of 392.5 min/night (SD=77 min) on weekdays and 506.4 min/night (SD=85 min) on weekends. Multiple regression analyses found that NSD was not a significant predictor of MVPA% on week days (adjusted R²=-0.15, p=0.944) or weekends (adjusted R²=-0.06, p=0.226).

Conclusions: NSD was not predictive of next day MVPA%, which may have been due to the small sample size and subjectively assessed physical activity. Further research should examine the connection between sleep and physical activity using objectively measured physical activity data collected throughout the day and in a larger sample.

Support: Support received from UNTHSC Intramural Grants (R16051 and R16160).

Sponsor: Support received from UNTHSC Intramural Grants (R16051 and R16160)

IRB/IACUC# 2013-015

Sleeping Safely: Perceptions and Practices of Parents and Caregivers

Purpose: the purpose of this study was to assess the perceptions of safe sleep among parents and caregivers.

Background: Infant mortality remains a persisting problem in the United States (MacDorman, et al., 2014). Despite the effort of American Academy of Pediatrics (AAP) to combat this issue, infant sleep safety remains a controversial topic with ambiguous definitions and inconsistent practices (McKenna & McDade, 2005). Given such debates, it is important to focus attention on exploring a community’s opinion of safe sleep.

Methods: A preliminary study utilizing a mixed method approach was conducted in Fort Worth, Texas. Surveys were administered at two daycare centers representative of a low and a high income community. Participants were asked about sleep positions, where, if at all, they received information about safe sleep, and they were asked to identify safe sleep positions from pictures of different sleep positions. Not wanting to identify babies by race or ethnicity a teddy bear was used to demonstrate four different sleep positions. A total of 48 parents/caregivers participated in the study.

Results: Our study found that there is confusion about what comprises safe sleeping position/arrangement for infants. Additionally, the recommendations by APA are not well disseminated as majority of our respondents selected side-sleep position as being safe for babies. Our results also found a relationship between where people receive information and how they perceive/practice safe sleep.

Conclusion: This study helped identify an important gap in knowledge and practice regarding safe sleep in the community that must be explored further.

Sponsor: N/A

IRB/IACUC# 2014-045
Sudden Infant Death Syndrome in Texas: a Geospatial Analysis

Purpose: to determine and explain the geospatial distribution of Sudden Infant Death Syndrome (SIDS) in Texas. The exact cause of SIDS is unknown, but it has been found to correspond to behaviors such as placing infants on their fronts to sleep, infants sleeping with soft bedding or toys in their crib, infants overheating, and exposure of infants to tobacco smoke. Geographic factors have by and large been de-emphasized in SIDS research, and as such represent a significant gap in the literature. However, factors such as temperature, demographics and socio-economic status may provide valuable insight into the underlying reasons behind the geographic distribution of SIDS in Texas.

Methods: Standard Mortality Ratios (SMRs) were calculated for each county in order to categorize Texas counties as “high,” “average,” or “low” SIDS. The resulting data was examined in a Geographic Information System (GIS) in order to determine its spatial distribution. Demographic data was collected from the U.S. Census Bureau in order to descriptively analyze high and low SIDS counties, and T-tests were conducted in order to examine similarities and differences within and between these counties. Temperature data from the PRISM Climate Group was collected in order to examine the potential relationship between low temperature and SIDS deaths per 100,000. A linear model was created to describe this relationship.

Results: 18 low and 54 high SIDS counties were identified by SMR. Low percentage of Hispanics and high percentage of vacant homes characterized the high SIDS group, while high percentage of Hispanics and low percentage of vacant homes characterized the low SIDS group. This difference was found to be significant at the p < 0.01 level. The temperature model was found to be significant at p < 0.05. This may be seen descriptively in that the high SIDS counties were clustered in the northeastern part of the state, where average temperatures are lower.

Conclusions: the relationship between SIDS and low temperature may in part be explained by behavior. In cold weather, parents may be more likely to cover their infants with soft bedding, not realizing the danger. Additionally, certain elements of Hispanic culture might serve as a protective factor against SIDS. This may bear further investigation. Furthermore, vacancy rates have long been used as a proxy for urban decay, and might indicate poor housing conditions. This may act to create an environment which promotes SIDS.

Sponsor N/A
IRB/IACUC#
Use of 1,3,5-Trimethylbenzene in Unconventional Shale Gas Hydraulic Fracturing Operations and Potential for Water and Soil Contamination

Introduction and Objective:
Hydraulic fracturing (fracking) of unconventional shale gas formations allows for extraction of natural gas in tight geologic formations.Large quantities of water, proppants and chemical additives are required during hydraulic fracturing. These chemicals have the potential to contaminate water and soil if not properly used and contained. The chemical's unique characteristics increase the potential for human exposure from contaminated water, soil and bioaccumulation in fish. The objective of this study is to examine the use of 1,3,5-Trimethyl benzene (TMB) as a chemical additive in fracking and the potential for human ingestion.

Methodology:
A meta-analysis was performed and articles related to 1,3,5-TMB evaluated. Databases searched included Science direct, PubMed, Scopus, Web of Science, ACS ChemWorx and TOXNET. Keywords searched include 1,3,5-Trimethyl benzene, Mesitylene, soil and water contamination, runoff, ground, surface and drinking water, fish kills, fracking fluids and petroleum industry. Published articles dates ranged from 1993-2012. Inclusion criteria were chemical properties of 1,3,5-TMB (Mesitylene), TMB water concentration, substantiality of TMB in water and soil, use of TMB in hydraulic fracturing. Exclusion criteria were health effects of TMB, air pollution, aerosolization of TMB, and toxicology studies on animals. All the relevant abstracts were evaluated with 150 articles reviewed in full-text.

Results:
This study confirmed 1,3,5-TMB used as a chemical additive in hydraulic fracturing. Published studies showed high concentrations of 1,3,5-TMB present in produced water from oil and gas production discharge. Migration of 1,3,5-TMB from accidental spills, uncontained fluids on pad sites, and holding ponds was found to increase the potential for municipal water, surface and groundwater contamination.
Migration of 1,3,5-TMB in ambient temperature water was found to be possible due to its high concentration being used at fracking site.

CONCLUSION:
The use of 1,3,5-TMB as a chemical additive in hydraulic fracturing was confirmed in this study. Published literature supports the ability of 1,3,5-TMB to contaminate surface and ground water used as municipal water reservoirs. Bioaccumulation of 1,3,5-TMB in fish was found to be possible due to its low partition coefficient.

Sponsor
N/A
IRB/IACUC#
Immunology (Abstracts in the 1200s)

1200  Oral  Classification: GSBS Student
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Age-related Thymic Involution Perturbs Negative Selection Leading to Autoreactive T Cells That Induce Chronic Inflammation (Inflamming)

The presence of chronic low-level pro-inflammatory factors in elderly individuals (termed inflamming) is a significant risk factor for morbidity and mortality. Recently, inflamming has been partially attributed to the persistent activation of immune cells thought to arise from latent viral infection, but the contribution of activated autoreactive T cells towards the development of inflamming remains unclear. To address our hypothesis that age-related thymic involution leads to the persistent release and activation of autoreactive T cells capable of inducing inflamming, we performed experiments including: adoptive transfer, kidney capsule transplantation, and tetramer detection of autoreactive T cells on a FoxN1 conditional knock-out (FoxN1-cKO) mouse model that mimics natural thymic involution while maintaining a young periphery. We found that thymic involution leads to T cell activation shortly after thymic egress, which is accompanied by a chronic inflammatory phenotype consisting of cellular infiltration into non-lymphoid tissues and elevated serum IL-6 and TNFα levels. Autoreactive T cell clones were detected in the periphery of FoxN1-cKO mice. A failure of negative selection, facilitated by decreased expression of Aire rather than impaired regulatory T cell (Treg) generation, led to autoreactive T cell generation. Furthermore, the young environment can reverse age-related Treg accumulation but not inflammatory infiltration. Together, these findings identify thymic involution and the persistent activation of autoreactive T cells as a source of chronic age-related inflammation (inflamming).

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IRB/IACUC# 2013/14-04-A04

1201  Oral  Classification: GSBS Student
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Extracellular Superoxide Dismutase Promotes Immature Neutrophil Egress from the Bone Marrow

Extracellular superoxide dismutase (ecSOD) regulates extracellular concentrations of reactive oxygen species (ROS) to protect tissues during infection and inflammation. Using three groups of mice with varying levels of ecSOD activity, we have previously shown that ecSOD activity enhances neutrophil recruitment to the liver, yet inhibits the innate immune response against Listeria monocytogenes (LM) leading to increased host susceptibility. However, it is unclear whether ecSOD activity affects neutrophil recruitment and function in a cell-intrinsic manner or by modulating the extracellular environment. Using adoptive transfer experiments, we observed that ecSOD activity does not affect neutrophil recruitment or function in a cell-intrinsic manner. Additionally, we determined that ecSOD activity protects the extracellular matrix (ECM) and leads to an increase in phenotypically immature neutrophils in the bone marrow and liver. Collectively, our data suggest that ecSOD activity inhibits degradation of the ECM and promotes egress of immature neutrophils out of the bone marrow and into the liver where they provide inadequate protection against LM. These studies highlight the potential therapeutic value of ecSOD inhibitors to enhance immune responses during bacterial infections.

Sponsor NIH-AI109630
IRB/IACUC# 2013/14-25, 2013/14-02
HIV-1 Tat and gp120 Regulate Astrocyte Tissue Inhibitor of Matrix Metalloproteinases-1 (TIMP)-1

Purpose:
While antiretroviral therapy (ART) has improved the quality of life and survival of HIV-1-infected patients, HIV-1-associated neurocognitive disorders (HAND) remain a major problem in over 30% of cases. All forms of HAND are associated with CNS inflammation. Astrocytes, the principal type of glial cells, are involved in signaling, homeostasis, and repair during CNS pathology. Some astrocytes become non-productively infected by HIV-1. The balance between matrix metalloproteinases (MMP) and their inhibitors must be tightly regulated during CNS inflammation. In the brain, tissue inhibitor of MMPs (TIMP)-1 protects human neurons from HIV-1-induced apoptosis and is mainly produced by astrocytes. Further, astrocyte TIMP-1 is differentially regulated during acute and chronic IL-1β-activation. However, the direct or indirect effects of astrocyte HIV-1 protein expression on TIMP-1 regulation are not well studied. Here, we investigated downstream effects of HIV-1 Tat and gp120 expression in astrocytes on the TIMP-1/MMP balance.

Methods:
Primary human astrocytes were transfected with HIV-1 protein-expressing plasmids (Tat72, Tat101, gp120JR-FL). First, HIV-1 Tat and gp120 expression levels were compared using RT²-PCR and western blot. Cell viability and proliferation were evaluated as measures of cytotoxicity using MTT and BrdU assays, respectively. Concurrently, time-dependent changes in TIMP-1 and CCL2 mRNA and protein levels were measured as indicators of astrocyte activation. Since C/EBPβ is a known TIMP-1 regulator, alterations in C/EBPβ mRNA and protein levels were analyzed.

Results:
HIV-1 Tat and gp120 expression in astrocytes significantly reduced cell viability. Transfected astrocytes showed higher cytokine and chemokine mRNA as well as protein levels. C/EBPβ mRNA expression was differentially altered in astrocytes expressing either HIV-1 Tat72, Tat101 and gp120 indicating potentially distinct underlying mechanisms.

Conclusions:
We propose that TIMP-1 is differentially regulated by HIV-1 protein expression in astrocytes, which mimic viral CNS reservoirs, and may have implications in HAND neuropathogenesis.

Sponsor
NINDS
IRB/IACUC# 2007-121
Independent of bacterial clearance, Interleukin-17A acts to exacerbate pulmonary inflammation in BALB/c mice infected with Mycoplasma pulmonis

Purpose:
Accounting for >50,000 deaths per year, lung infections are a leading cause of mortality in the United States. Chronic lung diseases complicated by infectious disease result in an additional 140,000 deaths. As a leading cause of pneumonia in man and animals worldwide, mycoplasmas cause persistent infections that induce debilitating chronic lung inflammation. An incomplete understanding on the pathogenesis of disease has contributed to the absence of effective vaccines against these organisms. Using a naturally occurring murine model mirroring human and animal infections, interleukin-17A (IL-17A) was found to increase within the lungs of susceptible BALB/c and resistant C57BL/6 mice inoculated with M. pulmonis. In a previous study, C57BL/6 mice deficient in IL-17 receptor expression were shown to have impaired clearance of mycoplasma. We hypothesized that IL-17A may have a different role in susceptible BALB/c mice. Consistent with this idea, we report that injection of neutralizing antibodies against IL-17A reduced respiratory inflammation in BALB/c infected with M. pulmonis. This was seen through abrogated lymphoid and neutrophil recruitment when compared to littermate controls. In addition, both gross lung and alveolar lesions were significantly reduced upon IL-17A neutralization. Surprisingly, blocking IL-17A did not alter bacterial burden, thus solely influencing the inflammatory process during infection in BALB/c mice. Interestingly, anti-IL-17A antibody administration did not have an effect mycoplasma infection in resistant C57BL/6 mice, suggesting that the IL-17A pathways differ between susceptible and resistant strains of mice.

Sponsor: N/A
IRB/IACUC#: 2013/14-01

Osteopathic Lymphatic Pump Treatment Does Not Alter Antibiotic Distribution in a Rat Model

Purpose:
Osteopathic doctors perform manual medicine treatments to promote the body to self-heal. The lymphatic pump technique (LPT) is one of these treatments and it has been shown to improve lymph circulation and delivery of immune factors. In 2010 we developed a rat model to study the effect of LPT on the lymphatic system. We found that 4 minutes of LPT significantly increased the lymph flow and the concentration of lymphocytes in the lymph. We also found that the combination of LPT and levofloxacin protected against Streptococcus pneumoniae-mediated pneumonia by reducing the concentration of bacteria in the lungs. Furthermore, LPT has been shown to increase the uptake of antigen from the interstitium; therefore, LPT may act as an adjunctive therapy during the treatment of pneumonia by enhancing the uptake and delivery of antibiotics. Specifically, we hypothesized that LPT would increase the concentration of levofloxacin in the lungs.

Materials and Methods:
Male, Fisher 344 rats with jugular vein catheters weighing between 200-300 grams were used. Rats were injected subcutaneously with 50 mg/kg levofloxacin and randomized into control, sham, or LPT groups. Control rats received no treatment or anesthesia, sham rats received anesthesia for 4 minutes, and LPT rats received LPT under anesthesia for 4 minutes. Ten minutes post-treatment, serum and bronchoalveolar lavage fluid (BALF) were collected and the concentration of levofloxacin was determined using a levofloxacin bioassay.

Results:
In serum, there was no significant difference (p value= 0.74) in the levofloxacin concentration between control (3.8±0.4 μg/ml), sham (3.9±0.6 μg/ml), or LPT (4.3±0.5 μg/ml). Similarly in the BALF, there was no significant difference (p value= 0.69) in the levofloxacin concentration between control (0.14±0.03 μg/ml), sham (0.10±0.03 μg/ml), LPT (0.12 ±0.03 μg/ml).

Conclusion:
In conclusion, the results from this experiment suggest that LPT does not enhance the delivery of levofloxacin to the lungs. Alternatively, LPT may act as an adjunctive therapy during the treatment of pneumonia by enhancing immune-mediated protection. Future studies are necessary to test this hypothesis.

Sponsor: N/A
IRB/IACUC#: 2012/13-37-A05
The Role of Lymph Flow on MTLn3 induced Breast Cancer

Purpose: Secondary lymphedema is the chronic accumulation of lymph with no definitive cure. At least 22% of axillary lymph node dissection and biopsies in breast cancer (BC) patients can lead to secondary lymphedema. There are no pharmaceuticals approved for lymphedema however manual medicine techniques have been designed to enhance lymph flow. Many clinicians fear manual medicine techniques, such as osteopathic lymphatic pump treatment (LPT), could promote metastasis in BC patients although there is a lack of literature supporting this notion. Our previous studies have shown LPT increases lymph flow and leukocyte concentrations in the lymph of rats. Physical activity increases lymph flow and has been associated with improved quality of life in BC patients and proposed as a modulator of the immune system. Therefore we proposed increasing lymph flow does not promote primary tumor growth.

Methods: To determine the effect of LPT on BC, rats were randomized on day 0 into control, sham and LPT groups and injected with MTLn3. The LPT group received LPT under anesthesia, the sham group received anesthesia and the control group did not receive LPT or anesthesia. Treatment was administered once daily at days 14-24 post-injection. At days 0, 7, 14, 21 and 25, primary tumors were excised, measured, weighed and prepared for histological examination. Axillary sentinel lymph nodes (SLN) were excised, weighed and leukocyte populations were measured.

Results: In the control rats, tumor weight increased significantly between days 14 (0.06 grams) and 25 (2.86 grams) post-injection. Tumor volume in situ increased significantly between days 14 (1.17 cm³) and 25 (2.75 cm³) post injection. Consistent with tumor growth, immunofluorescent staining revealed angiogenesis between days 14 and 25. Furthermore, SLN weight increased significantly (three-fold increase) and pathology confirmed metastasis by day 25. The number of T cells, B cells, NK cells, dendritic cells and macrophages were significantly higher in the SLN by day 25. LPT did not increase primary tumor size compared to control and sham groups. Interestingly, sham significantly increased SLN size (five-fold increase) when compared to control and LPT decreased SLN size when compared to sham.

Conclusions: Our results suggest LPT does not increase primary tumor growth and negated the effect of sham treatment on the sentinel lymph node. Therefore, future studies will focus on how LPT reduces sham induced enlargement and determine if LPT reduces tumor load or fluid in the SLN.

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IRB/IACUC# 2013/14-36-A05
Investigative Genetics (Abstracts in the 1300s)

**1300**  
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**Selection of an Ancestry-Informative Marker (AIM) Panel of INDELs**

**Purpose (a):**
In forensics, there are two main concerns with the marker systems currently used for human identification. First, the identification of the source of a biological sample found at a crime scene requires a comparison to a known reference sample. When no suspect is available for comparison, these genetic markers cannot provide any additional phenotypic information. In such cases, Ancestry-Informative Markers (AIMs) can be used as an investigative lead to law enforcement. A second issue commonly encountered is caused by sample degradation. When DNA is exposed to the elements, it can degrade to fragments of less than 200 base pairs (bps). The genetic markers currently used in forensic settings are called Short Tandem Repeats (STRs). The commercially available STR amplification kits generally yield amplified products that are 200-600 bps in length. Marker systems that yield short fragments (Methods (b):

INDELs, insertions and deletions in the genetic sequence as compared to a consensus reference sequence, are a bi-allelic marker system that can be easily multiplexed and analyzed using the instrumentation currently available in forensic laboratories. In this project, publically available genome data was used to select a panel of INDELs that can distinguish between three major global population groups; Caucasian, African, and East Asian. The markers were selected based on specific criteria; length of INDEL, allele frequency divergence, population substructure, and genetic location.

**Results (c):**
All INDELs were tested for departure from Hardy-Weinberg Equilibrium (HWE) and evidence of linkage disequilibrium (LD). Principal Component Analysis (PCA) of the markers indicate the AIMs ability to completely separate the three population groups. Additionally, analysis in STRUCTURE v2.3.4 gives statistical support for the presence of three separate population clusters.

**Conclusions (d):**
A robust panel of AIMs was chosen to distinguish between three major global population groups. By multiplexing these markers into a single reaction, the panel will provide a quick, reliable method for determining the ancestry origin of an unknown sample, which may provide significant benefits to forensic investigations.

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**IRB/IACUC#** 2010-132


**1301**  
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**Detection of intra-allelic sequence variants within Short Tandem Repeats using the Illumina ForenSeq DNA Signature Prep Kit and MiSeq Desktop Sequencer**

**Objective:** The goal of this study was to identify and characterize intra-allelic sequence variants that exist inside the short tandem repeat (STR) sequences captured by the ForenSeq DNA Signature Prep Kit panel for a Hispanic sample population (n=150).

**Materials and methods:** DNA from 150 Hispanic reference samples were used in this study. All samples were anonymized and collected according to IRB-approved protocols. The ForenSeq DNA Signature Prep Kit was used to barcode and generate sequence libraries so all 150 samples could be multiplexed. Sequencing was conducted on the MiSeq Desktop Sequencer, and data analysis was carried out using the ForenSeq Universal Analysis Software (UAS) and in-house Excel-based workbooks.

**Results:** All 27 autosomal STRs, 24 Y-STRs and 7 X-STRs included in the ForenSeq DNA Signature Prep kit were evaluated. A total of 31 loci were found to have sequence variation in at least one nominal allele. Within that group, 21 loci exhibited variation at greater than or equal to 3 or more nominal alleles. Although most alleles had only two varying sequences per nominal allele, some loci demonstrated a larger amount of variation within their nominal alleles, increasing the diversity and discrimination power at those sites.

**Conclusions:** These results demonstrated that intra-STR allelic sequence variation can be detected and characterized for the STRs captured with the ForenSeq Signature DNA Prep kit. Furthermore, the characterization of these sequence variants in STRs offers great potential as a means of further individualizing DNA samples from one another, opportunities for improved mixture de-convolution, and kinship analyses, such as identifying victims from mass disasters.

**Sponsor** Illumina  
**IRB/IACUC#** 2010-132
DNA is more susceptible to damage towards the distal end. Mitochondrial DNA sequencing was performed on specific samples to observe any repeat sequence and motif structure, and individualized based on unique sequence composition in regions flanking the repeat region. Further and then selected within a species based on the polymorphism observed among the individual samples. These loci would be more informative than existing panels of dinucleotide STR loci reported in the literature and used in wildlife genetics.

Each of the three primary bear species in North America: the American black bear, the brown (grizzly) bear, and the polar bear. These loci would be more informative than existing panels of dinucleotide STR loci reported in the literature and used in wildlife genetics. STRs often observed at tetranucleotide loci.

Hypothesis: The main objective of this study was to perform a preliminary identification of a suite of new tetranucleotide repeat STR loci, for each of the three primary bear species in North America: the American black bear, the brown (grizzly) bear, and the polar bear. These loci would be more informative than existing panels of dinucleotide STR loci reported in the literature and used in wildlife genetics. STRs are currently typed by PCR amplification followed by electrophoretic sizing that cannot identify polymorphisms in the repeat motif structure often observed at tetranucleotide loci.

Methods: In this study, barcoded, adaptor-ligated genome libraries were prepared for four individuals from each bear species from enzymatically fragmented ursine DNA to be interrogated by massively parallel sequencing. Preliminary libraries for the set of samples were size selected and quantified to ensure sufficient concentrations for downstream processing. These preliminary libraries were enriched for tetranucleotide STR sequence regions prior to sequencing using biotinylated RNA baits designed to capture twelve sequence motifs common to mammals. The enriched libraries were sequenced using the Ion Torrent™ Personal Genome Machine™ (PGM) and the data analyzed using the NextGENe® software using a Floton assembly method for de novo alignment to synthetically reference sequences based on the nucleotide structure of the targeted STR motifs as reference genomes for the bear species examined in this study do not exist. Loci were sorted by species and then selected within a species based on the polymorphism observed among the individual samples.

Results and Conclusions: Several tetranucleotide STR loci were identified within each bear species. Loci were characterized based upon common repeat sequence and motif structure, and individualized based on unique sequence composition in regions flanking the repeat region. Further characterization of individual alleles observed at the loci within and between the bear species is underway, and additional individuals will be typed at the optimized loci to establish allelic frequency distributions, genetic stability, and establish their value as individualizing markers. All unambiguous sequences identified in this study will be submitted to Genbank.

Sponsor
IRB/IACUC# 2010-120
**Effect of Dietary Methylmercury on the Gut Microbiome of Fathead Minnows (Pimephales Promelas)**

**PURPOSE:**
The purpose of this study was to investigate the effect of dietary methylmercury on the gut microbiome of fathead minnows. We hypothesized that consumption of methylmercury would induce a shift in the composition of the gut microbiome. This shift could render the gut susceptible to takeover by opportunistic pathogens. This shift could also increase the concentration of organisms capable of the biotransformation of mercury.

**METHODS:**
66 gut samples were obtained from the lab of Dr. Aaron Roberts at the University of North Texas. Methylmercury concentrations ranged from 0.02 to 5.5 parts per million. Bacterial deoxyribonucleic acid (DNA) was extracted, and the sequences for the 16S ribosomal ribonucleic acid (rRNA) were amplified by polymerase chain reaction (PCR). Amplicons were optimized and sequenced using the Ion Torrent™ Personal Genome Machine (PGM™) Sequencer® (Life Technologies™, Carlsbad, CA) with barcoded primers to identify the samples. Sequence data was analyzed using mothur.

**RESULTS:**
Data analysis revealed that the presence of dietary methylmercury induced a significant shift in the composition of the microbiome. Communities featured a decrease in order diversity, and an increased concentration of select taxa such as Fusobacteriales.

**CONCLUSIONS:**
The data supports our hypothesis that exposure to dietary methylmercury induced a shift in the composition of the fathead minnow gut microbiome. Further studies shall be devised to investigate the genome of those select taxa that flourished under these conditions.

**Sponsor**
N/A

**IRB/IACUC#**

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**Evaluation of the PowerSeq™ Auto System by Massively Parallel Sequencing**

Massively parallel sequencing (MPS) is potential technology for STR typing by forensic laboratories and that some of the CE-based limitations may be overcome by MPS. In this study, the PowerSeq Auto System (Promega) containing 23 STR loci and Amelogenin, was evaluated by MPS. The PCR products were size selected using the MinElute PCR Purification Kit (Qiagen). DNA libraries were normalized, pooled and sequenced on the MiSeq (Illumina; 2 x 250 bp). This multiplex STR system was tested for sensitivity of detection based on input DNA. The result showed that a broad range of the quantity of PCR products could be used for library preparation. In mixture study, the partial profile of minor contributor could be detected up to 19:1 mixture. These studies indicate that PowerPlex Fusion STR system and the Illumina MiSeq system can generate reliable DNA profiles with the types of samples and amounts of input DNA that are relevant to forensic analyses.

**Sponsor**
N/A

**IRB/IACUC#**
2010-132
Stated race/ethnicity is not a definitive indicator of patrilineal ancestry in males of major US populations. Evolutionary analyses of Y-linked SNPs provide clustering of Y-haplotypes defining haplogroups, whose geographic origins have been studied at least at continental levels. Lack of recombination allows haplogroup prediction even with Y-STR haplotype data. In this research we examined variations of predicted patrilineal ancestry of individuals grouped by their self-described race/ethnicity. Y-STR haplotype data, encompassing 23 STR loci, on 936 unrelated males published by the US National Institute of Standards and Technology (NIST) were used to examine the Y-chromosomal diversity at the haplogroup level for the three self-described race/ethnicity groups, namely US Caucasians, African Americans, and US Hispanics. Of these samples, haplogroups of 814 Y-STR haplotypes were predicted with a Bayesian approach, from which haplogroup diversity was estimated for the three groups. The phenetic tree of the observed Y-STR haplotypes was drawn as a Median Joining Network (MJN) with the program Network, on which their haplogroup prediction and stated race/ethnicity information was superimposed to graphically demonstrate the differences of patrilineal ancestry among the three groups. These predictions were used to estimate the proportions of male ancestry from European, African, and Native American gene pools. Predominantly most (90.85%) US Caucasians had predicted male European ancestry, while the Hispanics and African-Americans had much lower levels of male European ancestry; 62.95% and 31.14%, respectively. Contributions of male African ancestry in Caucasians, Hispanics and African-Americans were approximately 4.27%, 15.23% and 67.47% respectively. Lastly, all three groups exhibited variable amounts of male Native American ancestry; namely, 0.31%, 0.69%, and 14.72%, respectively for Caucasians, African-Americans, and Hispanics. At the haplogroup level, the coefficient of haplogroup diversity (Gst) was 18.15%, suggesting that the three groups differed substantially with respect their male ancestral haplogroup lineages. In contrast, these three groups had 812 distinct 23-locus haplotypes; none of which were shared across the three groups. Only two haplotypes were observed twice each, one in African-Americans, and one in Hispanics. The 328 Caucasians had all distinct haplotypes. These resulted in a coefficient of haplotype diversity (Gst) of 0.26% at the haplotype level. Together these results suggest that while there is virtually no haplotype sharing across these three groups, each of them exhibited considerable amount of haplogroup sharing, and hence prediction of male lineages is not definitive from the stated race/ethnicity of individuals with Y-STR haplotypes defined by the 23 loci of this study.
Clostridium difficile Ribotype 027 Virulence Phenotype Influences Disease Severity when Compared to Ribotype Non-027 Strains in the Hamster CDAD Model

Introduction: C. difficile ribotype 027 (RT027) is the epidemic strain found primarily in North America, and, recently, a strain of C. difficile has been named a superbug by the CDC. Studies have suggested an enhanced virulence phenotype for RT027 such as increased toxin production, but the impact on disease severity on in vivo models is not well understood. This study describes the in vitro characterization of important virulence factors for several RT027 and non-RT027 C. difficile clinical isolates, and how these characteristics may impact disease severity in the hamster C. difficile associated disease (HCDAD) model.

Materials and Methods: Six RT027 and six non-RT027 clinical isolates were evaluated in vitro for total spore counts and Toxin A/B titers in 72H broth cultures. Spore counts were generated from heat/ethanol shock culture samples and plated onto CCFA containing 0.1% taurocholate, and toxin A/B titers were determined from spent broth with the tgcBIOMICS ELISA assay. The HCDAD studies involved infecting male Golden Syrian hamsters with 72H broth cultures of two RT027 and two non-RT027 isolates, followed by subcutaneous administration of 10 mg/kg clindamycin 24H post-infection. One group of infected hamsters was orally treated with 20 mg/kg vancomycin once a day for 3 days following clindamycin administration, while the other group remained untreated. Survival was monitored for 11 days after infection and 3 hamsters were euthanized at set time points to determine cecal fluid associated the CFU/spore counts and Toxin A/B titers.

Results: The RT027 and the non-RT027 strains generated similar mean CFU/mL in 72H broth cultures, while the mean spore counts were 548 spores/mL for the RT027 strains and 273 spores/mL for the non-RT027 strains. In addition, the 72H broth-associated mean toxin A/B titers were 2.8-fold higher for RT027 strains when compared to the 72H titers of non-RT027 strains. In the HCDAD studies 14% of the non-027 infected hamsters became moribund, while 71% of the hamsters infected with the RT027 isolates became moribund. The mean cecal fluid Toxin A/B titers for RT027 infected hamsters were 2.3 to 9-fold higher than the titers for non-RT027 infected hamsters.

Conclusion: The results highlight that C. difficile ribotype isolates, when compared to non-RT027 clinical isolates, have enhanced virulence that corresponds to a more severe disease in the HCDAD model. Understanding why these strains have this phenotype, in vivo as compared to in vitro, is important for treatment as new ribotypes, with varying virulence, are continuously emerging.
Conclusion:
Trends were observed.

Methods to determine the true rate of side effects caused by medications: A case study with antiretroviral medications and diarrhea.

Introduction:
There have been discrepancies between the rates of adverse events reported in the medication's package insert and what have been seen in clinical settings. This difference causes confusion for clinicians and patients and interferes with pharmacists’ attempts to establish the necessary rapport with patient to improve compliance.

Hypothesis:
The incidence of selected adverse event for a class of medication would not be same as those found the package insert.

Goals:
The goal of this project is to conduct a systematic review of current literature to identify the true rate of adverse events associated with common Antiretroviral (ARV) medication regimens.

Methods:
A systematic search of primary literatures was conducted to evaluate the incidence rates of selected adverse events associated with most customary medication regimens recommended by HIV (Human Immunodeficiency Virus)/AIDS (Acquired Immune Deficiency Syndrome) medical practice guidelines. Initially, inclusion and exclusion criteria were established. The keywords collected were used to search the primary literatures and documents produced during the drug approval process. Finally, the gathered data was tabulated and analyzed to determine “true” rate of adverse events.

Results:
The incidence rates of diarrhea among HIV infected—treatment naive—males and non-pregnant females ages: 18-65, were extracted from various sources including: the medication's package insert, pertaining briefing document, clinical trials submitted to FDA, and published—unpublished phase III clinical trials. The medication regimens under investigation included: efavirenz (EFV)/ emtricitabine (FTC)/tenofovir (TDF) (Atripla), raltegravir(RAL)/ FTC/ TDF, and rilpivirine(RPV)/ FTC/ TDF (Complera). The values reported, varied from one source to another. For example, the rate reported in Atripla’s package insert was 9%, and yet nothing was documented in its briefing document. In addition, the average rates (all causes and grades) extracted from submitted clinical trials—published and unpublished phase III clinical trials, were respectively: 22.9% (10.14%-35.6%) and 13.43% (0%-33.9%). The same method was used for the other two medication regimens, and similar trends were observed.

Conclusion:
Preliminary results of case study show the rate of diarrhea reported in package insert was different from what was extrapolated from published and unpublished phase III trials. Further analysis will be conducted to confirm this finding.

Sponsor: N/A
IRB/IACUC#: 2015-009

Next-generation sequencing and cytokine analysis of bronchoalveolar lavage samples from mechanically ventilated trauma patients

Purpose: Mechanically ventilated trauma patients are at high risk for ventilator-associated pneumonia (VAP). VAP diagnosis relies on several clinical factors including the identification of a specific pathogen by culture-dependent techniques. Often, patients exhibit signs of VAP, yet the hospital lab is unable to culture a pathogen from a bronchoalveolar lavage (BAL) sample. We hypothesize that these culture-negative, presumptive positive patients are infected with potentially pathogenic bacteria that are not detected by traditional culture techniques.

Methods: Culture-positive and -negative hospital results were tested again by Sanger and next-generation sequencing (NGS) on the Ion Torrent PGM. Sample cytokine levels were determined using a Bio-Plex Pro Human Th17 cytokine panel.

Results: No significant difference was seen between the identification methods in culture-positive BAL. However, NGS analysis of culture-negative BAL identified hundreds of bacterial genera, including a group of patients that exhibited similar bacterial composition, diversity, and abundance. This group was significantly different from other culture-negative BAL that were dominated by one or two suspected pathogens. Culture-negative BAL contained significantly less IL-1β, IL-6 and TNF-α than culture-positive BAL.

Conclusions: NGS is a valuable method for pathogen identification, particularly for difficult to culture BAL. Culture-positive BAL exhibit less bacterial diversity and increased cytokine production than culture-negative BAL. The grouping of culture-negative BAL with similar characteristics may denote a core lung microbiome.

Sponsor: N/A
IRB/IACUC#: UTSW-STU 062011-0135
Neuroscience (Abstracts in the 1500s)

1501  Poster  Classification: GSBS Student
Presenter: Haydee Izurieta  Department: Pharmacology & Neuroscience
Authors: Haydee Izurieta Munoz, University of North Texas Health Science Center at Fort Worth; Nathalie Sumien, University of North Texas Health Science Center at Fort Worth;

Effects of an acid-sensing ion channel modulator on inflammatory pain

Purpose
The objective of this study was to evaluate GL-001 as an anti-nociceptive compound in an animal model of thermal and inflammatory pain. Acid-sensing ion channels (ASICs) are membrane-bound ion channels that are sensitive to protons and non-proton ligands. In particular, the ASIC3 channel subtype is highly sensitive to decreases in extracellular pH and is found predominantly in peripheral sensory neurons, making it a potential modulator of pain sensation. Non-proton ligand activators and blockers of ASIC3 have been documented to affect nociception in both humans and animal models. As the compound GL-001 shares structural similarity with the non-proton ligands of ASIC3, the hypothesis is that GL-001 will interact with the channel in a similar manner leading to decreased nociception.

Materials and methods
Sixty male and female C57BL/6J mice (2-3 months old) were fed either a control diet or the control diet supplemented with 6.25g of GL-001 per kg of diet for one week prior to and throughout the nociceptive tests. To assess thermal hyperalgesia, the distal portion of the tail of the mice was dipped in a water bath set at 52°C and the latency to withdraw their tails was used as a measure of pain sensitivity. To induce inflammatory pain, the mice were injected with 4% formalin in their right hindpaw, and their nociceptive behavior (licking the injected paw) was recorded and timed. Statistical analyses (t-test for the thermal hyperalgesia, and ANOVAs for the formalin test) were performed with alpha set at 0.05.

Results
Preliminary results indicated that neither sex nor treatment affected the latency to withdraw the tail in the thermal hyperalgesia test, even though the treated mice took 10% longer latencies than the controls. For the formalin test, males and females seemed to respond differently to the stimulus. The female mice treated with GL-001 seemed to recover faster than the controls, which was supported by main effects of treatment in the last 30 minutes of the test.

Conclusion
Our preliminary data suggest a potential effect of GL-001 on nociception, especially related to inflammation. Further, females seemed to be more responsive to GL-001 than males. Further studies will be required to determine the preferred dose of GL-001 for beneficial effects, and identify which ASIC subtypes might be involved in its mechanism of action.

Sponsor  N/A
IRB/IACUC#  2013/14-16

1502  Poster  Classification: TCOM DO Student
Presenter: Jacob Wilson  Department: Texas College of Osteopathic Medicine
Authors: Jacob Wilson, University of North Texas Health Science Center at Fort Worth; David Donahue, MD, Cook Children’s Medical Center;

A Reliable Method for MRI Volumetric Assessment of Hippocampal Resection Following Anterior Temporal Lobectomy

Purpose:
Surgical management of temporal lobe epilepsy in children is an established management of temporal lobe epilepsy (TLE). Surgery for TLE ranges from standard anterior temporal lobectomy (ATL) to selective resections which seek to spare temporal neocortex. Cortical dysplasia (CD) represents the most frequent non-neoplastic cause of TLE in children. Extent of resection (ER) of cortical dysplastic processes has been correlated with seizure control. The goal of this study was to design and test a standardized protocol based on anatomical boundaries for pre-operative (pre-op) and post-operative (post-op) imaging in order to measure hippocampal ER.

Medical records and neuroimaging of a 2 year old developmentally delayed female TLE patient with CD in her right temporal lobe were reviewed. Seizure semiology, electrodiagnostics, and imaging studies indicated independent bilateral temporal dysfunction with the most severe deficit of activity in the right temporal lobe. Pathological analysis of temporal neocortex and mesial structures disclosed evidence of cortical dysplasia in all specimens.

Pre-op MRI studies were performed using a Seimens Verio 3T unit generating 3 sequences: 1) T1 Magnetization Prepared Rapid Gradient Echo 3D with 1.0mm slice thickness, 2) T2 Turbo Spin Echo (TSE) Axial with 4.0mm slice thickness and, 3) T2 TSE Coronal with 3.0mm slice thickness. Post-op MRI studies were performed using a Seimens Esspres 1.5T unit generating 3 sequences: 1) T1 Spin Echo (SE) Axial with 5.0mm slice thickness, 2) T2 TSE Axial with a 5.0mm slice thickness and, 3) T2 TSE Coronal with a 3.0mm slice thickness. Studies were co-registered via Hermes, a product of Hermes Medical Solutions, which rendered multiple image studies into one file. The resulting 3D brain map was then loaded into Amide, a free image viewing tool for registering and analyzing medical data image sets, which allowed a slice by slice evaluation of both pre-op and post-op images.

After hippocampal boundaries were identified on each coronal slice, a region of interest (ROI) was created outlining hippocampal area. Amide calculated ROI areas for each slice and summed ROI areas to yield hippocampal volume.

Analysis of ROI yielded pre-op hippocampal volume of 2.691 cm³ vs. post-op volume of 0.259 cm³. ATL in our patient removed 96.25% of the hippocampus, leaving 3.75% of hippocampal tail remaining. Analysis completed after construction of protocol used to determine hippocampal anatomical borders. This project successfully designed and tested a standardized protocol based on anatomical boundaries for pre-op and post-op imaging in order to measure hippocampal volume ER. This protocol will allow for measurement of ER in future studies of TLE in pediatric populations.

Sponsor  N/A
IRB/IACUC#  CCHMS 2009-063
Acid-sensing ion channel modulation by nonproton ligands: the influence of divalent cations

1. The acid-sensing ion channel (ASIC) is emerging as a potential mediator for a variety of pathologies, such as stroke, pain, and mental health diseases. Despite their involvement in multiple age-related pathologies, the ability to selectively target the ASIC subtypes remains unidentified. As their name suggests, ASICs are activated by an increase in extracellular protons, however other ASIC ligands include natural venom toxins, guanidine containing compounds, and calcium. Nonproton ligands, like 2-guanidine-4-methylquinazoline (GMQ), have been identified to selectively activate the peripheral ASIC3 via the nonproton ligand sensor domain (NPLSD). A pair of glutamates in rat ASIC3 (E79 and E423) responsible for GMQ activation is present in the structural determinant chicken ASIC1, despite having no direct modulation effect on the channel. We previously showed that cASIC1 could be activated by GMQ following a based on a partially activated channel state. Interestingly, low calcium concentrations cause the peripherally located ASIC3 subtype to be partially activated. We proposed that direct nonproton ligand activation of ASIC3 is possible due to the actions of the transmembrane domains (TMD) where calcium sensitivity resides. Additionally, the introduction of ASIC3 TMDs into a GMQ insensitive ASIC subtype (cASIC1) will reveal nonproton ligand sensitivity.

2. Chimeric receptors combining the extracellular, transmembrane, and intracellular domains of rat ASIC3 and chicken ASIC1 were generated to individually isolate the calcium and nonproton ligand effects on channel activation. Each chimeric receptor was assessed for function using whole cell patch clamp electrophysiology.

3. We confirmed that rASIC3 is activated and held open when extracellular calcium concentrations are reduced with minimal proton influence (pH 8.0). Low-calcium-activation of rASIC3 is further enhanced by the addition of GMQ in a concentration dependent manner. These effects are absent in cASIC1. The chimera termed cASIC1 (rASIC3-TM/ITC) is comprised of the extracellular domain of cASIC1 and the transmembrane/intracellular domains of rASIC3, and can be activated by GMQ in the absence of calcium, although its sensitivity to GMQ is reduced. Thus, GMQ activation was introduced in cASIC1 by replacing the transmembrane domains with those of ASIC3.

4. This data suggests that the ASIC3 TM domains dictate NPLSD influence on channel activity. Fully understanding how we can interrupt or enhance channel activation will allow us to preferentially target these ion channels, potentially leading to the promotion of developing novel therapeutics to interact with ASICs.

Sponsor
IRB/IACUC#

Alcohol Regulates HIV-1-Mediated Astrocyte Inflammatory Responses Via cPLA2 Signaling Pathway

Alcohol (EtOH) abuse and HIV-1 remain significant public health problems. Globally, drinkers have approximately 70-77% higher risk of HIV-infection than non-drinkers. The prevalence of alcohol abuse among HIV-positive individuals has been estimated to be between 29-60% in the United States. Many studies showed that neurodegeneration in alcohol abusers include exacerbated neuroinflammation and oxidative damage. However, how EtOH regulates HIV-1-induced astrocyte neuroinflammation is unknown. Thus, we explored mechanism(s) involved in alcohol-mediated activation of human astrocytes with HIV-1 and subsequent alterations in their inflammatory functions.

Alcohol exposure altered the morphology of astrocytes, proinflammatory responses and induced cytotoxicity in a dose-dependent manner. Time-dependent changes were also evaluated. Alcohol and HIV-1 co-treatment decreased cell viability and proliferation, while increasing apoptosis and mitochondrial depolarization. Alcohol and HIV-1 together increased the levels of proinflammatory molecules, IL-1β, TNF-α, CXCL8, TIMP-1 and more importantly, arachidonic acid, known to be downstream of cPLA2. Consistent with this observation, phospho-cPLA2 levels were augmented in HIV-1 and EtOH co-treatment as compared to HIV-1 or EtOH alone. COX2 was upregulated as measured by real time PCR and western blot, whereas co-treatment of HIV-1 and EtOH decreased CYP2E1 levels as compared to EtOH alone. In summary, our results demonstrate that EtOH-mediated astrocyte inflammation and cytotoxicity in context of HAND occurs via cPLA2 signaling.

Sponsor
NIH RO1NS48837 to AG
IRB/IACUC# 2007-121
CB1 Receptor Antagonist, ATDP 32,456, as an Emergency Treatment Modality for Synthetic Cannabis Overdose in Mice

ATDP 32, 456 is a proven agent for blocking the effects of cannabinoids at the CB1 receptor. We sought to determine if the suppression of locomotor activity by Delta(9)-THC, JWH-018 and other synthetic cannabinoids could be alleviated with administration of ATDP 32, 456. The suppression of locomotor activity of mice was measured after administration of cannabinoids and after different rescue doses of ATDP 32, 456 given via the intraperitoneal route, 1-hour later. We noted a statistically significant reversal of locomotor activity suppression and inhibition of synthetic cannabinoid effects when mice received 3, 10 or 30 mg/kg ATDP 32, 456. These data support the use of ATDP 32, 456 as an acute treatment method for cannabinoid intoxication, though formulation compatible with intravenous administration would be required for a rapid response.

Sponsor
NIH-NIDA
IRB/IACUC# 2010/11-02-A04
Chronic Intermittent Hypoxia increases oxidative stress and inflammation

Background: Inflammation has been linked with sleep apnea. Sleep apnea is a common comorbidity associated with neurodegenerative disorders, such as Parkinson’s disease and Alzheimer’s disease. Furthermore, neurodegenerative diseases have also been linked with inflammation. A possible mechanism underlying increased inflammation in these disorders is oxidative stress, a hallmark of neurodegeneration. To examine the role of oxidative stress on inflammation, we used chronic intermittent hypoxia (CIH), an established model for the hypoxemia associated with sleep apnea. CIH consists of recurring events of low oxygen followed by reoxygenation.

Statement of Hypothesis: We hypothesize that CIH causes oxidative stress, which induces inflammation.

Materials and methods: To test this hypothesis, plasma from adult male rats subjected to 7 days of CIH (3 minute periods of hypoxia (10% oxygen) and 3 minute periods of normoxia (21% oxygen) for 8 hours per day) or normoxia (room air) were tested for AOPP, an indicator of oxidative stress, and circulating inflammatory markers (such as IL-1β, IL-10, IL-4, IL-6). Additionally, a group of rats was administered a neurotropic AAV with shRNA for AT1a receptors in their forebrains and instrumented with telemetry for blood pressure recording prior to CIH treatment to determine the effects of angiotensin on CIH hypertension and oxidative stress.

Significant results: Our results showed that CIH significantly increased circulating oxidative stress and inflammation. Interestingly, IL-1β, IL-2, and TNF-α inflammatory markers were associated with oxidative stress, unlike IL-10, IL-4, and IL-6 inflammatory markers. These markers were positively associated with IL-1β. Knockdown of angiotensin 1 receptors in the forebrain blocked the diurnal hypertension and CIH induced oxidative stress, indicating the involvement of CIH hypertension and central angiotensin receptors in CIH induced oxidative stress.

Conclusions: These results indicate that both neurons and macrophages contribute to CIH induced oxidative stress and inflammation and that CIH oxidative stress and inflammation is dependent on central angiotensin receptors and CIH hypertension.

Sponsor Texas Garvey Foundation; William and Ella Owens Medical Research Foundation; Graham & Carolyn Holloway Foundation; UNTHSC Intramural Grant; IAA DR Institute Grant; Alzheimer’s Association New Investigator Research Grant NIRG-14-321722; PO1 HL088052; and RS

IRB/IACUC# 2011/12-36
Concomitant Mutations of Sodium Channels SCN8A and SCN2A Cause Dravet Syndrome Phenotype

Purpose: To report a unique case of Dravet Syndrome (DS) and investigate the relationship between inherited SCN2A and de novo SCN8A mutations in our patient; to determine whether a de novo SCN8A mutation can cause DS; to review the genetic causes of DS phenotype and the need for thorough genetic evaluation for SCN1A-negative DS cases.

Methods: In this observational, retrospective case study, we focused on patient records analysis including whole-exome sequencing, EEG, and MRI.

Results: This study found reason to believe that the de novo SCN8A mutation acted as a phenotypic modifier of the inherited SCN2A mutation, resulting in DS. The study also found a significant need for genetic evaluation beyond SCN1A mutations. In addition, Stiripentol was found to be an effective treatment for DS in this patient.

Conclusions: Based on our findings and those of relevant studies, our patient’s de novo SCN8A mutation likely acted as a phenotypic modifier of the inherited SCN2A mutation potentially through a “two-hit” mechanism. The vast array of genetic etiologies of DS warrants thorough genetic testing beyond the most common SCN1A mutation. Stiripentol, though currently an investigative drug, shows promise as an effective therapeutic agent in our patient and potentially other cases of non-SCN1A DS.

Sponsor: UNTHSC Summer Research Fellowship

IRB/IACUC#: 1509

Human cerebral organoids generated using urinary epithelial cell-derived induced pluripotent stem cells

Background: Human induced pluripotent stem cells (hiPSCs) provide a great promise for the success of novel disease model and regenerative medicine. Such remarkable cells may be derived using virtually any types of somatic cells through cell reprogramming and used for addressing questions relevant to the physiopathological development of human organs. The generation of hiPSCs using somatic cells that are obtained by noninvasive approaches would be ideal for the further development of hiPSC-based models to address childhood disease. Given the pluripotency in hiPSCs, we anticipate that hiPSCs generated from cells isolated in urine samples can be used for creating a three-dimensional organoid model system to recapitulate human brain development.

Purpose: We desire the generation of transgene-free hiPSCs using urinary epithelial cells collected from the urine samples of health donors. We will further test cellular pluripotency and the capacity of forming three-dimensional cerebral organoids (minibrains) in these hiPSCs.

Method: We use a polycistronic, self-replicating RNA system to express four transcription factors SOX2, KLF4, OCT4, and MYC in urinary epithelial cells that are isolated from the mid-to-late stream urine samples of healthy individuals. We also generate cerebral organoids from urinary epithelial cells-derived hiPSCs and other bona fide human pluripotent stem cell (hPSC) lines using an established differentiation protocol.

Results: Urinary epithelial cells were successfully collected from four individuals, cultured, and reprogrammed into hiPSCs. Reprogrammed urinary epithelial cells express pluripotency markers and form cell types showing biomarkers for all three germ layers in undirected differentiation. The bona fide hPSCs have been used to optimize the procedure of building three-dimensional cerebral organoids. After matrigel embedding, the hPSC spheres that were precommitted to neuronal differentiation further developed complex structures that resemble discrete but interdependent cerebral regions, including forebrain, hippocampus, cortex, hindbrain, and a neural stem cell zone. These organoids stain positive for TUBB3 (a biomarker for neurons), GFAP (a biomarker for astrocytes), and SOX2 (a biomarker for neural stem cell populations).

Conclusions: Our preliminary data suggest that hPSCs can reproducibly form minibrains in a defined culture condition. We will use the optimized procedure to test the capacity of urinary epithelial cells-derived hiPSCs in forming three-dimensional cerebral organoids (minibrains) and further establish a suitable model for studying brain developmental abnormalities associated with childhood disease.

Sponsor: American Federation of Aging Research, Glenn Foundation, American Osteopathic Association

IRB/IACUC#: 2014-101
Mechanisms by which estradiol (E2) suppress neuronal cox-2 gene expression

Purpose:
Data from culture and animal models indicate that 17β-estradiol (E2) deprivation increases susceptibility to neurodegenerative and neuropsychiatric diseases. E2 plays a pivotal role in attenuating inflammatory response in the brain by suppressing expression of proinflammatory genes; however, the molecular mechanisms by which E2 suppress neuronal pro-inflammatory genes are not well established. The pro-inflammatory cyclooxygenase-2 gene (cox-2) is selectively expressed in neuronal populations of the amygdala, hippocampus and cortex. Upregulation of cox-2 expression has been implicated in cascades of deleterious effects that promote neuronal injury and dysfunction. The goal of this study is to elucidate the molecular mechanisms by which E2 suppress cox-2 expression in a neuronal context.

Methods:
To characterize the effect of E2 on cox 2 in a neuronal system, we used the AR-5 immortalized rat neuronal cell line. This cell line was developed by Kasckow et al. from rat embryonic amygdala cells. We first determined that the cell line constitutively expresses COX-2 protein by Western blots and immunocytochemistry and mRNA and hnRNA by RT-qPCR. To assess whether the E2 effect was mediated by ER-alpha (ERα) and/or ER-beta (ERβ), we treated the cells with E2, Diarylpropionitril (DPN), and propyl-pyrazole-triol (PPT). COX-2 mRNA and hnRNA levels were analyzed by RT-qPCR following treatments with the ligands.

Results:
Twenty-four hours of E2 exposure reduces neuronal COX-2 mRNA and hnRNA levels. E2 and DPN treatment led to suppression of COX-2 mRNA and hnRNA after 24hrs. In distinction, PPT had no effect.

Conclusions:
Collectively, the data indicate that E2 suppresses neuronal cox-2 expression through ERβ.

Sponsor
IRB/IACUC#
The Effects of Androgens on COX2 signaling in Oxidatively Stressed Dopamine Neurons

Hypothesis: We hypothesize that under oxidative stress conditions, the androgen, testosterone, will increase COX2 induced alpha-synuclein expression, leading to apoptosis in dopamine neurons.

Materials and Methods: To test our hypothesis, we exposed a dopaminergic cell line (N27 cells) to a sublethal concentration of the pro-oxidant, tert-butyl hydrogen peroxide (H2O2) for 24 hours and assessed the role of testosterone on COX2 signaling.

Results: Under low oxidative stress conditions, COX2 protein levels are low and alpha-synuclein expression and apoptosis are absent. However, under oxidative stress conditions, COX2, alpha synuclein, and apoptosis were increased, and these factors were exacerbated by testosterone.

Conclusion: Our data shows that androgens may mediate the gender differences observed in PD by activating COX2 mediated inflammation and oxidative stress in dopamine neurons.

Sponsor National Institute of Health grant F32 NS061417 and AHA BGIA4180116 to RLC and NIH T32 AG020494 to SH

IRB/IACUC#
The Role of Sleep Apnea Induced Oxidative Stress in Stroke Pathogenesis and Recovery

Purpose: Obstructive sleep apnea (OSA) is a common, but under-diagnosed comorbidity among patients with a number of age-related disorders, including stroke, Alzheimer’s disease, and Parkinson’s disease. Many of the risk factors for sleep apnea, such as obesity, are modifiable and treatment of sleep apnea itself can limit its systemic effects. Because of these facts, understanding the role of OSA in more serious diseases may promote awareness and early diagnosis, thus preventing serious adverse health outcomes.

Given the knowledge that sleep apnea increases oxidative stress, in order to investigate the effects of sleep apnea on the pathogenesis of and recovery from stroke, we used chronic intermittent hypoxia (CIH) as an animal model of sleep apnea in rats.

Methods: 12 rats underwent behavioral testing and were then randomly assigned to chambers with either a constant normoxic environment or one that simulates the chronic intermittent hypoxia of sleep apnea. Cerebral ischemia was induced in rats by occlusion of the middle cerebral artery. After a day of recovery, cognitive impairment, oxidative stress, and the size of the ischemic lesion was measured.

Results: The experiment showed that CIH increased the size of the stroke lesion in the brain. In this setting, CIH did not appear to alter circulating oxidative stress protein measures or acute stroke behaviors.

Conclusion: Based on these results, sleep apnea co-morbidity can have deleterious effects on stroke outcomes.

Sponsor: Medical Students Training in Aging Research, American Federation for Aging Research
IRB/IACUC#: 2013-14-18-A05

Treatment with Losartan Improves Baroreflexes in Obese Zucker Rats Coincident with Enhanced Response of Nucleus Tractus Solitarius (NTS) to Increased Arterial Pressure

Obese Zucker rats (OZR) have impaired baroreflex-mediated responses to acute rises in mean arterial pressure (MAP) coincident with the development of hypertension. In addition, the NTS becomes less responsive, with reduced phenylephrine (PE)-induced c-Fos expression and smaller physiological responses to glutamate in the NTS. Here, we determined if treatment with the angiotensin-AT1 receptor antagonist, losartan (LOS) improves baroreflexes and the PE-induced c-Fos expression in NTS of OZR. Baroreflex-mediated changes in HR to PE-evoked rises in MAP (40 mmHg) were measured in conscious rats implanted with femoral catheters. Rises in MAP were sustained with PE, and then rats were perfused after 90 min to examine NTS c-Fos expression. Treatment with LOS (for 5 wks) normalized MAP in OZR vs. LZR (untreated: 128±2 vs. 115±3 mmHg, with LOS: 111±3 vs. 112±2 mmHg; at 14.1 wks). LOS treatment enhanced PE-induced reductions in HR in OZR but not LZR. (untreated: 43±10 vs. -101±9 -bpm; with LOS: -75±12 vs. -112±11bpm). Although LOS improved PE-induced reductions in HR in OZR, responses in LOS-treated OZR were still smaller vs. LOS-treated LZR, suggesting a partial restoration of baroreflexes. PE-induced c-Fos expression in NTS was less in untreated OZR vs. LZR (30±5 vs. 50±6 counts). Treatment with LOS enhanced PE-induced c-Fos expression in OZR (54±11 counts), but not LZR (58±11 counts), rendering comparable PE-induced c-Fos expression in LOS-treated OZR and LZR. These data suggest that LOS improves hypertension, baroreflexes, and NTS function in OZR. Further study is needed to determine whether improved function by LOS is explained by normalization of MAP in OZR.

Sponsor: AHA GRNT18880005.
IRB/IACUC#: 2013/14-11-A05
Background: In order to reduce preventable prehospital death on the battlefield there needs to be an increase in prehospital medical documentation. The purpose of this study was to determine if there is a lack of training on utilizing Department of the Army Form 7656/Tactical Combat Casualty Care card during pre-deployment medical training at Tactical Combat Medical Care course, at the Center for Predeployment Medicine and the AMEDD Center and School. This form captures prehospital injury and intervention data from point of injury to definitive medical treatment.

Methods: A direct observational study of prehospital medical documentation was conducted on simulated Combat Casualties by Military Medical Providers, utilizing Department of the Army Form 7656/Tactical Combat Casualty Care card. Completion of one form during trauma lane training, per simulated combat casualty satisfied the inclusion criteria for qualitative results. Our hypothesis was there is no training deficit on Department of the Army Form 7656/Tactical Combat Casualty Care card at Tactical Combat Medical Care course.

Results: During the period studied, every other week over four months January – April 2013, 130 Department of the Army (DA) Form 7656/Tactical Combat Casualty Care (TCCC) cards were collected and evaluated from 131 simulated combat casualties. The quantity of the form completed was 99.20% with an accuracy of completed prehospital medical documentation at 80.70%.

Conclusion: Leaders enforcing standards will be the driving force for increased prehospital medical documentation. This study demonstrates there is not a lack of training at Tactical Combat Medical Care course on completing Department of the Army Form 7656/Tactical Combat Casualty Care card.

Keywords: DA Form 7656, Prehospital Medical documentation, Prehospital battlefield death.

Sponsor N/A
IRB/IACUC# 382121-1 From: Brooke Army Medical Center IRB N/A (Manikins had been used)
**1602**  
**Poster**  
**Classification:** GSBS Student

**Presenter:** Sean Dolan  
**Department:** Pharmacology & Neuroscience

**Authors:** Sean Dolan, University of North Texas Health Science Center at Fort Worth; Michael Gatch, Ph.D., University of North Texas Health Science Center at Fort Worth;

**Abuse liability of the novel benzofuran 6-APDB**

Benzofurans, sold online as “benzo-fury,” represent a class of designer drugs that have gained popularity on the ever-expanding market of “legal highs.” Users report that these compounds produce entactogen-like effects similar to MDMA. The current study aims to investigate the behavioral effects and abuse liability of the novel benzofuran 6-APDB. The locomotor effects of 6-APDB were tested in male Swiss-Webster mice over an 8-hour period in an open-field assay of locomotor activity. The discriminative stimulus effects of 6-APDB were tested in separate groups of male Sprague-Dawley rats trained to discriminate cocaine, methamphetamine, or MDMA from vehicle. The rewarding effects of 6-APDB were tested in male Swiss-Webster mice using a conditioned place preference assay. 6-APDB produced locomotor stimulation at 5 and 10 mg/kg starting 30-minutes post-injection and lasting approximately 3 hours. 6-APDB fully substituted for the discriminative stimulus effects of MDMA at 1 mg/kg, but produced low levels of drug-appropriate responding for cocaine- and methamphetamine-trained rats at the same dose. 6-APDB produced conditioned place preference. Our results indicate that 6-APDB produces hyperlocomotion, conditioned place preference, and discriminative stimulus effects similar to MDMA, suggesting that 6-APDB may have potential for abuse. The substitution of 6-APDB for MDMA, but not cocaine or methamphetamine, suggests that this compound may be used as a substitute for MDMA in a club or rave setting, especially as MDMA becomes more difficult to obtain.

**Sponsor** National Institute on Drug Abuse  
**IRB/IACUC#** 2012/13-52-A04; 2012/13-53-A05

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**1603**  
**Poster**  
**Classification:** GSBS Student

**Presenter:** Vuvi H. Nguyen  
**Department:** Integrative Physiology

**Authors:** Vuvi Nguyen, University of North Texas Health Science Center at Fort Worth; Howe Liu, University of North Texas Health Science Center at Fort Worth; Armando Rosales, University of North Texas Health Science Center at Ft. Worth; Rustin Reeves, University of North Texas Health Science Center at Fort Worth;

**Anatomical observation of the dorsal scapular nerve- A series of cadaver study.**

Purpose: The impingement of the dorsal scapular nerve (DSN) often leads to shoulder weakness and scapular pain radiating to the upper limb. This nerve originates from a branch of the root of C5 in the brachial plexus and typically pierces the middle scalene muscle to innervate the levator scapulae, rhomboid minor, and rhomboid major muscles. Due to its anatomical location, the DSN is difficult to dissect and thus, is not often shown to medical students in lab. The purpose of this study is to show and educate medical students on the variable anatomy of the DSN. 

Materials and Methods: Studies were conducted on 3 embalmed adult Caucasian cadavers in which the origin, anatomical route, and muscular innervations of the DSN were dissected and documented. 

Results: It was found that the DSN originated from C5 spinal nerve root in two cadavers whereas in one cadaver, the DSN branches from C4. The route of the DSN varies either by passing anteriorly to the scalene muscles or piercing through the middle scalene muscle in order to travel posteroinferiorly to its targeted muscles. The DSN innervated only the rhomboid muscles in one cadaver and in the other two cadavers, this nerve innervated the rhomboid muscles as well as the levator scapulae muscle. 

Conclusions: The variations of the DSN spinal contribution, route, and muscle innervations are identified in this study. Such variations will help clinicians become better aware of its anatomy in order to make the appropriate diagnosis and treatment plan to patients with pain related to DSN impingement.

**Sponsor** n/a  
**IRB/IACUC#** n/a n/a
**Association Between Self-Reported Symptoms and Biological Measures of Heavy Metal Exposure**

**Purpose.** The objective of this study was to evaluate the relationship between self-reported symptoms and biomarkers of lead and cadmium in urine and blood of people exposed to these heavy metals.

**Methodology.** Blood and urine measures of lead and cadmium were grouped into quartiles. A correlation matrix was created to assess the linear relationship between urine and blood levels of metals and a scatter plot was used to visualize this relationship. A chi-square test was then used to assess independence between the frequencies of self-reported symptoms by quartiles of biological measures. Logistic regression was used to analyze the relationship between symptoms in the lowest quartile compared with those in higher quartiles.

**Results.** There was a significant (p < 0.05) association between self-reported symptoms and biological measures of heavy metal exposure, where those with higher exposures to heavy metals experienced more symptoms. There is also a significant association between lead levels in urine and blood.

**Conclusion.** This study shows that there is a positive relationship between self-reported symptoms and biological measures of heavy metal exposure, where those with higher exposures to heavy metals experienced more symptoms. There is also a significant association between lead levels in urine and blood.

**Can cadaver racial disparity affect medical education?**

**Purpose (a):** The study of anatomy is a cornerstone of clinical knowledge. Human pathology is known to have different presentation across different races. In this study, we decided to elucidate the racial disparities of willed-body donors (WBDs) at UNTHSC.

**Methods (b):**

Demographic data was collected from 222 WBDs from the UNTHSC Department of Anatomy. Information such as age, race, sex, residence zip code, birthplace, education level, marital status, place of death, cause of death, military statues, and occupation were all examined. All data were compiled and analyzed using SAS 9.3 and Microsoft Excel.

**Results (c):**

Our analysis of the WBDs (n=222) demonstrated racial proportions as 96.43%, 2.23%, 1.34%, and 0.00% for Caucasian, African-American, Latino, and all other races respectively.

**Conclusions (d):**

Our findings suggest that many racial groups are essentially excluded from anatomical studies at the University of North Texas Health Science Center. We also believe that the level of education obtained may influence the decision for body donation, as our donors have higher average education levels compared to the average US population. The results of this study have important implications for medical education at a time when more minorities, as well as people with low socioeconomic status, are gaining access to our healthcare system.
Results

Changes in Health Knowledge and Lifestyles After Participating in a Research Study.

Methods

A telephone survey was administered to parents/legal guardians of children who participated in two initial studies conducted at the UNT Health Science Center (UNTHSC). The survey assessed if the parents/legal guardians became more aware of their child’s health after participating and whether they made a change in the child’s lifestyle. Questions used in the initial study were re-administered in this study. In the initial study, children were sent a report characterizing the child’s lab results as normal or abnormal. Wilcoxon-Signed Rank test was used to compare means pre and post, and Fisher’s Exact Test was used to compare willingness to participate in future studies between parents of children who received normal and abnormal results. A total of 61 surveys were completed.

Results

Since completing the study, 55.7% of the parents/legal guardians reported a change in their child’s diet, while 70.5% reported a change in their child’s physical activity. Parents/legal guardians of children who received both normal and abnormal results were more likely to report making their child eat healthy and exercise regularly as well as describe their child as not being overweight during the follow-up data collection as compared to the original study (Abnormal p=0.001, Normal P=0.0024). Lastly, total of 84% of parents/legal guardians belonging to the abnormal subgroup and a 100% of parents/legal guardians in the normal subgroup reported that they would be likely to participate in future studies as well as let their child participate in future studies (p=0.330).

Discussion/Conclusion

By highlighting such benefits, the public’s perceptions of clinical research can be broadened, encouraging more individuals to consider participating. The goal was to show that by participating in research, individuals can learn more about their own health, or more importantly, their child’s health. This knowledge can then translate to lifestyle changes beyond the scope of a study.

Sponsor

n/a

IRB/IACUC

2014-111

Comparing Long Term Hemodialysis Access Survival between two Non-Autogenous Conduits

Objectives: In end stage renal disease population, there has been an increase in the utilization of non-autogenous conduits for hemodialysis access over the past decade. In this study, we compare long term functional patency between two non-autogenous conduits: bovine biograft and polytetrafluoroethylene (PTFE).

Methods: Study include 120 grafts placed in 98 patients between January 2011 and June 2014 in our institution. Various statistical analyses were run via Univariate methods and Kaplan-Meier and Cox regression to evaluate time to loss of patency and identify its predictors. Log rank tests were used to compute differences in survival functions between both groups. Follow-up began at the first time the graft was used for dialysis and ended with an event such as death or study closure.

Results: There was no difference in the survival for functionality between PTFE and biograft (Table 1). There was a six fold increase in the loss of functional secondary patency in PTFE compared to biograft (HR: 6.8 95%CI: 1.7-26.3, P=0.006). The survival function for secondary patency was higher for biografts compared to PTFE (x²=7.69, p=0.02). Functional secondary patency at 6months, 1 year and 18 months for biograft and PTFE are 76%, 72%, 72% and 52%, 46%, 46% respectively. Graft infection rates were higher for PTFE compared to biografts (21% Vs 15%). The predictors of patency loss were high-BMI and hyperlipidemia.

Conclusions: In our cohort, intervention-free access survival and thrombosis-free access survival are similar between biografts and prosthetic conduits. But, bovine biografts have a significant advantage over PTFE with regards to access survival until abandoned. Patients with high BMI and hyperlipidemia attracted close graft monitoring to improve access survival.

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JHU-NA_00042446
Differences in physical and psychological outcomes among patients who were and were not admitted to an inpatient physical rehabilitation facility 3 months after acute traumatic injury

Purpose:
After experiencing a traumatic injury, many patients are recommended to receive inpatient physical rehabilitation to continue their recovery. Even with recommendations from the acute care therapy team to continue care at an inpatient rehabilitation facility, some patients are unable to be admitted for a variety of reasons. The objective of the current analysis was to examine differences in perceived functional and psychological outcomes between (1) individuals who were admitted to an inpatient physical rehabilitation hospital after an acute traumatic injury, and (2) patients who were recommended and but not admitted to inpatient rehabilitation.

After obtaining hospital IRB approval, patients admitted to a Level I trauma center for acute injury were approached to participate in this prospective, longitudinal study. After meeting inclusion criteria, 505 patients completed informed consent and were enrolled into the study during hospitalization. Of these, 60 (8.4%) patients were identified with recommendations by the therapy team to continue care in inpatient rehabilitation; 50 patients subsequently were admitted to an inpatient rehabilitation facility and 10 were not. Eight of ten subjects that did not admit to an inpatient rehabiliation facility as recommended completed a three month follow up. Patient-perceived physical and emotional function was evaluated three months after initial injury using the Veterans RAND 12 Item Health Survey (VR12); all individuals were also screened for depression, posttraumatic stress disorder (PTSD), pain, and return to work. Wilcoxon and Fisher’s tests were conducted to identify differences between the two groups.

There were no differences in functional and psychological outcomes between the two groups during initial hospitalization. However, at three month follow up, a significant difference was found between groups for both emotional health and depression. No significant differences between groups were found for PTSD, pain, and physical function at three month follow up. Though not significant, patients who were admitted to an inpatient rehabilitation facility reported greater pain improvement at three month follow up when compared to patients who did not go to inpatient rehabilitation.

Patients receiving inpatient physical rehabilitation appear to fare better emotionally and psychologically three months after initial injury. These results suggest that admission to inpatient rehabilitation is an important factor in optimizing psychological health after injury. As such, recommendations across disciplines should be strongly considered when making discharge decisions from the acute care setting. Future research to provide evidence regarding the importance of inpatient rehabilitation in later outcomes post injury should be conducted to maximize later quality of life.

Sponsor
IRB/IACUC#: BRI-012-028
Drowning in North Texas: A Six-Year Retrospective Census

Background: Drowning as a cause of death is a substantial concern among many communities, coastal or otherwise. It ranks among the leading causes of mortality among all age groups, especially in the pediatric population. In the United States alone, drowning accounts for 6000-8000 deaths annually. Therefore, it is imperative to be aware of the most common risks and circumstances involved in drowning.

Method: In this study, data was collected from case files of drowning incidents that passed through a medical examiner’s office over a six year period in order to determine the following questions: what subpopulations are most at risk for drowning? Where do drowning incidents most commonly occur? And what are the risk factors and circumstances that prevented the victims from being extricated from danger?

Results: The data (n=234) indicated a predominance of male victims. In addition, an analysis of victims by age interval revealed a bimodal distribution with toddlers and collegiate age individuals being the most susceptible. With regards to location, swimming pools and lakes were the most common scenes of drowning. Identification of the lakes was performed to determine the sites where drowning occurred most frequently. One lake, Lake Lewisville, accounted for just over 25 percent of all recorded lake drownings in the area. Similarly, swimming pools and lakes were categorized as being private or public and inground or above ground. An overwhelming majority of the pools were determined to be private (82%) and inground (68%). Swimming pools also accounted for two-thirds of all pediatric drowning events. In the same vein, sufficient adult supervision was lacking in 90 percent of all pediatric drowning cases and barriers to pool entry were inadequate in 72 percent. In adult drowning incidents, alcohol use was found to be the most frequent risk factor present. Lastly, the phenomenon of “dry” drowning, in which the airways and lungs remain essentially free of the drowning medium, was considered and a novel set of criteria was generated to classify such cases. Eight percent of drowning events were identified as “dry” drowning but this sampling of individuals did not exhibit any discernible pattern with regards to demographics or circumstances.

Conclusion: Overall, this study corroborates and expands upon present knowledge and understanding of the epidemiology of drowning. Recognition of the most susceptible victims as well as the most likely circumstances surrounding drowning is invaluable to the formulation of strategies and the distribution of education to prevent drowning in the future.

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Effects of Cervicothoracic Junction Manipulation on Shoulder Strength and Electromyography Amplitude in Asymptomatic Adults

PURPOSE:
Recent studies have examined the relationship between spinal mobility restriction and upper quadrant muscle function in patients with shoulder pain with limited results. Little research has been conducted to examine the effects of cervicothoracic junction manipulation (CTJ) on shoulder strength and electromyography (EMG). The primary purpose of this study was to examine the immediate and carry-over effects of CTJ manipulation on shoulder strength of shoulder abduction (ABD) and external rotation (ER), as well as EMG amplitude of the anterior deltidoid (ADELT), mid-deltoid (MDELT), supraspinatus (SUPR), and infraspinatus (INFR) muscles. The secondary purpose was to determine the reliability of the strength and EMG testing protocol used in the study.

METHODS:
Twenty-four adults (7 men, 17 women, aged 29.8 +/- 9.8 years) were randomly assigned into two groups: manipulation group that received a sham CTJ manipulation (3 men, 9 women). A hand-held dynamometer (HHD) was used to determine shoulder strength, and EMG activity was recorded using a wired EMG unit and four tethered surface electrodes. Shoulder ABD and ER strength and EMG activity of the ADELT, MDELT, SUPR, and INFR muscles were collected simultaneously during maximal voluntary isometric contraction (MVIC) of shoulder ABD and ER. Two trials of MVIC were performed for shoulder ABD and ER, and the average of the two trials was used for statistical analysis. All participants were asked to come in two separate days. The within-day and between-day reliability of shoulder strength and EMG measurements was determined in the first two visits. The intervention was delivered during the second visit, which was within 24-48 hours of the first visit. To assess immediate and carry-over effects of CTJ manipulation (either manipulation or sham manipulation), the shoulder strength and EMG were collected before intervention, immediately post intervention, 15 minutes post intervention, and 30 minutes post intervention. To assess within-day intra-tester reliability, the shoulder strength and EMG activity were collected twice on the first visit, and again during the second visit before the intervention to determine the between-day reliability. Outcome measures consisted of shoulder abduction and ER strength in kilograms*force (kgf) and EMG root mean square (RMS) of the ADELT, MDELT, SUPR, and INFR muscles. Intra-class correlation coefficients (ICC) were used to determine intra-tester within-day and between-day reliability. Six separate 2x4 ANOVAs with repeated measures were used to analyze HHD and EMG data for between and within group comparison. Alpha level was set at 0.05 for all analyses.

RESULTS:
The results showed excellent within-day and between-day reliability for both HHD and EMG measurements (within-day reliability: ICC = 0.97-0.99 for HHD, ICC = 0.97-0.99 for EMG, and between-day: ICC = 0.94-0.96 for EMG). The ANOVA results revolted a significant group by time interaction for ER strength (p = 0.047), EMG RMS of SUPR (p = 0.041), and EMG RMS of INFR (p = 0.001), but not for shoulder ABD strength or the rest of the EMG data. Post-hoc analysis showed a significant decrease (p < 0.05) from pre-intervention to immediately post manipulation, at 15 minutes post manipulation, and 30 minutes post manipulation in the manipulation group only for all three significant variables (interactions).

CONCLUSIONS:
The results of this study suggest that a potential immediate inhibition carryover effect exists on shoulder EMG and HHD for shoulder ER post spinal manipulation and is possibly maintained for a period up to 30 minutes post technique.
Evaluation of Sport-Specific and Personal Factors in Relation to the Occurrence of Menstrual Irregularity in Female College Athletes

Purpose
Female collegiate athlete participation has significantly increased over the last quarter-century. Despite the known benefits of exercise for females, participation in sports may lead to alterations in menstrual cycle regularity. The prevalence of menstrual irregularities is believed to be associated with the type of sport played. Moreover, there is a correlation between female athletes who participate with reduced body fat, weight, and the onset of later menarche and menstrual cycle irregularities. The purpose of this study was to determine the relationship between Body Mass Index (BMI), body fat percent, type of sport, and other sport-specific and personal factors in relation to menstrual irregularities in college athletes.

Methods
All female athletes at Texas Lutheran University were invited to participate. The sample was composed of 94 participants from seven sports (Cross-Country, Track, Soccer, Volleyball, Tennis, Softball, Basketball). Each participant filled out a questionnaire, which assessed variables including their age at menarche, intensity of training session, menstrual history, and use of oral contraceptives, BMI, and body fat percentage. A binary logistic regression was used to investigate the predictive properties of the variables to predict the presence of menstrual irregularities. This model produced odds ratios of having an irregular menstrual cycle based on each independent variable. Statistical analysis was performed with SPSS and effects were considered statistically significant when p<0.05.

Results
The model explained 31.0% of the variance in menstrual irregularities and correctly classified 71.0% of cases. Sensitivity was 30.8%, specificity was 86.6%, positive predictive value was 46.1%, and negative predictive value was 74.8%. None of the six individual predictor variables were statistically significant. Female athletes who used contraceptives were 2.29 times more likely to exhibit menstrual irregularities than females who did not use contraceptives. Older age at time of menarche and females who played soccer were associated with an increased likelihood of exhibiting menstrual irregularities.

Conclusions
A predictive model of various personal and sport specific factors demonstrated a significant correlation with the alteration of normal menstruation. The use of contraceptives, older age at time of menarche and females who played soccer were associated with an increased likelihood of having menstrual irregularities. Healthcare providers such as physical therapists should be aware of the increased risk of developing menstrual irregularities with sport-specific and other personal factors.

Sponsor
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IRB/IACUC# 2015-018

Histopathology of the Superficial Zone in Human Articular Cartilage

Background: The surface and superficial zone (SZ) of human knee articular cartilage (hK-AC) exhibits variable properties of deterioration with aging and osteoarthritis. A standardized grading system for SZ cartilage would help elucidate the early stage pathogenesis of age-related cartilage degeneration.

Objectives: To establish such a grading system, the objectives were to (1) record key histological features from current grading systems, (2) introduce standards for digital histology images, (3) collect and evaluate images of hK-AC from a digital histology base, and (4) provide clear examples of each feature grade for a comprehensive atlas.

Methods: Key histological features for hK-AC were collected from the original reports of major grading systems for cartilage degeneration (Mankin, OARSI, ICRS). Properties (field of view (FOV), resolution) of traditional microscopy images were determined and guided an acquisition protocol for the images. Digital images with comparable properties were collected from a digital database on SlidePath (Leica Biosystems, IL). Images of 1, 3, and 20X were collected from each of 15 donor knee cartilage, across 4-6 sites on one medial femoral condyle, from n=6 young (21-40yrs), grade 1 and n=9 old (>61yrs), grade 1-3 samples. Images were assessed for clarity, and further processed under standardized cropping and resizing to achieve representative images for an atlas.

Results: An hK-AC image atlas was created. It contains representative images of SZ features with a standardized field of view and resolution according to the magnification. A table listing each feature to be graded was included on every image.

Conclusion: With the creation of a standardized grading system for the SZ of hK-AC, local features of cartilage degradation can be assessed. The same approach can be used to extend the grading system into deeper zones of cartilage. Utilizing a standardized FOV and resolution, researchers are guaranteed a consistent image for grading that will ultimately help us better understand the early pathogenesis of cartilage degradation.

Sponsor
American Federation for Aging Research

IRB/IACUC#
Injury Patterns and Treatment in Functional Fitness Competitions: A Case Report

Introduction: High-intensity functional fitness regimes, popularized by programs such as CrossFit, have produced a large population of regularly active participants in a short span of time. The evolution of such exercise programs into formal competitions has allowed athletes to pursue further athletic achievement, and, in some cases, earn monetary and other prizes for placing highly. The CrossFit® Games and CrossFit® Regional events are annual sanctioned competitions organized by CrossFit, Inc. which hosts the top athletes from around the world. As the pool of competing athletes continues to grow, a greater number of local-level events hosted by individual gyms, known as affiliates, have begun to emerge. While incident reporting by medical staff is implemented at CrossFit-sanctioned events, local level event hosts inconsistently take all necessary steps to ensure sufficient medical care is available for the participating athletes, which places athletes at greater risk of harm. This as well as proper antisepsis measures are of the utmost importance, as blood-borne exposure secondary to superficial hand abrasions, commonly referred to “hand rips”, in competition is very common.

Methods: Injury report data was collected during at the 2014 Dallas All Cities Open, a one-day local event hosted by CrossFit Dallas Central at the Texas State Fairgrounds Fair Park Coliseum. Athlete information was recorded upon their presentation to the medical station, including name, gender, age, affiliate, and a brief description of their injury.

Results: A total of 248 athletes representing 50 gyms and CrossFit affiliates participated, 8 of whom were unaffiliated (M=3, W=5), and placed into four divisions: Mens (M) Womens (W) Masters Men (MM) and Masters Women (MW), a Masters designation given to those age 40 or older. There were 134 M, 90 W, 13 MM, and 11 MW. A total of 43 athletes presented for injury treatment (17 M, 24 W, 2MW), and all injuries recorded were hand-related. Injury types were unilateral hand rips (HR, n=16), bilateral hand rips (HRB, n=19), simple blister (B, n=1), blood blister (BB, n=5), and combined type blister + hand rip (B+HR, n=2). Treatment predominantly consisted of triple antibiotic ointment, nonadherent dressing, and kinesiotape.

Conclusion: This is the first known documented account to detail injury types, treatment, and medical coverage of local-level functional fitness competitions. With the number of these events steadily increasing, the need for medical coverage, standardized treatment and antisepsis protocols, and education of event coordinators and athletes is of central importance to ensuring participant safety and injury prevention.
Is Birthweight a Predictor of Attention Disorders and Depression in School-Aged Children, 6-17 years?

Objective. There is a growing trend of increased diagnoses of mental health problems among school-aged children 6-17. ADHD/ADD and depression account for two of the top four mental health outcomes, affecting 6.8% and 2.1% of children (3-17 years), respectively. Our objective is to determine if there is an association between birthweight and ADHD/ADD, and birthweight and depression, among school-aged children in the United States. Because both low birthweight and macrosomia are associated with physical health problems in later childhood, we considered both low and macrosomial births as potential risk factors.

Methods. We conducted a cross sectional study using data from the 2011-2012 National Survey of Children’s Health (NSCH), a telephone survey of 95,677 households in the US. Using multiple logistic regression modeling (incorporating survey weights), we estimated the odds ratios associated with low birthweight and macrosomial birth as predictors of ADHD/ADD and for depression among children 6 to 17 years.

Results. Children with macrosomial birth weight (n = 7549) have a statistically higher odds of having depression when compared to healthy birth weights (n = 48681) (OR = 1.328; 95% CI: 1.002, 1.760). Low birthweight was not statistically associated with childhood depression. There is no statistically significant difference between birth weight and ADHD/ADD.

Conclusion. The study adds to the body of evidence that birth weight is a probable risk factor for some mental health outcomes in children. Knowing that macrosomia has a negative effect on mental health outcomes such as depression can lead to more caution and awareness in mental health status of school aged children. Although not statistically significant, the relation of birthweight to ADD/ADHD needs further study.

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CrossFit is a high-intensity functional fitness program that has experienced exponential growth since the introduction of its affiliate gym program in 2005. As part of the affiliation credentialing process, CrossFit coaches and trainers must complete a minimum two-day, hands-on CrossFit Level 1 Trainer Certification course. Given the rapid surge in participant numbers and the intense nature of the workouts, concerns have been raised within the exercise and fitness communities about the safety of CrossFit exercise programming and whether the Level 1 certification course provides sufficient training for coaches to appropriately manage and oversee their respective membership populations. The purpose of this study was to determine if level of certification is associated with risk of injury.

Data were collected using the 2013 CrossFit Participant Composite Survey (Ohio Health IRB 13-0023) to examine multiple aspects of an athlete's background. A multiple regression analysis was performed on 569 CrossFit affiliate members to determine if the certification level of coaching staff is associated with self-reported injury as a direct result of CrossFit participation. Members of coaches with only CrossFit-level certification were compared to members of coaches with CrossFit-level certification plus additional coaching/personal training certification. Analyses controlled for time in CrossFit, age, gender, race/ethnicity, and if the participant had experienced a sports related injury in high school or college.

There was no significant association between the level of certification and self-reported injury (OR: 0.866; 95% CI: 0.595 – 1.260). Compared to members with 0-3 months cumulative CrossFit experience, there is an increasing trend in reported injury complaint as cumulative time in CrossFit participation increases. Participants with 25+ months of experience had a 10.7 times increased odds of self-reported injury (OR: 10.703; 95% CI: 5.140 – 22.289). Age, gender, ethnicity, and history of a high school or collegiate sports-related injury were not associated with self-reported injury related to CrossFit.

This is the first reported evidence examining the influence of CrossFit coach certification on member self-reported injury. While it appears that having other training certification in addition to CrossFit-level certification does not significantly reduce likelihood of injury, further focused investigation into the training environment, programming, and individual athlete characteristics and backgrounds within the CrossFit community will be needed to solidify such findings.
Metaphyseal Distal Tibia Fractures: Cohort Study Comparing Outcomes of Patients Treated with Minimally-Invasive Plating vs. Intramedullary Nailing

Introduction: The optimal treatment of non- or minimally articular distal tibia fractures has been debated in the literature. In recent years, minimally invasive plate osteosynthesis (MIPO) and intramedullary nail (IMN) fixation have been commonly used to treat this injury pattern. Both treatment modalities use biology-preserving (indirect) techniques for fracture reduction but the implants' designs and their application are very different. There are few, limited studies that compare the clinical results and outcomes in patients with metaphyseal distal tibia fractures treated with MIPO vs. IMN. We hypothesized that there would be no difference in clinical or functional outcomes between these treatment modalities in a similar population.

Methods: We evaluated all patients with metaphyseal distal fractures (=4cm from the plafond) treated with MIPO or IMN at a busy urban trauma center by a single fellowship trained orthopedic trauma surgeon from 2003 to 2013. The senior surgeon treated this type of injury almost exclusively with MIPO technique until 2009, when technique and design improvements of IMN yielded a potentially superior alternative treatment method. Since then, we have used IMN almost exclusively for this problem. This has created two distinct cohorts of patients treated for a like problem by very different surgical methods. Clinical and radiographic evaluation at a minimum of one year follow up was obtained along with visual analog (VAS) pain scales, limb specific assessments (Olerud and Molander’s ankle score, American Orthopaedic Foot and Ankle Surgeon’s [AOFAS] ankle-hindfoot instrument), and whole-person assessment with the Short Form 36 (SF-36) tool.

Results: We studied 86 patients (43 MIPO and 43 IMN) with distal tibia fractures within 4 cm of the plafond with minimal or no articular involvement. Thirty-eight of 43 patients in the MIPO group and 26 of 43 patients in the IMN group met inclusion criteria for the study including greater than 1 year follow up. Complications of MIPO included three nonunions, two with malunion >5 degrees, no infections, one major wound complication, and four patients who had plates removed. Complications in the IMN group included 2 nonunions (both type 3 open fractures), one delayed union (type 3 open fracture, healed without surgical intervention at 65 weeks), 3 with malunion >5 degrees, two deep infections, and three patients undergoing removal of distal locking screws. Pain scores were similar between MIPO and IMN groups. Average AAOS ankle scores were similar between MIPO and IMN (86.6 vs. 77, respectively; P< 0.02). Average SF-36 v2 domain scores were similar between two groups, but the Olerud and Molander ankle scores were significantly better in the MIPO group (86.6 vs. 77, respectively).

Conclusions: Similar clinical results and functional outcomes were obtained when treating non- or minimally articular metaphyseal distal tibia fractures with MIPO or IMN except for one of two ankle scores that favored MIPO. Complications appeared to correlate with open fracture and high-energy injuries.

Sponsor: N/A
IRB/IACUC#: THR #00005191

Non-Autoimmune Diabetes Mellitus in a 12-Year Old Vietnamese-American Female with Congenital Hyperinsulinism (CHI)

Introduction: The occurrence of non-autoimmune diabetes mellitus in individuals with a confirmed diagnosis of congenital hyperinsulinism has previously been reported in individuals with a heterozygous inactivating mutation of the ABCC8 gene. We describe a patient with CHI who developed diabetes mellitus and review the proposed mechanism and treatment options.

Case Description: A 12-year old Vietnamese-American female presented with new-onset, antibody negative diabetes. As an infant, she experienced episodes of hypoglycemia and was found to have congenital hyperinsulinism caused by a maternally inherited ABCC8 gene mutation. The child’s hypoglycemia was treated symptomatically, without pharmacological or surgical intervention. During the ensuing 7 years, she remained asymptomatic. As a teen, she developed typical polyuria, polydipsia and was found to be hyperglycemic. Standard diabetes-related antibodies were negative. She was initially treated with multiple daily injections (MDI) of insulin, with plans to transition her to an oral hypoglycemic agent.

Conclusion: The cause of diabetes in individuals with CHI is unknown. Currently it is thought to be due to increased metabolic demand with unregulated insulin secretion, leading to pre-mature apoptosis of the pancreatic beta cells. An understanding of the pathophysiology of diabetes in CHI is important in determining treatment options.

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Potential health effects from exposure to Xylene (Dimethylbenzene) in residential communities experiencing unconventional shale gas extraction and processing operations.

Introduction: Xylene, a product of combustion is found in emissions from unconventional shale gas extraction and processing operations. Residential communities experiencing urban drilling may have an increased risk of exposure to Xylene from inhalation of emissions. Routes of entry into the human body are inhalation, ingestion and absorption. Xylene rapidly spreads throughout the body due to its high solubility in blood. It is highly lipophilic and may be retained in fatty tissues. It can cross the placental and blood-brain barriers (BBB).

Objective: To identify potential health effects from Xylene exposure in residential communities experiencing unconventional shale gas extraction and processing.

Materials and Methods: A meta-analysis of published literature was performed and articles retrieved from Pubmed (388), Scopus (353), EBSCO, Science Direct and Pneumonet (25). Keywords searched include xylene, dimethylbenzene and health effects of xylene. Abstracts were reviewed and articles pertaining to health effects retrieved in full text. No date restriction on publications was made for articles searched. Xylene was found in mixtures with other volatile organic compounds (Benzene, Toluene and Ethylbenzene), with literature referencing BTEX rather than the individual compounds. Articles that included combined effects of BTEX were excluded.

Results: Ambient air monitoring studies identified high concentrations of Xylene at various distances from unconventional shale gas operations. Published literature confirmed exposure to isomers of Xylene was associated with adverse health effects. Residential communities in close proximity to natural gas emissions may experience similar health effects. Short- and long-term health effects associated with Xylene exposure included neurological, respiratory and hematological impairment.

Conclusion: Short- and long-term exposure to Xylene among residents in close proximity to emissions from unconventional shale gas extraction may have an increased risk of neurological, respiratory and hematological adverse health effects. Children may be at an increased risk due to their unique physiological demand and high body fat.

Sponsor: N/A

IRB/IACUC#: N/A
Preoperative Hip Fracture Patient Risk Stratification Based on Objective Data

Hypothesis: Patients with isolated fractures of the proximal femur can be stratified for risk of post-operative complications.

Materials and Methods: A retrospective analysis of patients with isolated fractures of the proximal femur, taken from the Harris Methodist Hospital hip fracture registry, was evaluated with regards to preoperative objective data (Body Mass Index (BMI), Total Lymphocyte Count, Prealbumin, Albumin, Age, Vitamin D Level, American Society of Anesthesiologists (ASA) score) and the odds ratio of having a post-operative complication based on having abnormalities of these preoperative lab values. Post-operative complications were defined as transfusion, myocardial infarction, cardiac arrest, cerebrovascular accident, arrhythmia, ICU stay, surgical complication, respiratory failure, gastrointestinal complications, bacteremia/sepsis, acute renal failure, pulmonary embolus, pneumonia, deep venous thrombosis, urinary tract infection, and 1 year mortality.

Results: Preliminary statistical analysis demonstrates that patients with a BMI of <18.5 AND prealbumin <18 have a 5x greater risk of post-operative complications. Those with albumin <3.0 AND BMI 25-29.99 have a 4.94x greater risk, those with albumin <3.0 AND vitamin D level 30-80 have a 4.19 greater risk, those with albumin <3.0 AND vitamin D level <30 have a 2.69x greater risk, those with BMI <18.5 AND T-Lymphocyte count <1500 have a 2.42x greater risk. Having age 60-74 AND a BMI of 25-29.99 had a protective effect with an odds ratio of 0.37, and having age 60-75 AND a T-Lymphocyte count >1500 also had a protective effect with an odds ratio of 0.36.

Conclusions: Patients can be stratified for risk of post-operative complications based on preoperative nutritional status, as evidenced by the increased odds ratios of low preoperative nutritional labs as well as low BMI levels. There was significant limitation in further evaluating a set if criteria with greater than 2 variables as several patients did not have all laboratory values available preoperatively. This would allow for a prospective study to specifically seek out these variables.

Sponsor N/A
IRB/IACUC# 2014-056

Quality of Life Assessment in Transtibial Amputees using K2 vs K3 Prosthetic Feet

The functional level of transtibial amputees is used to determine the K-level classification of prosthetic feet that can be reimbursed. A lower K-level prosthesis lacks the technology of higher K-level prosthesis and thus may diminish the patient’s ability to perform daily tasks such as balance and gait while increases chances of expensive injuries due to trips and falls. Our hypothesis is that a K3 prosthetic will not only show improvements in daily tasks such as balance and gait but will also improve the patient’s quality of life.

Ten subjects with transtibial amputations secondary to diabetes and vascular disease were recruited. Subjects were asked to participate in two visits. A V-gait CAREN (Computer Assisted Rehabilitation Environment Network, Motek Medical, The Netherlands) system and a 12-camera Motional Analysis System were used to create virtual environments where subjects were assessed performing balance and gait task. These two visits were separated by a two week trial period in which subjects were randomized to wear a K2 or K3 prosthetic foot above, below or at their specific level of function. Data collected at both visits were evaluated alongside quality of life information gathered from the Physiological Cost Index, the Reintegration to Normal Living Index, and the SF-36 questionnaires.

Results were analyzed with pared t-tests. Subjects switching from a K2 to K3 level prosthesis showed a significant increase in SF 36 scores (p=0.0005). Those switching from a K3 to K2 level prosthesis expressed significant decrease in SF 36 scores (p=0.01). The quality of life domains most impacted in subjects switching from a K2 to K3 level were physical functioning, limitations due to physical health, as well as energy and fatigue. The only domain that was not impacted was social functioning. Subjects switching from a K3 to K2 level prosthesis expressed the greatest difference in limitations due to physical health, energy and fatigue, physical functioning and pain.

The results to this point confirm that K3 prosthetic feet lead to a greater quality of life. Providing higher functioning prosthetics to lower functional level amputees may not only lead to improved balance and coordination, but it may also lead to increased cost effectiveness due to an elevated level of function with less injuries and falls. Therefore, it is vital that the proper prosthesis is prescribed to transtibial amputees.
22 patients for Grade 2 falls, and 19 patients for Grade 1 falls. Students participants (extension, internal rotation, and external rotation), for a total of nine peaks of applied force. One group was provided determining the force at end feel. The participants performed three trials on each arm of three different motions of the shoulder on their fellow were recruited for this study, with a total of 208 participants. Expert examiners established a “gold standard” of the force applied when determining the force at end feel. The participants performed three trials on each arm of three different motions of the shoulder on their fellow students participants (extension, internal rotation, and external rotation), for a total of nine peaks of applied force. One group was provided access to train with the device, while another control group was not given access. Two assessment periods - one before training with the device, another two months after training – measured the usefulness of the device in an educational setting. The raw data was collected from Matlab and analyzed using SPSS software. Analysis focused on dependent variables including gender, side, motion, trials, and the overall force means compared to the “gold standard”.

Mean force of the student participants during the pre-assessment period was 2.11 kg with a standard deviation of 1.27 kg. For the student participants, an ANOVA of the three trials revealed no significant differences (p = 0.594). Women had a significantly lower (p = 0.00) mean than men (1.75 kg and 2.31 kg respectively). The three motions also had significant (p = 0.000) differences in values. Extension had the greatest applied force (2.38 kg), while external rotation had the least (1.78 kg). After two months of training to meet the “gold standard” of 3 kg of force, the trained group had a mean closer to that than the control (3.16 kg for trained, 2.58 kg for controls). No significant difference was found between left and right arm trials in pre or post assessment data. The first hypothesis that the sample of medical students would have a lower mean of applied force that the gold standard was supported. The greater applied force in extension suggests that the movement’s range motion has a firmer and more sudden end feel. The second hypothesis that the trained group would achieve a mean applied force closer to the standard was also supported.

Sponsor: N/A

IRB/IACUC#: 2014-059

Range of Motion Device for Evaluating Somatic Dysfunction

An integral part of the osteopathic medical education is the palpation exam, but few tools exist to provide an objective measure of appropriate force applied to find the soft tissue resistance at the end of the range of motion. The educational range of motion device utilized in this study is a hand-held tool with sensors to record the applied force during a range of motion test. This device can allow students to observe differences in technique among motions and trails for a more rapid understanding of proper palpation exam techniques. It was hypothesized that first year medical students utilizing the device would apply less force during palpation exams than experienced physicians (gold standard), and that the group allowed to train with the device would apply force closer to the “gold standard” in the post-assessment period. First year medical students were recruited for this study, with a total of 208 participants. Expert examiners established a “gold standard” of the force applied when determining the force at end feel. The participants performed three trials on each arm of three different motions of the shoulder on their fellow students participants (extension, internal rotation, and external rotation), for a total of nine peaks of applied force. One group was provided access to train with the device, while another control group was not given access. Two assessment periods - one before training with the device, another two months after training – measured the usefulness of the device in an educational setting. The raw data was collected from Matlab and analyzed using SPSS software. Analysis focused on dependent variables including gender, side, motion, trials, and the overall force means compared to the “gold standard”.

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Sponsor: N/A

IRB/IACUC#: 2014-059

Reducing falls in post-acute Medicaid patients enrolled in the Safe Transitions for the Elderly Patient (STEP) Program

The STEP Program is a hybrid transitional care model composed of interdisciplinary team members focused on reducing hospital readmissions, decreasing falls, and improving quality of life. Thus far, no transitional care program has been able to show a significant reduction in falls among post-acute, community dwelling older adults.

As the first physical therapy (PT) team to be included in a transitional care program, we sought out to identify potential fallers and reduce falls in this vulnerable population. The purpose of this paper is to evaluate the contribution of PT intervention in the STEP program, specifically as it relates to decreasing falls and falls risk.

We utilized a qualitative, subjective report instrument known as the 4-point Hopkins Falls Grading Scale (HFGS) with good face and content validity to discriminate between the severity and frequency of falls. A systematic, subjective history of falls and comprehensive fall risk assessment scores pre- and post- PT intervention were obtained and analyzed. All data was analyzed using SPSS, and according to the Shapiro-Wilk test, none of the fall data was normally distributed (all yielding p-values of .000). Therefore, we used the Wilcoxon Signed Rank Test to analyze the difference in medians for pre-STEP fall data at 3 months and post-STEP fall data.

Preliminary data of a subset of patients reveals promising results for the Hopkin’s Falls Grading Scale with 3 out of 4 grades showing a significant reduction in falls. The Wilcoxon Signed-Rank Test provided the following results. There was a significant decrease in number of Grade 4 Falls (p = .000). There was not enough evidence to support a significant difference in number of Grade 3 Falls (p = .065). There was a significant decrease in number of Grade 2 Falls (p = .000). Finally, there was a significant decrease in number of Grade 1 Falls (p = .004). Grade 3 falls showed no significant difference; however in our distribution, we only had 8 patients that reported Grade 3 falls, compared to 20 patients for Grade 4 falls, 22 patients for Grade 2 falls, and 19 patients for Grade 1 falls. These results confirm the need and importance of collecting pre- and post- PT intervention falls data. At this point in time, 3 out of 4 grades show a significant decrease in falls. The data suggests that transitional physical therapy is effective in showing a reduction in falls in older Medicaid patients recently discharged from the hospital.

Sponsor: Center for Medicare and Medicaid Services

IRB/IACUC#: 2014-90
Remote Damage Control Resuscitation

Purpose: Damage control resuscitation (DCR) is the accepted standard of care in military trauma care and is becoming an emerging practice in the civilian medical community. The presence of uncontrolled major hemorrhage, coupled with a delay in access to hemostatic surgical intervention, remains a primary contributor to preventable death in both combat and many domestic settings including rural areas and disaster sites. Therefore, the purpose of this translational policy research project was to adopt the US military’s Remote Damage Control Resuscitation protocols to civilian austere medical care. Methods: Civilian and military emergency care leaders throughout the world have sought a means to project DCR principles. The protocols have been taught at the US Army Center for Predeployment Medicine, Fort Sam Houston, TX, as well as by the Norwegian Naval Special Operations for several years, and were advocated for applicability in a civilian austere medical setting with minor modifications to accommodate their civilian counterparts. To spearhead the project, the Hemostatis and Oxygenation Research Network and the Remote Trauma Outcomes Research Network working groups reflected on military experiences from past conflicts, defined current capability gaps, and examined available and potential solutions for use domestic and abroad. Results: Although some military protocols needed to be adapted for the civilian application of Remote Damage Control Resuscitation, the principles of medical care in the military austere environment are similar to those in the civilian rural and maritime medical care settings. This work resulted in the proposed strategy “Remote Damage Control Resuscitation” to be used in civilian medical settings. The remote damage control resuscitation principles reinforce the importance of identifying and managing uncontrolled massive hemorrhage as part of a comprehensive approach to prehospital stabilization and enroute care. Conclusion: Continued efforts on behalf of The Hemostatis and Oxygenation Research Network and the Remote Trauma Outcomes Research Network will be paramount in the success and establishment of future RDCR programs both domestic and abroad.

Sponsor None
IRB/IACUC#
Skin Health on Our Team: Prevention of Pressure Ulcers in Athletic Individuals with Spinal Cord Injuries

OBJECTIVE: Focus group data were collected as a means to gather participant attitudes, beliefs, feelings and opinions in regards to informing the design of a pressure ulcer prevention study.

BACKGROUND: Little research has been done on pressure ulcers (PU) in healthy, active individuals with spinal cord injuries (SCI). Athletes, in particular, may be at greater risk for developing PUs due to prolonged vigorous movement. Despite this risk only 30.8% of all wheelchair athletes seek medical assistance for PUs.

METHODS: Participants were recruited following collegiate sports practices to participate in a focus group that assessed attitudes, beliefs, and feelings about PU prevention and intervention delivery preferences. Classic content analysis methods were used to determine frequencies of important themes. Basic demographics, sports involvement, and previous PU history were also collected.

RESULTS: Participants were male (N=8) with a mean age of 23 (SD) years; Caucasian (55%), and Hispanic/Latino (33%). All participants were actively competing in various wheelchair sports. Forty-four percent had a history of PUs but only 28% sought medical treatment. Focus group themes included: awareness, risk, prevention, and program solutions. Within PU awareness, 72% of comments concerned intrapersonal topics (e.g., beliefs, attitudes) followed by participants’ comments on past experiences (15%). Participants expressed a sense of isolation with PU occurrence resulting in frustration and a lack of ability to face the challenges coinciding with PUs.

CONCLUSIONS: This group of athletes with SCI believes skin health is crucial for overall health, ability to participate in sports, and quality of life. Although PU occurrence may not necessarily be due to laziness or lack of attention, that impression seems to be general consensus of other team members and society. Future recommendations include providing athletes with direct access to a wound care specialist, while interventions should emphasize best practices in compliance, motivation, and development of protective lifestyle behaviors.

Sponsor
IRB/IACUC# UTA-2014-0283

Suture Pattern Comparison: Are buried sutures strong enough for traumatic wound closure?

Purpose
Prior research has shown that an inverted, buried wound closure may offer potential benefit to wound healing in terms of increase blood flow and superior scar formation. It has been suggested that this might be beneficial in traumatic applications where compromised blood flow could negatively impact wound healing. Anecdotally, it is often stated in the literature that this type of suture pattern has insufficient strength for trauma applications, however a literature search yielded no empiric evidence to support this view. The objective of this study is to compare suture pattern strength to determine if a buried, intradermal vertical mattress suture has sufficient strength for trauma applications, with the added benefit of improved capillary blood flow and superior scar formation.

Materials/Methods
A freshly butchered porcine specimen was used. Several incisions will be made along the flanks and sutured with 3.0 monocryl suture, using 3 standard suture patterns and a buried inverted vertical mattress pattern. The wound margins were then distracted using and industrial grade tensiometer (Imada DS2-44). Data about suture pattern failure was gathered at varying intervals of lbs. of distraction and to failure. Failure was standardized with ultimate monocryl failure strength determined by breakage point of monocryl suture, and will be reported as failure of suture or of soft tissue. Results were then compared to determine comparative failure points of each suture pattern.

Conclusion/Discussion
Within tension limits facilitating adequate capillary blood flow, we believe the buried suture pattern will have a similar strength profile to other suture patterns. This provides for a method of suturing traumatic wounds that has been proven to increase capillary blood flow and is potentially beneficial in traumatized, devitalized wound margins; thus potentially increasing the wounds capacity for healing.

Sponsor
Intramural Grant - JPS Office of Research and Scholarly Activity
IRB/IACUC# 2014-15-16-T10
### Tactical Emergency Medical Support

**Purpose:** The scene of a law enforcement special operation presents numerous barriers to traditional Emergency Medical Services access; thus, there is a need for medical support of law enforcement special operations to be performed by well-trained and properly equipped tactical medics who can operate effectively within the perimeter. Though military and law enforcement special operations are unique, similarities exist in the realm of tactical medical. Therefore, the purpose of this translational research project was to adopt the US military's Tactical Combat Casualty Care guidelines, which are currently considered to be the standard of care for military prehospital medicine, to civilian tactical law enforcement.

**Methods:** In 2005, the TCCC guidelines were adopted by US Army Special Operations for use in the Global War on Terrorism and training began at the Center for Predeployment Medicine, Fort Sam Houston, TX. When later considering adaptation of the guidelines to civilian special operation use, the Committee on Tactical Emergency Casualty Care was formed to determine the extent to which the three phases of tactical care—Care under fire (Direct threat care), Tactical field care (Indirect threat care), and Tactical Evacuation Care (Evacuation care)—needed to be modified.

**Results:** Some specific content areas and provider competencies were amended; otherwise, each phase was determined applicable and modified in name change only. In addition, the overall structure and decision-making of the TCCC model was applicable to civilian special operation use. The austerity and danger of the operational environment require that the tactical medic be trained with a unique set of decision-making skills to be able to constantly balance the benefit of a particular intervention against the special risks inherent in performing the intervention in the environment. Modification of techniques, establishing priorities, and ongoing assessment of risk permit the tactical medic to provide the greatest good for the most people without exposing himself to unnecessary risk.

**Conclusion:** The principles of medical care in the military tactical care environment are similar to those in the civilian tactical care environment. Although some TCCC content needed to be adapted for the civilian law enforcement, the phases of tactical care and the principles and flexibility of the system were efficiently and effectively incorporated.

**Sponsor** n/a

**IRB/IACUC#** n/a

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### The Effects of Hearing Loss on Balance in Older Adults: A Systematic Review

**Purpose:** Falls due to poor postural control are a common problem within the older adult population, leading to many negative outcomes such as fractures, hospitalization, and even death. Traditionally, three sensory inputs – visual, vestibular, and somatosensory – are associated with the control of balance and have been investigated for their potential contribution to increased risk of falls. However, recent epidemiological research has brought attention to the notion that other sensory impairments, such as hearing loss, may affect balance. The purpose of this review is to systematically document the recent evidence linking hearing loss to balance impairments and increased risk for falls in seniors, and to present various hypotheses regarding the mechanisms by which auditory impairments may affect balance.

**Methods:** A literature search was performed using the key terms: hearing loss, auditory impairment, older adults, elderly, balance, falls, hearing aids, hearing devices, gait, locomotion, cognition, and postural control. The databases PubMed, Scopus, CINAHL, Cochrane, ScienceDirect, and Medline were queried for articles published between January 2000 and June 2014. An initial screen was performed based on titles and abstracts. A total of 346 articles were found. A second reviewer who is an expert in the field screened the articles based on the relevance to the topic and narrowed the inclusion number to 72 articles. Literature reviews and articles about pediatrics were excluded from this review, which further narrowed the inclusion number to 47 articles.

**Results:** The evidence from the literature supports a link between hearing loss and balance deficits. Four main theories exist that may explain why and how hearing loss may affect an older adult’s balance: (1) The Physiological Theory; (2) The Social Theory; (3) The Perceptual Theory; (4) The Cognitive Theory. The evidence strongly supports The Cognitive Theory; substantial evidence supports The Social Theory; not enough evidence is currently available in the literature to support or refute the Perceptual Theory and the Physiological Theory.

**Conclusions:** The consequence of hearing loss on a person’s ability to maintain balance has not gained attention until recently and minimal research on the effects of hearing loss on balance exists. This report informs healthcare professionals about potential consequences of hearing loss on an individual’s postural control and the need for further research to be performed.

**Sponsor**

**IRB/IACUC#**
The Perfect Storm: Predicting Injuries in Professional Ballet Dancers

Hypothesis: Injuries in a professional or semi-professional ballet dancer are significantly associated with perfectionism and fewer rehabilitation hours as measured by the Multidimensional Perfectionism Scale (MDS). Injuries will be treated more often with osteopathic manipulative therapy (OMT) than other interventions (e.g. physical therapy, chiropractic, and other.)

Method: University institutional review board approval was obtained to conduct this prospective, cross-sectional pilot study to examine the prevalence, severity, and predictors of musculoskeletal injuries. Ballet dancers between the ages of 20-60 with a past professional or semi-professional ballet performance history of 5-years or longer with a history of one or more performance injuries during their careers were recruited. MDS scores, the number of lifetime dance injuries, and whether or not OMT was utilized were analyzed.

Results: Forty-eight ballet dancers (mean age + SD = 30.15 + 7.48) chose to participate in the survey. Total lifetime moderate injuries (requiring recruitment. MDS scores, the number of lifetime dance injuries, and whether or not OMT was utilized were analyzed.

Conclusion: In support of our hypotheses, ballet dancers may experience more musculoskeletal injuries due to high levels of perfectionism, feelings of inferiority, and fewer hours of necessary rehabilitation. Dancers with a history of multiple overuse injuries sought OMT more than other therapies, although pre-existing illnesses may have influenced the results.

Sponsor: N/A

IRB/IACUC#: 2013-233

The use of virtual reality and a sub-threshold vibratory noise as a tool to enhance sensory reintegration and postural control among patients with diabetic peripheral neuropathy.

Purpose:
Peripheral neuropathy frequently occurs among patients with diabetes and can result in many complications, including plantar sensory loss. Diminished sensation alters the sensory weighting mechanism, causing individuals to become increasingly reliant on visual stimuli to maintain adequate balance and postural control. The purpose of this study was to evaluate the clinical usefulness of a virtual reality- (VR) based sensory reweighting and balance training program that incorporates principles of the stochastic resonance theory in subjects with diabetic peripheral neuropathy.

Methods:
Seven subjects, ages 63 to 69 years old, with peripheral neuropathy due to type II diabetes have completed the study; enrollment is ongoing. This study was conducted using a V-Gait CAREN system. Subjects were fitted with vibratory devices placed around both ankles and underwent increasingly challenging postural stability activities over the course of 6 one-hour sessions. Visual dependency was reduced by manipulating the lighting conditions and applying visual distractions from the VR. Subjects received an acute application of a sub-threshold vibration throughout the duration of each session. Pre- and post- measurements of fall risk and standing balance were assessed at visits 1 and 8 using the Activity Balance Confidence (ABC), Falls Efficacy, and Clinical Test of Sensory Interaction for Balance (CTSIB). Data was analyzed using paired t-tests.

Results: Post training analysis showed a significant improvement in ABC score (p=0.02) but not with Fall Efficacy score (p<0.09). Sway and stability index did not reach significance on any components of the CTSIB when measured independently. However, combining sway and stability resulted in significant improvements in standing balance during conditions of eyes closed/firm surface (p=0.04), dome/foam surface (p=0.05), eyes open/foam surface (p=0.05), and dome/foam surface (p=0.04).

Conclusions: Subjects improved overall balance and sensory selection strategy as indicated by an improved ability to control both the amplitude and velocity of their sway during conditions of altered visual and somatosensory information. Preliminary results support the use of a sub-threshold background noise as an adjunct to a VR- based balance and sensory re-integration training program for individuals at risk for falls due to diabetic peripheral neuropathy.

Sponsor: Texas Medical Research Consortium RI 6026

IRB/IACUC#: 2012-007
Treating the Homeless Patient: Different Attitudes Among Pre-Clinical Medical Students

Background: Locally, ~2,123 people are homeless. Most of these have multiple physical and mental illnesses requiring consistent medical treatment that is delivered intermittently. Inadequate medical treatment for the indigent and homeless could potentially be a function of biased healthcare professional attitudes toward the homeless patient. Our previous research examined treatment attitudes of medical students (MS1-4), residents, and physicians and showed that MS3-4 students were cynical and judgmental about the homeless condition and they resented treating the homeless patients more than any other group. Here, we examined if there were any changes in attitudes towards treating the homeless in 2nd year medical students assessed in 2013 in comparison to a different group of 2nd year medical students assessed in 2014.

Hypothesis: Attitudes about treating the homeless will significantly differ between two groups of 2nd year medical students.

Methods: A cross-sectional between-group comparison of attitudes toward treating homeless patients was conducted in 2nd year medical students MS2_1 (n=66) and MS2_2 (n=72). All ages and race/ethnic groups were eligible to participate. The Health Professionals' Attitudes Toward the Homeless Inventory (HPATHI) and the Attitudes Toward the Homeless Questionnaire (ATHQ) were used to quantify attitudes. Socio-demographic data were analyzed using frequency distributions and chi-square analyses. Group differences in HPATHI and ATHQ scores were analyzed using general linear modeling to correct for unequal group sizes. Statistical significance was determined using a 95% CI and a p-value of 0.05.

Results: We found the MS2_1 group was significantly more judgmental in that they reported that ‘homelessness was self-inflicted’ (p=0.013), and that they believed that ‘alcoholism is a personal weakness’ (p=0.001). The MS2_1 thought that ‘homelessness was not related to health issues’ (p=0.038). The MS2_2 rated themselves significantly higher than the MS2-1 group as ‘going into medicine to help the needy’ and that ‘social injustice is an important healthcare issue.’ Gender and race were not influencing factors on these results.

Conclusion: These results suggest that 2nd year medical students assessed in 2013 had a substantial bias towards treating homeless patients and had very poor insight on the biological basis for addiction. These data warrant a larger investigation to determine if this was just a cohort effect that has since been resolved, or if the educational requirement and coursework that the 2013 group of medical students experienced was different than that received by the 2014 students. Nevertheless, curriculum that adequately prepares students to practice real-world community medicine in special needs populations like the homeless is important, as is the need for more in-depth curriculum to teach the biological basis for addiction.

Sponsor: N/A
IRB/IACUC# 2012-215
A Case Report on Low Back Pain in the Third Trimester of Pregnancy addressed with Osteopathic Treatment

Purpose: The objective of this case report is to document the use of osteopathic manipulative articular, myofascial, soft tissue, and muscle energy techniques as safe adjunctive treatments for low back pain in the third trimester of pregnancy. The author describes a case of worsening low back pain in an obstetrical patient who was a G1P0 33 year old female in the 36th week of gestation and constantly on her feet at her workplace. The patient complained of stiffness in her lumbar spine as well as pain in the area of the round ligaments in the anterior pelvis. Following two osteopathic manipulative treatment sessions in addition to the patient stretching at home and using a massage therapist, the patient gained increased pain relief in her lumbar spine and sacrum as well as her anterior pelvis along the pubic symphysis. This enabled the patient to continue working her regular job up until the time of a full term vaginal delivery at 39 weeks.

Methods: The author employed the use of the PROMOTE study OMT protocol developed by Dr. Kendi Hensel in order to address the patient with third trimester low back pain in this case report. The patient was treated twice using a series of techniques found in the PROMOTE study with great overall improvement in the patient’s pain. The author used seated thoracic articulation, cervical soft tissue, occipito-atlantal decompression, thoracic inlet myofascial release, lateral recumbent scapulothoracic soft tissue, lateral recumbent lumbar soft tissue, abdominal diaphragm myofascial release, pelvic diaphragm myofascial release, sacroiliac articulation, pubic symphysis decompression, and frog-leg sacral release. These OMT techniques were used in sequence to address the patient with third trimester low back pain.

Results: In this case report, a multimodal approach was taken to address the patient’s back pain in the third trimester. The patient utilized home stretches and also attended massage therapy in addition to undergoing OMT treatments twice at the doctor’s office. The techniques from the PROMOTE study were utilized with great success in the patient and greatly relieved the patient’s low back pain in the weeks leading up to delivery. Through the treatments the patient was able to continue working and also was able to improve her ability to stay active in an exercise program in the weeks leading up to delivery.

Conclusion: This case study does not prove that osteopathic treatment is the sole factor responsible for the improvement in low back pain within the third trimester of pregnancy. However, the case study does show that osteopathic manipulation was a vital component to the improvement that was shown in the pain and function of the patient in this particular case study. Further studies are indicated to focus more on the aspects of preparing the pelvis for the labor and delivery process as well as addressing other postural factors and improving overall hemodynamic functioning.

Sponsor Dr. Peggy Smith-Barbaro--faculty sponsor and Principal Investigator
IRB/IACUC# 2015-025

Analysis of Approach and Motion Velocities in Dominant Hands While Performing Daily Activities

Analysis of Approach and Motion Velocities in Dominant Hands While Performing Daily Activities

Previous studies have shown individual force sensors to be a simple means of providing feedback about the environment to a robot. Combining the data of velocity in two phases (approach and motion) from a touch sensitive surface glove can provide insight into the neural processes that govern muscle movements during approach, pushing, and pulling of an object. The analysis of these interactions may be used to streamline the motions of a robot to simulate the average adult human’s movement while performing simple tasks. Data from dominant hand positions and velocities from ten people was collected using a motion capture system (Motion Analysis Corp, Santa Rosa, CA). There were five females and five males with ages 23-51. Quantitative data of both motion and velocity was collected on five trials and averaged across the cohort for analysis. The average minimum velocity during approach for a push movement was 0.546 meters/second, 0.579 meters/second, and 0.632 meters/second for a cylinder weight of three, five, ten pounds respectively. Trends show that as weight increases, so does the minimum velocity of approach in the palm position. Future analysis of these data will include providing information for building simulated and eventually physical human-robot interaction systems to aid in daily activities.

Sponsor N/A
IRB/IACUC# 2011-161
Brief OMT Improves Range of Motion, Reduces Pain & Anxiety As Shown by Interleukin 1-Beta Levels

Hypothesis: Brief osteopathic manipulative therapy (OMT) will improve range-of-motion (ROM), reduce pain-related anxiety and self-reported somatic pain perceptions as indicated by salivary Interleukin-1 Beta levels (IL-1B). Methods: A prospective 2-week longitudinal treatment intervention trial was designed to examine treatment efficacy of one brief OMT session to improve trunk ROM while reducing anxiety and pain perceptions in 25 acute pain patients for up to 2-weeks later. Salivary IL-1B was analyzed as a biomarker of pre- and post-OMT inflammation, psychosomatic pain and anxiety.

Results: Brief OMT delivered one time was significantly related to improved ROM in trunk flexion (t = 2.84, p = 0.009), reduced anxiety as measured by the Generalized Anxiety Disorder questionnaire (F=11.20, p=0.0000). A statistical trend in reduced pain perceptions was evident 2-weeks later (F=23.07, p=0.0000). Levels of IL-1B were significantly correlated to mood and anxiety (r =-0.47, p = 0.05) in the 2-week follow-up condition. Improvement in trunk side bending (right side) after OMT was significantly correlated to reduction in pain related anxiety (r=-0.43, p=0.04).

Conclusion: These results suggest that one brief session of OMT effectively increased ROM, reduced pain and anxiety that lasted up to 2-weeks. These OMT benefits were associated with increased post-OMT levels of the inflammatory biomarker, IL-1B. OMT seemed to provide physical pain relief benefits while also reducing psychological pain perceptions and pain-related anxiety.

Sponsor: N/A
IRB/IACUC#: 2013-197

Effect of Whole Body Vibration on stroke patients: A Systematic Review

Introduction and Purpose: Stroke is one of the major medical disorders that affect patients’ daily functional mobility. From last decade, whole-body vibration therapy (WBV) has been introduced and getting more used for patients with stroke. However, up to date, about using the WBV, the following questions are still uncertain: which stage of patients with stroke can really benefit from the WBV, what WBV intervention parameters should be provided, and what assessment instruments could be applied to evaluate the WBV effectiveness. Therefore, the purpose of this review is aimed to answer these questions by analyzing relevant articles.

Methods: Two researchers performed literature search by using Ovid Medline, Scopus, Medline, Cochrane and PubMed independently. Eligible studies published from 2000 through April 2014 were selected. The keywords for search were whole body vibration, stroke, cardiovascular accident, hemiplegia, hemiparesis, functional performance, posture, balance, strength, and rehabilitation.

Result: Eleven articles were qualified for the purpose of this review. WBV could be used alone, or combined with therapeutic exercise. It seemed that patients with subacute and chronic stroke could benefit more from the WBV, while the acute one does not. The intervention parameters in these studies are: once per week to five times per week, duration from 3 to 12 weeks, frequency of vibration from 5 to 45 Hz, amplitude from 0.44 to 8 mm. More than ten measurements had been described for outcome assessment in these articles. It demonstrated that the WBV could improve activity of daily living (measured by Barthel’s index), and functional mobility (measured by timed up & go - TUG 10-MWT, 6-MWT, walk speed and cadence and Tinetti Gait Test). However, it is controversial if the WBV is able to improve 1) balance in term of Berg Balance Scale (1 study said yes while other two said no), 2) muscle strength and flexibility (3 said yes, while other three said no), and 3) spasticity (one with yes and two with no in term of Modified Ashworth Scale showed improvement in lower extremity).

Conclusion: Whole body vibration therapy is an effective therapy that can be used independently or combined with others. It demonstrated that patients with subacute and chronic stroke can benefit more. People with stroke used the WBV varies. Its main effects are on improvement of ADL and functional mobility, but its effect on balance, strength, flexibility and spasticity is uncertain, further study may be needed.

Key Words: whole-body vibration, WBV, stroke, rehabilitation

Sponsor: N/A
IRB/IACUC#: N/A
Evaluation of a Physical Exam Test for Determination of Leg Length Discrepancy Versus the Standard Postural X-ray Series in Low Back Pain Patients

Objective: To determine if the hip (pelvic) swing test for short leg is equivalent to the postural x-ray series for determination of leg length discrepancy in patients with low back pain.

Methods: Patients between the ages of 18 and 65 years who presented to the UNTHSC Department of OM with low back pain and a short leg on clinical exam were enrolled in the study. A hip swing test was performed with the patient barefoot. The test was repeated with heal lifts of various heights to determine which height allowed for equal rotational motion of the hips. The height of the correct heal lift was recorded in the patient’s chart. Each patient was then referred to Radiology Associates for a postural standing x-ray series. The measure of sacral base unleveling was recorded. The correlation between physical exam test and postural x-ray results was analyzed using a kappa correlation.

Results: 30 subjects participated in the study. All subjects underwent the hip swing test and postural standing x-rays. There was a positive correlation (P value) between heel lift height, as determined by physical exam test, and sacral base unleveling measured with imaging.

Conclusion: The study shows that the hip swing test may be as reliable and clinically applicable as postural standing x-rays in the evaluation of leg length discrepancy in patients with low back pain. These findings have the potential to alleviate the need for x-rays in the future, thus saving money and reducing the risk of radiation exposure to patients.

Sponsor: N/A
IRB/IACUC#: 2014-057
Use of Yoga in Children with Autism: A Systematic Review of Literature

Purpose and Hypothesis
Research examining the use of yoga in children has suggested benefits related to a variety of outcomes; however, there is no review that synthesized research findings for children with autism. The purpose of this review was to examine the evidence concerning the use of yoga exercises for children with autism. Safety concerns, potential benefits and practical application are discussed.

Materials and Methods
The databases searched included PubMed, PsychINFO, CINAHL, Cochrane, OVID, PEDro, ProQuest, Access Physiotherapy, and Hooked on Evidence. The search was conducted using the following keywords: ‘yoga’, ‘autism’, and ‘autism spectrum disorder’. Titles and abstracts were assessed manually according to the following criteria: (1) children with autism spectrum disorder, and (2) intervention (yoga program). An additional search, the reference lists of the relevant articles, was explored manually. We screened those articles for duplicate and selection criteria.

Results:
Seven of the 107 articles that were retrieved met the inclusion criteria. Across all studies, a total of 153 children (age range 13 to 16 years old) with autism were investigated. All studies reported improvements following participation in yoga exercises.

Conclusion
The result of this review suggests positive effects of yoga exercises in children with autism. The results should be interpreted with caution given the strength of evidence and the quality of reviewed studies and that the number of studies that examined the effects of yoga exercise in children with autism is low.

Sponsor: N/A
IRB/IACUC# 2014-063
Methodological considerations of label-free neuroproteomics: A case study involving a rat model of chronic methamphetamine exposure

Purpose: This presentation is aimed at evaluating label-free quantitative neuroproteomics methodologies to reveal biological pathways associated with chronic methamphetamine exposure in rats.

Methods: Striatal samples were harvested from drug-treated and naïve animals (adult male Sprague-Dawley rats). After a urea-based protein extraction and sample preparation following routine proteomics workflows, data-dependent LC-MS/MS analyses were run on a hybrid linear ion trap–FTMS instrument. Parameters evaluated in the context of detecting statistically significant changes in protein expression elicited by methamphetamine in the rat striatum included the choice of database search engines (Mascot and SEQUEST) and the method by which label-free quantitative information was obtained (spectral counting, MS/MS total ion currents from identified spectra, and precursor-ion abundance). Identifications were validated using the Scaffold software suite, whose label-free quantification and statistical modules were used for processing data files and organizing results. Additionally, bioinformatics was performed using Ingenuity Pathway Analysis (IPA).

Results: We queried our mass spectrometry-based proteomics data using the Mascot and SEQUEST search algorithms separately and conjointly for complementary protein identifications. For label-free quantitative analysis, identified proteins were revealed as differentially expressed following evaluation of quantitative method, along with the use of appropriate statistical analysis (G- and t-tests, p

Conclusions: Although our study focused on methodical aspects of quantitative label-free shotgun neuroproteomics initially, IPA of our results not only captured processes already recognized to be impacted by methamphetamine exposure (dopamine and serotonin biosynthesis, oxidative stress, cell signaling, etc), but also revealed protein associations hitherto unknown at proteome level. Thus, the latter would be worthy of future pursuit in the framework of mechanistic interpretations and as potential neurobiological indicators or consequences of methamphetamine abuse.

Sponsor Supported by the Robert A. Welch Foundation, BK-0031, and a Medical Student Research Program at the University of Florida College of Medicine

IRB/IACUC#
The Role of Anxiety in the Arterial Pressure Response to Chemoreflex Stress

Background: Anxiety disorders are remarkably prevalent in the United States, with an estimated 25% of the population suffering from some kind of anxiety disorder. Many studies have elucidated the link between high anxiety and cardiovascular disease (CVD), indicating a link between mental disorders and cardiovascular control. This study tested the hypothesis that the State-Trait Anxiety Index (STAI) and modified Borg Anxiety Scores can predict the blood pressure response to voluntary apnea.

Methods: STAI surveys were given before experimentation, with separate scores calculated for state (conditional/situational anxiety) and for trait (background/intrinsic anxiety). 10 young and healthy subjects (5 male, 5 female) were recruited. Subjects had no reported anxiety disorder and were not taking any anxiety medications. Subjects were exposed to 12% oxygen and then initiated 6 end-expiratory apneas with a 2 minute recovery period in between each apnea. Blood pressure, heart rate and the nadir of SaO2 were measured. Prior to and immediately after each apnea, subjects were asked to rate their level of anxiety on a modified Borg scale (6-20) to capture an instantaneous measure of acute anxiety.

Results: We found that trait anxiety had a significant correlation with increases in mean arterial pressure ($r = 0.725$, $P = 0.027$) and with changes in systolic blood pressure ($r = 0.856$, $p = 0.003$), but not diastolic pressure ($P>0.05$). There was a trend for a correlation between state anxiety and changes in systolic blood pressure ($r = 0.6$, $P = 0.082$), but no trend or significant correlation for diastolic or mean arterial pressure ($P>0.05$).

Modified Borg scales did not predict the systolic, diastolic or mean arterial pressure response ($P>0.05$)

Conclusion: We conclude that background/intrinsic anxiety (trait) is a better predictor of arterial pressure responses to apnea than conditional/situational anxiety (state). Furthermore, instantaneous anxiety as measured via modified Borg scale failed to adequately predict this pressor response. This study offers evidence that psychological functioning and not instantaneous anxiety can alter the physiological response to acute chemoreflex stress.

Sponsor
IRB/IACUC# 2014-080
Acid-sensing ion channel proton sensitivity is modulated by a guanidine containing dietary supplement

Acid-sensing ion channels (ASICs) belong to the epithelial/degenerin family. ASICs are sodium selective and are sensitive to extracellular protons specifically those following ischemia and injury. The ASIC1a subtype has been implicated centrally in the neurodegeneration following ischemic stroke while ASIC3 is involved in pain sensation and is expressed peripherally. Protons and inflammatory mediators can activate or modulate ASIC1a and ASIC3, suggesting that ASICs can be a pharmacological target for ischemic stroke and pain. The large extracellular domain of ASICs offers multiple sites for interacting with protons and guanidinium group containing compounds. Guanidinium compounds such as 2-guanidine-4-methylquinazoline (GMQ), amiloride, and agmatine are known to modulate the electrophysiological properties of ASICs. Here we identified a dietary supplement, GL-001 that shares molecular similarity to these ASIC ligands and modulate ASICs. We utilize whole-cell patch-clamp electrophysiology to determine the interaction of GL-001 with endogenous human ASIC1a (hASIC1a) and transiently expressed rat ASIC3 (rASIC3). Our data suggests that GL-001 reduces the hASIC1a pH sensitivity at physiologically relevant supplement concentrations consistent with suggested dietary supplementation. The rASIC3 peak current amplitude and steady-state current is reduced in the presence of GL-001. In the absence of extracellular calcium, GL-001 reduces the rASIC3 proton sensitivity by shifting pH-activation profile to lower pH. This suggests that the effect of GL-001 on rASIC3 is calcium dependent. Future studies will focus on determining the effect of GL-001 on the rASIC3 window current and other ASIC3 properties to resolve the mechanism of action of the GL-001 influence on channel activity.

Sponsor N/A
IRB/IACUC#
An Evaluation of Prenatal Behaviors in a Rural Texas Community

Purpose: Appropriate prenatal care for mothers is an important part of maternal health and should be a public health concern. Mothers need to be adequately educated on appropriate health practices during their pre-conception, prenatal, and post-conception time periods. This study was aimed to assess the behaviors of reproductive age women in a rural community concerning their prenatal care and to see if age and education level played a role in their behaviors.

Methods: 46 women completed a survey that was given out at the Perryton Health Center in Perryton, Texas. The study was given to women of reproductive age 18-45 who were pregnant at the time or had been pregnant. The survey asked about their most recent pregnancy and the behaviors associated: how early they sought prenatal care, tobacco use, folic acid supplementation, and flu vaccination.

Results: 41% of the respondents were 18-25 years old; in that age group, the average time of their first prenatal visit was 6.94 weeks, 15.8% were smoking while pregnant, 52.6% got their flu shot, and 63.2% took prenatal vitamins every day. 44% were 26-35 year olds; the average time of their first visit was 6.59 weeks, 5% were still smoking, 55% got their flu shot, and 70% took prenatal vitamins every day. 15% were aged 36-45; the average time of their first visit was 6.28 weeks, 14.3% were still smoking, 71.4% got their flu shot, and 42.9% were taking their prenatal vitamins every day.

Conclusions: It is important to educate women on safe behavior during the prenatal period. This data shows that younger moms seek prenatal care later and are less likely to get the flu shot. But when it came to smoking and taking prenatal vitamins, both the youngest and oldest age groups had poor behaviors. This information can help healthcare providers know what to focus on in their patient encounters and what the patients should be asked about and educated on.

Sponsor
IRB/IACUC# 2014-079

Assessing the Obstetric Patient’s Knowledge of Pregnancy

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Conclusions: It is important to educate women on safe behavior during the prenatal period. This data shows that younger moms seek prenatal care later and are less likely to get the flu shot. But when it came to smoking and taking prenatal vitamins, both the youngest and oldest age groups had poor behaviors. This information can help healthcare providers know what to focus on in their patient encounters and what the patients should be asked about and educated on.

Sponsor
IRB/IACUC# 2014-079
Cervical Cancer Screening Among Refugee Populations in Tarrant County

Cervical cancer is the second most common cause of cancer mortality among women, with most cancer deaths among women of developing countries. It is also the most easily preventable cancer in women. This study evaluates cervical cancer screening practices among several refugee populations in Tarrant County: Burmese, Bhutanese, Somalian, and Congolese. Many factors influence participation in cervical cancer screening among refugee women. Such factors include knowledge about cervical cancer, cultural beliefs, financial concerns, access to health care, physician characteristics, and time in the United States. The study aimed to investigate the impact of time in the United States on cervical cancer screening. Data for this study were obtained from a project called the Building Bridges Initiative. As part of this program, trained refugee Lay Health Educators reached out to refugee women in their communities with education and assistance in receiving cervical, breast, and Hepatitis B screenings. The Lay Health Educators consented and interviewed women who met the inclusion criteria during the baseline assessment. For the purposes of this study, the following baseline questions were examined: “Have you had a Pap test?” and “What was the date of your last Pap test?” in addition to demographic information and time of arrival in the United States. The association of arrival in the United States and screening, as well as qualitative data from comments shared during the group education sessions are presented to illustrate barriers to screening. Rates of cervical cancer screening among refugee populations are far below that of the recommended rate in the United States as outlined by Healthy People 2020. Therefore, refugee populations in the United States, especially when resettling from countries with a high incidence of cervical cancer, are in need of culturally and linguistically tailored cancer education prevention and intervention programs.

Sponsor
IRB/IACUC# 2014-084

Contributors to Depressive Symptoms Among Pregnant Women

The Division of Reproductive Health of the CDC has made mental health conditions of pregnant woman a top priority (CDC, 2013). Depression during pregnancy (AKA Perinatal Depression) often goes undiagnosed; therefore, identifying potential risk factors for screening purposes is important for all health professionals. The current study examined whether race / ethnicity predicts depression symptomatology in pregnant women. Additionally, current identified risk factors for perinatal depression (maternal stress, anxiety level, social support, relationship status, education level, healthcare coverage, and employment status) were analyzed in this study.

Participants in this study (n=454) completed a survey and were recruited from the Tarrant County WIC clinics and UNT Health OB/GYN clinic at Harris Methodist Hospital. African American, Caucasian, and Hispanic pregnant women were eligible to complete this questionnaire. Variables examined in this study included demographic information and psychosocial measures (depressive symptoms, anxiety, and stress-level). Simple and multiple logistic regressions were utilized to predict depression symptomatology (no depressive symptoms vs mild, moderate, or major depressive symptoms). Models controlled for perceived stress, anxiety, social support, age, employment status (employed, student, not employed), health insurance (yes, no), marital status (married or in a relationship, not in a relationship), highest education (less than high school, high school or GED, more than high school), and recipient of WIC (yes, no). Odds ratios and 95% confidence intervals are presented.

Participants were Caucasian [n=193 (42.5%)], African-American [n= 103 (22.7%)], and Hispanic [n=158 (34.7%)]. Depressive symptomatology was present in 158 participants (34.7%). Unadjusted analyses showed that African American women had 1.7 times greater odds of having depressive symptoms (95% CI [1.008-2.721]) as compared to Caucasian women, but no differences were observed between Hispanic and Caucasian women. Additionally, stress, anxiety, social support, WIC assistance, education-level, and marital status were all individually predictive of depressive symptoms in unadjusted analyses. However, in the adjusted model, only anxiety predicted perinatal depressive symptomatology. No differences were observed by race/ethnicity.

This study shows the high percentage of pregnant women with depressive symptoms. Although individual analyses of race/ethnicity were significant, overall it was not predictive of depression symptoms in pregnant women. Follow-up studies are needed to help health professionals identify risk factors of perinatal depressions and direct patients to appropriate treatment.

Sponsor
IRB/IACUC# 2013-014
Determinants of Urinary Bisphenol-A Concentrations During Pregnancy

Purpose: Given the short half-life (5-6 hours) of bisphenol-A (BPA), a suspected endocrine disruptor, we examined whether urinary concentrations of bisphenol-A (BPA) among pregnant women were correlated with 24 hour self-reported consumption of canned beverages and/or canned/prepackaged foods.

Methods: Pregnant women (n=306) were recruited from the University of Oklahoma Medical Center Women’s and High Risk Pregnancy clinics in Oklahoma City, Oklahoma. Banked urine specimens were analyzed for total (free BPA + conjugates) urinary BPA concentrations (mg/L). Participants were asked to self-report the number of servings of canned beverages, canned foods and prepackaged foods within the last 24 hours. Spearman rank correlation coefficients were used to identify statistically significant correlations between log-transformed urinary concentrations of BPA and self-reported measures of canned beverage and canned/prepackaged food consumption. Linear regression analysis was also performed, adjusting for specific gravity, BMI, age, smoking, income, race, education, and consumption of coffee within the past 24 hours.

Results: The majority of women were non-white, reported an annual household income below $30,000 and were not active smokers (<15 ng/ml cotinine). Median urinary concentrations of total BPA were 2.15 ng/mL (sd = 7.86). Less than one-third of women had consumed canned beverages (30%), canned foods (32%), or prepackaged foods (23%) in the previous 24 hours. Log-transformed total urinary concentrations of BPA were not found to be statistically correlated with the consumption of canned beverages or canned/prepackaged foods. After adjusting for covariates using linear regression, we still did not observe any significant associations.

Conclusions: Maternal concentrations of total urinary concentrations do not appear to be correlated to the consumption of canned beverages or canned/prepackaged foods in the previous 24 hours, the hypothesized main routes of exposure to BPA in human populations.

Evaluation of the UNTHSC Campus as a Mother-Friendly Worksite

Objective

Mothers face numerous barriers with breastfeeding specifically returning to work. Lack of privacy and storage to breastfeed or pump, and accepted break times are reasons to cease. Texas created the Mother-Friendly Worksite Initiative in 1995 which offers certification for worksites that meet certain criteria including “Flexible work schedules with breaks and work patterns providing time milk expression, access to a private location(s), not a bathroom and clean and safe water source for washing hands and cleaning equipment, and access to hygienic refrigeration to safely store breastmilk.” This pilot research project evaluated breastfeeding-friendliness on the UNTHSC campus and sought to assess steps to become a mother-friendly worksite.

Materials and Methods

Fifteen MPH students and one DrPH student were assigned UNTHSC buildings and asked to evaluate the assets and barriers to breastfeeding on campus. The assessment, conducted with photographs and journaling ascertained whether there were already designated places to breastfeed, pump, and/or store milk.

Results

The results found three lactation-designated areas on campus and surrounding buildings. Two lactation rooms were private with locked doors but neither were labeled as such. The third lactation area was located in a restroom with a curtain and chair. None of the three lactation areas had refrigeration to store expressed breastmilk.

Conclusions

To become a certified mother-friendly worksite, UNTHSC needs to 1) increase lactation spaces on campus; 2) generate policy that facilitates faculty, staff, and students to take breaks to pump or breastfeed, and 3) create designated spaces for patients and guests to breastfeed and pump.
Gender Differences in the Arterial Pressure Response to Apnea

Background: Gender-based differences in basic physiology receive intense scrutiny within the scientific community. These differences can potentially explain the mechanisms of various health outcome disparities among the genders. It has been widely documented that women and men respond differently to physiological stress—especially in the response to sympathetic stimulation. Women are considered “cardiac responders” (increasing heart rate and contractility) while men are considered “vessel responders” (increasing systemic vascular resistance). Up to this point, no study has tested this hypothesis with apnea. This study tested the hypothesis that women receiving metoprolol will decrease their arterial pressure and heart rate response to hypoxic voluntary apnea compared to men.

Methods: For this pilot study, 2 men and 4 women were recruited. Each of the women was in the early follicular phase of her menstrual cycle (day 1-4 post menses). No women were taking hormonally active medications. Each subject was exposed to 12% oxygen via Douglas bag for 5 minutes. The subject then initiated 3 voluntary apneas. Beat-to-beat arterial pressure (Finometer) and O2 saturation (Nellcor pulsoximeter) were measured. Each subject repeated the experimental condition with (a) a full blocking dose of intravenous metoprolol (average=0.1 mg/kg) and (b) the same dose of normal saline.

Results: Males and females exhibited similar responses in systolic, diastolic and mean arterial pressure to voluntary hypoxic apnea with and without metoprolol (all P>0.05, repeated measures two-way ANOVA).

Conclusions: This preliminary study has shown that women in the early follicular phase of menstruation respond similarly to men with hypoxic apnea in terms absolute arterial pressure. This potentially implicates the role of estrogen and progesterone in this phenomenon. Future studies will quantify the role of menstrual cycle phase and comparison to other physiological stressors.

Sponsor
IRB/IACUC# 2014-138
Identifying Primary Factors Responsible for the Decline of Obstetric Care by Rural Texas Family Practice Physicians

There is a well-documented decline of family practice physicians (FPs) providing OB, and the known reasons behind the decline are varied and complex. The purpose of this study is to assess which factors are most responsible for the decline in OB provided by FPs, with a specific focus on those in rural Texas communities. Specifically, it seeks to determine:

1.) What rural FPs are currently providing OB services?
2.) What are the primary factors/barriers responsible for the decline of OB services provided by rural FPs?

A statewide survey of self-identified rural FPs targeted the degree of OB services currently provided and graded factors/barriers responsible for the decline of obstetric care in their personal practices. Current OB practice characteristics were divided into 3 primary categories: currently performing, previously performed, or never performed. Individual factors/barriers were graded using a scale of 1 through 5 and ranked according to highest arithmetic average. The survey was distributed in both physical and online forms to various professional FP societies in Texas and the data and statistical analysis were recorded in Qualtrics online survey software.

35 FPs volunteered to participate. 2 respondents did not self-identify as rural and were excluded from the analysis. Of the remaining 33, we found that 85% felt as if they had received adequate OB training in residency, yet only 29% were currently performing vaginal deliveries as part of their practice. Another 43% had previously performed vaginal deliveries but were not currently, and 29% had never performed vaginal deliveries as part of their practice. Of those adequately trained in OB, lifestyle (4.36), family (4.00), and sleep issues (3.75) accounted for the top three factors, followed by liability (3.41) and difficulty obtaining back-up coverage (3.14). The lowest ranked factors/barriers were hospital privileges (2.11), concern with skill level (1.96), and credentialing barriers (1.79).

This data confirms that qualified FPs are declining to provide OB care. Primary factors responsible include lifestyle/family-related issues, liability, and poor back-up coverage. Factors of least concern were credentialing barriers, concern with skill level, and hospital privileges. This study confirms that non-medical factors are affecting medical care in rural areas, and future solutions must take these factors into account.

Sponsor n/a
IRB/IACUC# 2013-167
Seroprevalence of high-risk human papillomavirus types among substance abusing women screened for cervical and anal cancer.

Purpose. Prevalence studies of HPV in the general US population have provided important baseline data for monitoring HPV vaccination efforts. As the field of HPV progresses, funders are calling for HPV studies to be conducted in more meaningful and high risk populations to uncover new leads in HPV infection. Our primary objective in this cross-sectional study was to estimate the seroprevalence of high-risk HPV (hr-HPV) among a high risk population - substance abusing women. Further investigation was conducted to assess concordance of hr-HPV infection between cervical and anal sites.

Methods. Women were recruited from Nexus Recovery Center – the largest female only substance abuse recovery center in DFW. Cervical and anal pap smears were used to collect samples for hr-HPV co-testing. HPV results were received from 318 cervical samples and 243 anal samples. Chi-square and t-tests were used to determine differences in hr-HPV status by age, race, smoking, high risk sexual activity, cytology, and concordance.

Results. Seropositivity for cervical hr-HPV was 29%. Anal hr-HPV was observed significantly more often (32%) compared to cervical sites. Seropositivity for hr-HPV among women with abnormal cervical cytology was 63%; for those with normal cervical cytology hr-HPV was 47%. However, only 39% of abnormal anal cytology tested seropositive for hr-HPV. hr-HPV status differed by age and cervical cytology, but not by race, smoking, sexual activity, or anal cytology. Of those testing positive for either cervical or anal hr-HPV, nearly half (46%) had infection concurrently at both sites.

Conclusion. Our study population demonstrated higher rates of cervical and anal hr-HPV infections compared to US women (23% and 19%, respectively). As expected, hr-HPV status differed by cervical cytology results. Contrary to our hypothesis, hr-HPV status was similar regardless of anal cytology results. This unexpected finding may suggest a different ability of anal hr-HPV clearance, or it could reflect the younger age of our study group given the older age predilection of anal dysplasia. Concordance of hr-HPV between cervical and anal sites is generating a separate study of type-specific hr-HPV at cervical, anal, and oral sites. Our findings lend importance to determining whether anal Pap smears and/or anal hr-HPV testing should be included in well woman exams and also presents baseline HPV prevalence for the first time in this high risk population.

Sponsor. Cancer Prevention Research Institute
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