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Research Appreciation Day

April 15, 2016

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Receptor Pharmacology & Drug Delivery (Abstracts in the 2000s)
Woman’s Health (Abstracts in the 2100s)
Conclusions:
Epworth Sleepiness (ES), as well as among OSA and DepE. Specifically, for those who met criteria for ES, a significant positive correlation was shown between the

SDB was found to be elevated among the Mexican American population in this study, with significant associations being shown among ES and

Objective:
Sleep-disordered breathing (SDB), such as found in excessive sleepiness (ES) & obstructive sleep apnea (OSA), has been recognized as a common
occurrence in the elderly. SDB has been linked to a number of negative health outcomes in older persons, as well as both cognitive dysfunction and depression. Research shows that the likelihood of depression increased with the frequency of SDB. Likewise, breathing problems during sleep may also be linked to early mental decline and Alzheimer’s disease in Mexican Americans, a new study suggests. There remains, however, a dearth in the literature regarding the impact of SDB on the link between depression and cognition in this population. This study seeks to address the gap in knowledge on the relationship of SDB on depression-related cognitive impairment in Mexican Americans.

Methods:
Data were analyzed from 516 Mexican American participants from the Health and Aging Brain among Latino Elders (HABLE) study. Excessive sleepiness (ES) was determined based on having a score ≥10 on the Epworth Sleepiness Scale (ESS). Obstructive Sleep Apnea (OSA) was identified as those with a score ≥3 on the STOP-BANG Sleep Apnea Questionnaire. Depression-related cognitive impairment was determined based on the DepE (Depression endophenotype), which was coded on a five-point scale with the GDS-30. Linear regression models were utilized with the DepE as the dependent variable and the Epworth Sleepiness Scale, as well as the STOP-BANG Sleep Apnea Questionnaire, serving as two separate, independent variables. Covariates included age, gender, education, BMI, hypertension, dyslipidemia, and diabetes mellitus. Significance was set at p<0.05.

Results:
SDB was found to be elevated among the Mexican American population in this study, with significant associations being shown among ES and DepE, as well as among OSA and DepE. Specifically, for those who met criteria for ES, a significant positive correlation was shown between the Epworth Sleepiness Scale (B[SE]= 0.93[0.27], t=3.47, p=0.001) and DepE. Additionally, among those who met criteria for OSA, a significant positive correlation was also shown between the STOP-BANG Questionnaire (B[SE]= 0.98[0.23], t=4.21, p<0.001) and DepE.

Conclusions:
Elevated ES and OSA show an increased risk for depression-related cognitive impairment (DepE) among Mexican Americans. Potential implications include treatment of ES and OSA as a means of therapeutic intervention for individuals with DepE. Further research should continue examining the effects of other SDB conditions on DepE, as well as exploring the role of DepE on SDB.

Sponsor
American Federation for Aging Research
IRB/IACUC# 2012-083

Workforce Enhancements in Healthy Aging and Independent Living
Purpose: Older adults are among the fastest growing age group in the United States and use many health care services, have complex conditions, and require professional expertise to meet their health care needs. Having a geriatric workforce capable of carefully managing the medical conditions of seniors to assist with healthy independent lifestyles is important. The University of North Texas Health Science Center expanded unique partnerships with Texas Christian University, JPS Health Network, and United Way’s Area Agency on Aging to create the Workforce Enhancement in Healthy Aging and Independent Living (WE HAIL) Program. As the only Geriatric Workforce Enhancement Program awarded in Texas, WE HAIL advances geriatric education by aligning learning objectives and activities with community needs of an aging population. Program innovations take cross-sector approaches to integrate evidence base programs into health professional training, and expand training opportunities for rural areas and underserved populations. Applying a Rapid-cycle Continuous Quality Improvement (RCCI) method, WE HAIL provides training enhancements for the following learner groups: 1) undergraduate and graduate students; 2) faculty; 3) family medicine residents; 4) practicing health care professionals, including physicians, nurses, physician assistants, pharmacists, physical therapists, social workers, and dieticians; and 5) caregivers of older adults. Methods: Data will include trainee demographic information through the HRSA-GWEP Performance Report for Grants and Cooperative Agreements (PRGCA), feedback from trainees on usefulness, intention to use, and suggestions for future activities, and pre-post measures for practitioner knowledge, skills, and effectiveness. Additional data includes older adult outcomes from program-specific validated tools, and cross-program measures using Centers for Disease Control Healthy Days (4-items) and National Health Interview Survey Utilization (4-items). Results: Five Innovation teams of interprofessional faculty and community organizations, including Meals on Wheels, Senior Citizen Services, Alzheimer’s Association and James L. West Alzheimer’s Center, convened to plan and develop enhancements in existing programs. New programs are proposed for a Geriatric Certificate for Family Medicine Residency Programs, and a Geriatric Professional Leadership Institute. Proposed enhancements and new programs will be implemented during 2016-2018 to impact over 2,000 health professions students, almost 100 family medicine residents, over 500 primary care practices, and over 2,000 older adults and their caregivers. Conclusions: WE HAIL collaboration will deliver quality training enhancements and increase the number of geriatric-trained primary care providers to meet the needs of older adults at individual, community and population levels.

Sponsor
Health Resources and Services Administration (HRSA), Federal Award No - U1QHP287350100, Geriatrics Workforce Enhancement Program
IRB/IACUC#
Single leg standing (SLS) is one of the most commonly used balance assessment instrument in clinical settings. However, when a person stands on one leg, there may be many factors that may affect the person’s static standing ability. These factors could be external ones like surface firmness, shoes on or off, or standing leg straight or bent, or the internal factors like foot flat or dominant when kicking a ball. So far, there was still lack of studies investigating how these factors may affect the SLS. Therefore, the purpose of this study was to investigate whether these external and internal factors may affect the SLS assessment.

Methods.
Twenty-eight young subjects (age in average?) were selected with selection criteria for this study. Each of them was asked to stand on the balance platform with single leg standing for 20 seconds under the following 6 different external affecting conditions: surface firmness (hard versus soft with a foam), shoes on and off, and leg straight versus bent. All subjects have their left legs as the supporting legs and the right leg as the kicking legs when they jumped to shoot a basketball or kicked a soccer ball. To avoid fatigue effect on data results, the order of conditions for being tested was randomized. Also, the internal affecting conditions including foot flatness and leg dominance were compared.

Results.
There were no statistical significance (p > 0.05) noticed no mater shoes on or off under other conditions. The surface firmness affects the SLS only on the left side (p < 0.016) when the leg was straight with shoes off or when the leg was bent regardless of shoes on or off. Significant differences (p < 0.001) were identified between leg straight versus leg bent regardless of surface firmness or shoes on or off. The flat foot as an internal affecting factor could only make significant differences when a subject stood on a foam with shoes off and leg bent (p < 0.05).

Conclusions
This study showed that knee bending or not, and surface firmness for dominant or non-dominant leg or flat or non-flat foot to stand on could make significantly different results of SLS assessment. Clinicians should keep these affecting conditions in mind and be precautious when using the SLS for balance assessment.

Vitamin D and cognition in Hispanic patients
Introduction: Recent research has shown an association between vitamin D deficiency and cognitive functioning. There is also evidence to suggest that there may be a relationship between low levels of vitamin D and Alzheimer’s disease. A review revealed there was minimal research on low vitamin D levels in minorities, particularly in Hispanics. This issue is particularly salient to Hispanics as they are the fastest growing aging population in the US. Additionally, the cost of Alzheimer’s disease to the US is estimated to be $226 billion in 2015, and Hispanics and African American make up the highest racial population with the disease.

Methods: A literature review used search terms including vitamin d deficiency, cognition, Alzheimer’s, Hispanics, and Mexican-American, resulting in approximately 100 abstracts.

Results: The articles reviewed demonstrated strong evidence of the relationship between a vitamin D deficiency and cognition. They also revealed an increased risk of Alzheimer’s disease (AD) and other types of dementia in the context of a low vitamin D level. Interestingly, AD is a disorder of progressive memory loss and cognitive dysfunction, but in those few studies that performed cognitive testing, a low vitamin D level correlated with poor executive functioning. Memory testing has yielded equivocal results. These studies used white participants and may not therefore reflect the general population. A multiethnic cohort study showed the mean vitamin D level of the sample as 19.2 (11.7) ng/mL, with 26.2% of participants being vitamin D deficient, and 35.1% insufficient. The mean serum vitamin D levels were lower for African-American and Hispanic participants compared with white participants. Various reasons for these differences have been hypothesized including cultural differences in vitamin D intake, incidence of renal insufficiency, place of birth, and less vitamin D production due to more highly pigmented skin.

Conclusion: Hispanics are the fastest growing ethnic population in the US and have higher rates of obesity, liver disease, tobacco use, heart disease, diabetes, metabolic disorder, stroke, and hypertension. Many of these disorders are related to vitamin D, and all are associated with cognitive deficits. It is unknown at this time if vitamin D supplementation will reverse cognitive deficits. Therefore, it is important to add Hispanic cohorts to future studies to explore the relationship between vitamin D and cognition.
The Effects of Cardiovascular Risk Factors on Depression in Elderly Mexican Americans

Objectives: The Mexican American population is the fastest growing segment of the aging population in the United States and as such they face a disproportionate burden of health issues such as cardiovascular disease (CVD) and depression. Although evidence exists linking depression and CVD, the link between risk factors for CVD and their association with depression have not been explored, especially among the Mexican American population. This study seeks to look at the relationship between depression and CVD risk factors specifically among the Mexican American population.

Methods: Data were analyzed from 525 participants (High CVD n=159; Low CVD n=131) from the Health and Aging Brain among Latino Elders (HABLE) study. Risk factors for CVD include hypertension, dyslipidemia and diabetes mellitus. A CVD risk score was created combining the risk factors with the high CVD group including all three risk factors and the low CVD group consisting of just one risk factor. Medical diagnosis was based on clinical lab work. Depression was measured through the use of the Geriatric Depression Scale and its associated four subscales (dysphoria, meaninglessness, apathy, and cognitive impairment). Linear regressions were utilized to analyze the relationship between CVD risk factors and depression. Covariates included age, gender and education.

Results: Within the total sample, overall CVD risk was shown to be significantly associated with increased apathy (B[SE]= 0.17[0.07], t=2.3, p=0.01). When stratified by level of CVD risk, those in the high CVD risk group showed a significant positive association with total GDS score (B[SE]= 1.68[0.67], t=2.50, p=0.013) as well as with dysphoria (B[SE]=0.66[0.31], t= 2.17, p=0.03), apathy (B[SE]=0.36[0.15], t=2.51, p=0.012) and cognitive impairment (B[SE]= 0.36[0.17], t=2.20, p=0.05). The low CVD risk group showed no significant correlations to the GDS or it’s associated subscales.

Conclusion: Hypertension, dyslipidemia and diabetes mellitus, all of which are risk factors for CVD were found to be associated with depression among Mexican American elders. However, this association was specific to level of risk, with the high risk CVD group showing the greatest link with geriatric depression as well as with its associated subscales (dysphoria, apathy, and cognitive impairment).

Sponsor Medical Student Training in Aging Research
IRB/IACUC# 2012-083
The effect of dietary curcumin intake on age associated neurobehavioral dysfunction

We hypothesized a combination treatment of dietary curcumin and CR to improve age associated neurobehavioral dysfunction better than either treatment alone, via attenuation of inflammation and oxidative stress. Middle-aged (15 months) and aged (20 months) male and female C57BL/6 mice were grouped under four dietary interventions, (1) regular chow fed ad libitum (AL), (2) curcumin at 0.7g/kg body weight in AL (CURAL), (3) caloric restriction (CR) and (4) curcumin w/ CR (CURCR) and were kept under these interventions for 16 weeks. We administered a behavioral battery after eight weeks of dietary intervention that included tests for cognitive and psychomotor function. To measure oxidative stress and inflammation we collected plasma and red blood cells and used factory manufactured kits to detect pro and anti-inflammatory cytokines and glutathione status. CR and CURCR significantly improved various aspects of motor function including wire suspension, rotordod and bridge walking performance, indicative of cerebellum functioning, when compared to age matched control (AL) for both sexes, whereas only CURAL improved optomotor function, indicative of vision, in middle aged males and females and aged males. All three interventions had significant effects on pro and anti-inflammatory cytokines, KC-GRO concentration was significantly decreased in CR and CURCR in the middle aged males and aged females group and was correlated to body weight; TNF-α concentration was significantly decreased in both CURAL and CURCR in middle aged males and there was a significant decrease in C-reactive protein in aged males under CURCR. There were no significant differences in the redox state across groups. Based on results from the motor tests and blood based biomarkers and earlier data on cognitive function, dietary curcumin can be used as a CR mimetic for certain components of healthy functional aging but the benefits may not entirely be related to its anti-inflammatory and anti-oxidant effects. Future studies should include different doses and a tapered down caloric restriction regimen.

Sponsor
P01 (Program project grant) AG022550 National Institutes of Health, National Institute on Aging
IRB/IACUC#  2011/12-30-A04

Dementia Care in Tarrant County

Purpose: The purpose of this research is to analyze local resources and barriers that will affect the quality of life of the patient and their family as the disease progresses.

Methods and Materials: Information was collected from the Alzheimer's association, WHO, CDC, Texas Department of aging and disability services, and local organizations.

Results: For each stage of dementia several community resources are suggested.

Conclusions: Patients and their family need to be aware of the various resources they can obtain for management of dementia.

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IRB/IACUC#
Chronic intermittent hypoxia induces oxidative stress and inflammation in brain regions associated with neurodegeneration

Age is the highest risk factor for the development of neurodegenerative diseases (ND), such as Alzheimer’s disease (AD) and Parkinson’s disease (PD). As life expectancy increases, the incidence of ND is projected to rise accordingly. Increased ND incidence will be associated with high healthcare costs. Currently, no cure exists for ND and diagnosis occurs at advanced stages, which foreshadows a financial healthcare crisis. Therefore, early identification of patients at risk for ND may provide opportunities for more effective therapies. Since ND is associated with increased oxidative stress (OS) and inflammation, these markers could be used to identify patients at risk for ND. Multiple environmental factors can be an oxidative stressor, and thus exacerbate inflammation induced ND risk. One such environmental factor that increases OS is sleep apnea (SA), a common ND comorbidity. However, it is unknown if SA induced oxidative stress activates neuroinflammation in areas associated with ND. To model SA in rats, chronic intermittent hypoxia was used. Male rats were exposed to six minute chronic intermittent hypoxia (CIH) cycles, during which oxygen levels were rapidly decreased from 21% to 10% then returned to normal room air levels, eight hours a day during the light phase for seven days. Plasma and tissue from hippocampus (HIPP), entorhinal cortex (ETC), substantia nigra (SN), rostral ventrolateral medulla (RVLM), and solitary tract nucleus (NTS) were collected and tested for levels of OS and inflammation, using Advanced Oxidative Protein Products (AOPP) and multiplex immunoassays, respectively. OS markers and inflammation were elevated in the plasma of rats exposed to CIH compared to control rats. Differences in neuroinflammatory markers within tissues were observed. Specifically, inflammatory markers in the RVLM were significantly decreased in animals exposed to CIH while TNF-a and IL-6 were elevated in the SN. TNF-a was positively associated with plasma OS and the cytokine associated with inflammatory cell recruitment, KC-Gro, exhibited the same pattern in the ETC. The ETC and SN are areas associated with initial neurodegenerative processes in AD and PD, respectively.

CIH may contribute to processes involved in early ND pathology by elevating OS and inflammation in critical brain regions. These results indicate that SA can exacerbate ND by increasing OS-induced neuroinflammation. Therefore, treatment of SA could be one consideration in preventing ND.

**Sponsor**
Texas Garvey Foundation Grant, a William and Ella Owens Medical Research Foundation grant, a Graham & Carolyn Holloway Foundation grant, an UNTHSC Intramural Grant, an IAADR Institute Grant, and the Alzheimer’s Association; New Investigator Research Grant

**IRB/IACUC#**
2014/15-50-A05
The purpose of this study is to evaluate patient and tumor characteristics, treatments, and outcomes of patients at Cook Children’s Medical Center (CCMC) who were diagnosed with primary osteosarcoma from January 1, 1992 to December 31, 2013. Prior to the use of systemic chemotherapy, the survival rate for osteosarcoma patients was poor at 15-20% for two year survival. Current five year survival is more than 60% in non-metastatic disease with the addition of systemic chemotherapy. However, patients with metastatic disease at diagnosis have a lower 5 year survival of about 30%. This study will evaluate the outcomes of patients with osteosarcoma at CCMC relative to the outcomes noted at other institutions and in previous literature. It will also evaluate various potential prognostic factors to determine if they significantly affect patient outcomes. Researchers conducted a comprehensive retrospective chart review with the patients abstracted from the Cook Children’s Cancer Registry. The population consists of patients diagnosed with and treated for primary osteosarcoma at CCMC from 1992 to 2013.

The 5 year overall survival for the population is 66.9% ± 6.1. The 5 year Event Free Survival for the population is 62.2% ± 6.6. The 5 year survival for patients with metastases at diagnosis is 50% ± 13.9. The 5 year survival for patients without metastases at diagnosis is 72.3% ± 6.8. The 5 year survival of patients diagnosed from 1995 to 2003 is 70.0% ± 8.9. The 5 year survival for patients diagnosed from 2004 to 2013 is 64.2% ± 8.8. Survival rates for patients diagnosed with osteosarcoma at CCMC are consistent with the literature. Survival rates have not changed in the past 20 years for osteosarcoma.
Radiotherapeutic Bandage for the Treatment of Skin Cancer

Purpose: It is currently estimated that one in every five Americans will develop skin cancer. Squamous cell carcinoma (SCC) is the second most common type of skin cancer and occurs in cells just beneath the outermost layer of the epidermis. Radiation therapy is used in the clinic against inoperable tumor lesions and in patients that cannot undergo surgery, as well as to treat recurring lesions after a primary surgical approach (i.e., Mohs micrographic surgery). We have previously reported on the incorporation of Holmium-165 (165Ho) nanoparticles into electrospun nanofibrous mats (“bandages”) for potential use in the treatment of SCC. A 165Ho-containing polymer nanofibrous bandage was prepared via electrospinning using 165Ho-iron garnet nanoparticles (165HoIG) and polyacrylonitrile. These bandages can be manipulated for easy application to tumor lesions, and can be made on a large scale; they are made radioactive (to holmium-166; 166Ho) just prior to therapy using a process called neutron-activation. The goal of the present study is to test our radiotherapeutic bandage against SCC in an animal model, to determine clinical relevance.

Methods: Polyacrylonitrile polymer bandages containing 165HoIG were prepared as previously reported. The radiotherapeutic bandages were then produced via neutron-activation in a thermal neutron flux of 1.8 × 10¹³ neutrons/cm²·s for 1.33 h using a 1 MW nuclear reactor. Female athymic nude mice were injected with human Colo-16 SCC cells subcutaneously and after eight days (average tumor volume: 35 ± 8.6 mm³) received no treatment, or were exposed to non-radioactive or radioactive (92.5 ± 18.5 MBq) bandages for approximately 1 h (n = 10 per group). After treatment, tumors were measured over fifteen days, tumor volume ratios (TVRs) compared and histopathology performed.

Results: Fifteen days after treatment, the TVR of the radioactive bandage treatment group was 3.3 ± 4.5, while TVRs of the non-radioactive or radioactive bandages were 33.2 ± 14.7 and 26.9 ± 12.6, respectively. At the time of necropsy, there was mild focal epidermal hyperplasia surrounding a small area of epidermal ulceration in the radioactive bandage group. No other examined tissue (i.e., muscle, liver, lung, spleen and heart) showed significant lesions.

Conclusions: Our radiotherapeutic bandage exhibits promising efficacy against SCC of the skin in a mouse model. It can be individually tailored for easy application on tumor lesions of all shapes and sizes, and could complement or possibly replace surgery in the clinic.

Sponsor: Sigma Xi
IRB/IACUC#: 2012/13-48-A04

Focal Nodular Hyperplasia (FNH) of the Liver Following Treatment of Childhood Cancer

Purpose: The purpose of this case study is to describe three different patients with complicated malignancies in their past medical history who received the diagnosis of FNH. The report will highlight the clinical features of each case, describe the diagnostic modalities utilized and increase awareness of FNH as a long term sequela of chemotherapy and radiotherapy used to treat childhood cancers.

Methods: Medical records of three patients treated at Cook Children’s Medical Center who were identified to have FNH were collected. Medical history, medications, clinician notes, imaging, surgical reports, and pathology reports were all reviewed systematically. A literature review was conducted using PubMed, Scopus and UpToDate.

Results: Two of the three patients had been successfully treated for metastatic and recurrent Wilms' tumors; the third had been successfully treated for embryonal rhabdomyosarcoma of the pelvis. All three patients required chemoradiation leading to extensive follow up for the long term side effects of their therapy. All three cases of FNH were found incidentally on imaging, which was either routine or based on symptoms unrelated to the liver. The lesions were first identified an average of 9 years after completion of cancer therapy. Two of the patients underwent surgical biopsy while the third was diagnosed based only on imaging. A watchful waiting approach was applied to all three children and they are all doing well without any hepatic complications, although the lesions often continue to increase in size slowly.

Conclusions: The pathogenesis of FNH is thought to be due to a vascular insult leading to ischemia and subsequent remodeling of the hepatic tissue with reperfusion. It is commonly found in adult women on estrogen therapy. The exact mechanism of its development in children is unknown; however, there appears to be a correlation with a past medical history of childhood malignancy and chemoradiation therapy. It is possible to make the diagnosis based on imaging alone to avoid more invasive diagnostic procedures, if the lesions are characteristic and if they are not suspicious for metastatic or recurrent disease. A watchful waiting approach is recommended in all cases of focal nodular hyperplasia of the liver.
Nitric oxide- and cisplatin-releasing amine-modified mesoporous silica nanoparticles for the treatment of non-small cell lung cancer

Purpose:
Lung cancer is the leading cause of cancer related death in the United States; non-small cell lung cancer (NSCLC) is the most common type and it is a challenge to treat in the clinic. Studies have shown that cisplatin-loaded nanoparticles are efficacious against NSCLC and can reduce the nephrotoxicity associated with cisplatin. Previously, nitric oxide (NO) was shown to enhance the efficacy of chemo- and radiotherapies in vivo; thus, the aim of this study was to develop a NO- and cisplatin-releasing wrinkle-structured amine-modified mesoporous silica (AMS) nanoparticle for improved NSCLC therapy.

Methods:
The AMS and NO- and cisplatin-loaded AMS materials were prepared and characterized. Platinum (Pt) drug loading was analyzed using inductively coupled plasma-mass spectrometry (ICP-MS), and NO release and in vitro release of cisplatin from AMS materials were investigated. Cytotoxicity of functionalized AMS nanoparticles were tested against human NSCLC cell lines, H596 and A549, and compared with that against normal lung cell lines, WI-38 and BEAS-2B. Pt cellular uptake studies were then performed using these four cell lines. The results were then compared to those obtained for cisplatin.

Results:
For both NSCLC cell lines, the toxicity of NO- and cisplatin-loaded silica nanoparticles (NO-Si-DETA-cisplatin-AMS) was significantly higher than that of silica nanoparticles loaded with only cisplatin (Si-DETA-cisplatin-AMS). In contrast, the toxicity of NO-Si-DETA-cisplatin-AMS toward normal lung cell lines was not significantly different from that of Si-DETA-cisplatin-AMS (normal lung fibroblast cells WI-38) or was lower than that of Si-DETA-cisplatin-AMS (normal lung epithelial cells BEAS-2B). The calculated therapeutic index of NO-Si-DETA-cisplatin-AMS was higher than that of Si-DETA-cisplatin-AMS and free cisplatin, based on both WI-38 and BEAS-2B data. When treated with Si-DETA-cisplatin-AMS, Pt cellular uptake was highest in BEAS-2B, then H596, WI-38 and A549, which corresponds to the toxicity data, and Pt uptake was higher in NSCLC cells when treated with NO-Si-DETA-cisplatin-AMS, compared to Si-DETA-cisplatin-AMS; however, differences in Pt uptake were not statistically significant.

Conclusions:
The NO-induced sensitization of tumor cell death demonstrates that NO is a promising enhancer of platinum-based lung cancer therapy, and our new therapy may be useful to enhance efficacy of Pt therapy in the clinic.

Sponsor
IRB/IACUC#
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 (surgery, radiation, and chemotherapy); this necessitates the development of more effective, less toxic therapies for diagnosed patients. Methylene blue (MB), a blue dye with noted medicinal applications, has received recent consideration as a potential neurotherapeutic due to its ability to infiltrate the blood-brain barrier (BBB), improve cellular processes within distinct brain cell compartments and types, and preferential accumulation in the brain. While MB displays these advantages, 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 submicron-sized nanoparticles (NPs) composed of the biodegradable/biocompatible co-polymer, poly(lactic-co-glycolic) acid (PLGA). Our lab, as well as others, have shown the application of PLGA NPs as potential cancer therapies, as well as their preferential accumulation in the brain, as a means to improve passive drug delivery. With this knowledge, our goal is to develop a MB-loaded PLGA NP capable of permeating the BBB in order to treat GBM, based on our hypothesis that encapsulation of MB into PLGA NPs will enhance accumulation in cancerous brain regions, resulting in reduced tumor size and prolonged survival.

In this study, we formulated and characterized MB-loaded PLGA NPs via particle size, surface charge, drug loading, and encapsulation efficiency. Additionally, we analyzed their in vitro effects to establish biological, and potentially therapeutic, activity. Following MB loading and comparison to blank NPs, we obtained preparations comparable to those published sized at 162.4nm, a surface charge of -31.7, and drug loading and encapsulation efficiency values of 2.2% and 29.2%, respectively. With this data, MBNPs were further analyzed and determined to produce a peak release at 24hrs. Additionally, in vitro cell death studies, MBNPs were found to induce cell death comparable to, if not better than, free MB, in GBM cell lines. Lastly, MBNP treatment enhanced cellular metabolism, an capability noted in free MB. We are currently completing additional studies on MBNPs’ effects in vitro, as well as establishing a protocol for a PK study.

In conclusion, our formulation displays MB’s therapeutic potential, displayed by its enhanced effectiveness in in vitro studies compared to free MB.

Tolfenamic Acid and Curcumin Analogs Effectively Inhibits Pancreatic Cancer Cell Growth

Tolfenamic Acid and Curcumin Analogs Effectively Inhibits Pancreatic Cancer Cell Growth

Background: Curcumin (Cur) is a natural phenol of the plant Curcuma longa that has been tested for anti-cancer activity in pre-clinical and clinical studies. The therapeutic efficacy of Cur is greatly impacted by its low bioavailability. Synthetic analogs of Cur are under testing to overcome this limitation. Cur analogs, EF31 and UBS109 have shown anti-cancer activity in colon and pancreatic cancers. Small molecule Tolfenamic acid (TA) is known to inhibit human cancer cells and tumor growth in mouse models for some human cancers. TA is known to target Specificity protein 1 (Sp1) transcription factor that mediates the expression of several genes associated with cancer including survivin, a key member of inhibitor of apoptosis proteins family.

Purpose: Combination treatments have been tested to address the issues related to efficacy and drug resistance. In this project, the anti-cancer activity of EF31 and UBS109 was tested in combination with TA.

Method: Human pancreatic cancer cells, L3.6pl and Mia PaCa-2 were grown in DMEM media with 5% fetal bovine serum. Cells were treated with DMSO (control) or EF31 or UBS109 or TA or EF31+TA or UBS109+TA and cell viability was measured at 48 hour post treatment using CellTiter-Glo (Promega) kit. The effect on apoptosis was assessed by determining the activity of caspase 3/7 (Caspase-Glo kit) and the expression of cleaved PARP (Western blot). The effect of individual and combination treatment(s) on the expression of Sp1 and survivin was evaluated by Western blot analysis.

Results: TA in combination with EF31 or UBS109 resulted in an induction of cell growth inhibition which is accompanied by increased caspase 3/7 activity and upregulation of PARP cleavage. The combination treatment(s) also showed a modulation in the expression of Sp1 and survivin.

Conclusions: TA combination with EF31 or UBS109 increases pancreatic cancer cell growth inhibition potentially by inducing the apoptotic pathways. When compared to TA, TA and Cur analog(s) is more effective in pancreatic cancer cells. These new combinations of anti-cancer molecules provide preliminary evidence for the therapeutic efficacy in treating pancreatic cancer.
Factors affecting awareness of Hepatitis B status among Bhutanese, Karen, Somali, and Central African Refugee populations in Tarrant County: Building Bridges Initiative (BBI)

Background: Hepatitis B Virus is reported to be the leading cause of liver cancer in the United States, and 90% are foreign born. The CDC recommends HBV screening for newly arrived refugees who have lived in countries with a high prevalence of chronic HBV infection. Nearly 14,000 refugees resettled in Texas in 2014. Currently, limited data is available on refugee awareness of HBV. This study aims to investigate what factors influence their awareness of HBV status.

Methods: Four community health workers conducted outreach and baseline assessments in their respective communities (i.e. Bhutanese, Burmese, Somali and Central African). Means, t-tests, and chi-square tests evaluated the influence of time in the US, education, and group on awareness of self-reported Hepatitis B status at baseline.

Results: Approximately 350 women have participated in BBI. 60% had heard of hepatitis B. Only 26% were aware of their Hepatitis B status. The bivariate analysis showed nearly half of the central African women were aware for their HBV status (47.3%) in comparison with associated with awareness of HBV status.

Conclusion: Majority (74%) of refugees are unaware of their Hepatitis B status. Time in the U.S., nor formal education influence HBV status awareness. However, awareness between regions shows that the differences within ethnic groups (traditions, health care beliefs) need to be considered. Refugee populations remain in need of culturally and linguistically appropriate cancer prevention programs.

Racial Disparities and Mortality Rates for Ovarian Cancer in Texas, 1999-2009

Background: Ovarian cancer is the leading cause of gynecological cancer-associated deaths, being the fifth most common of all cancer-associated deaths among women. Regional variation in mortality rates can be due to race and ethnicity, their distribution, varied reproductive patterns, tubal ligation, socioeconomic status, access to healthcare and diet. Other risk factors such as family history, early menarche, and late menopause, and nulliparity have also been identified.

Hypothesis and Objective: The hypotheses of this study are: 1. Race is a predictor of mortality rates for ovarian cancer. 2. There is a significant difference in demographics, socioeconomic status and ovarian cancer mortality rates between 1999 and 2009 years in the counties of Texas. 3. Access to health care, age, lack of insurance, and reproductive pattern, are significant geographic variables associated with ovarian cancer mortality in Texas. The objective is to test these hypotheses.

Materials and Methods: A cross-sectional study was conducted using the demographic and access to healthcare county level data obtained from the US Census Bureau 2000 and County Health Rankings and Roadmap website for the years 1999 and 2009 for women in Texas which were matched with the age-adjusted death rates (AADR) for the same periods obtained from the Texas Department of State Health Services and Texas State Data Center. Two sample t-tests were performed to evaluate the difference between the trends of 1999 and 2009. Correlation coefficient and multiple regression model analysis were performed to analyze the relationship between mortality rates and uninsured adults and between primary care provider rate (PPR) and socioeconomic status, respectively. Spatial analysis including mapping and hot spot analysis was also performed to find significant clusters.

Results: Income level, education, and poverty levels improved significantly from 1999 to 2009 in white women but not in blacks. The average family size of whites (2.86) was significantly less than blacks (3.28). The PPR was negatively correlated to the mortality rates. Low median household income in past 12 months was significantly related to AADR (p-value= 0.01). Eastern Texas showed consistently high AADR from 1999 to 2009. Hot spot analysis revealed very few significant clusters in central and north Texas.

Conclusion: Racial disparities and geographical factors can play an important role in predicting the disease outcome.
Evaluating reconstituted high density lipoprotein nanoparticles as target specific Doxorubicin carriers using fluorescence spectroscopy.

Doxorubicin, also known as Adriamycin, is an anthracycline antibiotic which first gained clinical prominence in the early 1970’s as an effective antitumor agent. It is still used today to treat a spectrum of cancers like lymphoma, bladder, stomach, lung, breast, ovarian, and several others. Due to its production of free radicals to attack tumor cells, Doxorubicin interferes with mitochondrial phosphorylation and also induces cardiotoxicity. Thus, efficient and biocompatible delivery methods are needed for targeted drug delivery to overcome systemic toxicity. To maintain a high level of growth, tumor cells overexpress Scavenger receptors type B-1 (SR-B1). This cellular characteristic can be used to target and selectively deliver doxorubicin to tumor cells by packing it in reconstituted high density lipoprotein (rHDL) nanoparticles, which bind selectively to SR-B1 receptors. Nanoparticles as target-specific drug delivery agents are increasingly used in cancer therapy to enhance bioavailability and to reduce off target toxicity of anti-cancer agents. Several different formulations of rHDL nanoparticles to incorporate doxorubicin were synthesized. Doxorubicin’s intrinsic fluorescence was used to photophysically characterize the properties of loaded rHDL nanoparticles including absorption, emission, excitation, steady-state and time resolved anisotropy measurements, and quenching to study drug shielding by nanoparticles. Overall the fluorescence properties of the rHDL: doxorubicin complex may reveal valuable novel characteristics of this drug delivery vehicle that may be particularly applicable when used in systemic (intravenous) therapy.

Sponsor
IRB/IACUC#
Fluorescence lifetime was used for fluorescence lifetime-based imaging of cancer. The intensity of the HA-ADOTA probe at 560 nm and 605 nm can be used as the sensing signal for detecting hyaluronidase. Recovery in the fluorescence lifetime imaging microscopy (FLIM) was also used to image hyaluronidase activity in cancer cells.

Results: The heavily ADOTA labeled hyaluronic acid (HA-ADOTA) has a red shift in the peak emission wavelength (605 nm), a weak fluorescence signal and a short fluorescence lifetime due to efficient self-quenching. In the presence of enzyme hyaluronidase, the brightness and fluorescence lifetime of the sample increases with a shift in the peak emission to its original wavelength at 560 nm. The ratio of the fluorescence intensity of the HA - ADOTA probe at 560 nm and 605 nm can be used as the sensing signal for detecting hyaluronidase. Recovery in the fluorescence lifetime was used for fluorescence lifetime-based imaging of cancer.

Conclusions: Our results show the ability of this the HA-ADOTA probe to detect activity/level of hyaluronidase in biological samples. Due to long fluorescence lifetime of the dye, it can be also be used to remove the background in cellular images. In future, this novel technology can be used to design a small device which can be used in primary care settings for the screening of cancer.

Sponsor UNTHSC intramural grant R16120 (R.F.), Sigma Xi grants in aid of research G20141015656984 (R.C.), UNTHSC pre-doctoral bridge grant R16171 (R.C.), NIH grant R01EB12003 (Z.G) and NSF grant CBET-1264608 (I.G).

IRB/IACUC# 2016-026
**Isolation and Characterization of a Group of TS-FK228 Analogues**

FK228 (Istodax/Romidepsin) is an FDA approved anticancer drug for the treatment of human cutaneous T-cell lymphoma and peripheral T-cell lymphoma via the inhibition of class I histone deacetylases (HDACs). Fermentation of Chromobacterium violaceum No. 968 is still the main preparation method for the large-scale production of FK228 for its research and clinical applications. Interestingly, we previously discovered the production of authentic FK228 by Burkholderia thailandensis MSMB43. During a pilot scale production of FK228 through the fermentation of B. thailandensis MSMB43, we unexpectedly isolated and purified one labile compound (thiosulfinate-FK228, TS-FK228, existed as isomers) which is structurally similar to FK228 but distinctive from their cytotoxic effects against tumor cells. Through LC-MS analysis and subsequent chemical synthesis of five TS-compounds from the prepared FK228 and FK228 analogues (thailandepsins, TDPs), we were able to prove that the oxidation of the disulfide bond in FK228 is derived from silica gel during the course of silica gel chromatography rather than through de novo biosynthesis by perspective bacterial strain. We showed that one of the TS-FK228 isomers has similar HDAC inhibitory activities with FK228, but has higher antiproliferative activities than FK228 against representative human cancer cell lines.

**In Vitro Study to Identify a Novel Combination Treatment for Ewing Sarcoma**

Introduction: Ewing sarcoma (ES) is an aggressive tumor that predominantly occurs in young adolescent populations. Chemotherapy used to treat ES is associated with long-term morbidity. The objective of this study was to identify an effective combination treatment option for treating ES. A fusion protein EWS-FLI1 is associated with >85% of ES incidences and mithramycin (Mit) is known to target this fusion protein and is currently in clinical trials. We investigated the combination of Mit to induce the efficacy of Doxorubicin (Dox), a widely used chemotherapeutic agent for treating ES patients.

Methods: ES cell lines CHLA9, CHLA10, and TC71 were cultured in laboratory and treated with increasing concentration of Mit or Dox. Cell viability was assessed using CellTiter-Glo luminescent assay at 48 hour post-treatment. Optimized doses for Mit and Dox were used for combination treatment. Western blot analysis was used to evaluate the apoptotic markers, caspase 3, cleaved PARP and Bcl2. Real-Time PCR was used to evaluate the expression of EWS-FL1 downstream targets. RNA was extracted using Trizol reagent (Invitrogen) and subjected to cDNA synthesis using Superscript III reverse transcriptase. PCR was carried out with cDNA using TaqMan primer-probes specific for ID2, LDB2, NROB1 and NCOR1.

Results: The results of current study illustrated that Mit or Dox treatment resulted in a dose and time dependent decrease in ES cell proliferation. Mit down-regulated the EWS-FL1 downstream targets (ID2, LDB2, NROB1 and RCOR1) in TC71 cells. Combination of Mit+Dox enhanced the anti-proliferative effect in ES cell lines which was accompanied by modulation of apoptotic markers.

Conclusion: This investigation provides evidence for the use of Mithramycin for enhancing the efficacy of chemotherapeutic agents. In vivo assays are underway to confirm in vitro results. These pre-clinical studies will have clinical implications for treating Ewing Sarcoma patients. The proposed combination to induce chemotherapy response is highly helpful since it can be tested to reducing chemotherapy dose(s) and addressing the issues related to side-effects.
Tolfenamic Acid Sensitizes Ewing Sarcoma Family Tumor Cells to Chemotherapy

Ewing sarcoma family tumor (EFT) is the second most prevalent bone and soft tissue tumor observed in children and young adolescents. Patients with metastatic disease have poor outcome with 5-year overall survival rate less than 30%. Current chemotherapeutic options are causing limited progress in the management of EFT. Our aim was to identify novel targets and less toxic agents to improve the efficacy of standard care offered to EFT patients. Specificity protein 1 (Sp1) transcription factor is known to be upregulated in various cancers and is frequently linked to poor prognosis. In this study, Tolfenamic acid, an inhibitor of Sp1 was tested to sensitize EFT cells to commonly used chemotherapeutic agent Vincristine (Vin). The effect of TA or Vin or TA+Vin on cell viability was evaluated by CellTitre-Glo assay and caspase 3/7 activity was measured by Caspase3/7 Glo assay. Western blot analysis was performed to determine the expression of Sp1, survivin, and cleaved-PARP. Apoptotic cell population was measured by Annexin V staining. Results showed a dose and time dependent decrease in cell viability with both agents while the combination of TA+Vin caused a significantly higher response as compared to individual treatments. This inhibition of cell viability was accompanied by the inhibition of Sp1 and survivin expression and an increase in the apoptotic markers i.e. Annexin-V positive cells, caspase 3/7 activity and the levels of c-PARP. Our results suggest that TA+Vin combination treatment provides an effective therapeutic strategy for the treatment of EFT.

Sponsor N/A
IRB/IACUC#
Racial Variation in Annexin A2 (AnxA2) Gene Expression and Poor Outcome in Triple-Negative Breast Cancer

Background: Triple-negative breast cancer (TNBC) is identified by the absence of three major receptors that drive most breast cancers and is a health disparity issue due to its disproportionate occurrence in African American (AA) women. Previous studies have identified elevated levels of AnxA2 in TNBC cell lines, but its association with racial variation and outcomes is unknown.

Methods: AnxA2 gene expression was evaluated in TNBC and non-TNBC cases from The Cancer Genome Atlas (TCGA) RNAseqV2 database. Associations between clinical outcomes and AnxA2 gene expression were tested in a genome wide association study of combined publicly available datasets.

Results: AnxA2 gene expression was elevated in TNBC in comparison to other breast cancer subtypes. Furthermore, AnxA2 gene expression is elevated in AA women and is associated with the disproportionate occurrence of TNBC. High expression levels of AnxA2 is associated with reduced overall survival (hazard =2.66; 95% confidence interval [CI] = 1.14 – 6.25, P = 0.0192), reduced relapse free survival (hazard = 1.45; 95% confidence interval [CI] = 1.12 – 1.89, P = 0.0051), and reduced distant metastasis free survival (hazard = 1.7; 95% confidence interval [CI] = 1.00 – 2.91, P = 0.048). AnxA2 gene expression was not associated with poor outcome in other subtypes, indicating the specificity of AnxA2 contribution to the aggressive behavior of TNBC.

Conclusion: AnxA2 overexpression is associated with racial variation and is a potential prognostic candidate for TNBC. AnxA2 has potential prognostic value, implicating a role for AnxA2 in the aggressive biology of TNBC in AA women.

Sponsor
This work was supported by the National Institute on Minority Health and Health Disparities Grant 1P20 MD006882.

IRB/IACUC# 2016-009

Colorectal cancer mortality is decreasing but not the average person-years of life loss: Findings from a population-based study

Purpose: Colorectal cancer death rate decreased by about 2 percent per year in the 1990s and this decline accelerated to about 3 percent per year during 2001 to 2010 in the US. The objective of this study was to investigate whether the average person-years of life loss (APYLL) has improved in a similar fashion over time. We also investigated the effects of cancer stage at diagnosis on person-years of life loss (PYLL) since it is one of the major factors that influences the survival of cancer patients.

Methods: A total of 509,738 patients diagnosed with only colorectal cancer in their lifetime in 1988-2012 were identified from the Surveillance, Epidemiology, and End Results (SEER) registries. We used life expectancy from the US population life table adjusted by year of death, sex, and race to estimate person-years of life loss. PYLL were calculated for 111,704 patients, who died during the follow up period due to colorectal cancer, by subtracting age at death from expected years of life at that age. To estimate the effect of early diagnosis on PYLL by controlling the effects of sex, race, and marital status, we have fitted a multiple linear regression.

Results: Average PYLL was 16.3 years and showed an increasing trend from 14.6 years in 1988 to 17.4 years in 2012. Effects of stage at diagnosis on PYLL by controlling the effects of sex, race, and marital status, we have fitted a multiple linear regression.

Results: Average PYLL was 16.3 years and showed an increasing trend from 14.6 years in 1988 to 17.4 years in 2012. Effects of stage at diagnosis on PYLL by controlling the effects of sex, race, and marital status, we have fitted a multiple linear regression.

Conclusion: Average person-years of life loss has been increasing steadily over the last two decades for colorectal cancer patients in the US. This increasing trend might be attributed to diagnosis at later stage and transition of the disease at younger age. It is evident from our study that early diagnosis might be one of the most effective ways to save person-years of life loss due to colorectal cancer.
Activation of a putative membrane androgen receptor increases the efficacy of the chemotherapeutic agent, temozolomide, in a human glioblastoma cell line

Glioblastoma Multiforme (GBM) is a form of brain cancer with very poor prognosis such that the life expectancy of a person with this disease is about one year after diagnosis. Moreover, current treatment regimens are only able to extend the life span by mere months. Based on recent studies from our lab that identified a putative membrane androgen receptor (mAR), which when activated is capable of promoting cell death, we investigated whether exploitation of this receptor could increase the efficacy of current chemotherapeutic agents to combat this deadly and invariably lethal cancer. Using the human glioblastoma cell lines, A172 and T98G, our studies have shown that activation of the mAR (using testosterone or dihydrotestosterone conjugated to bovine serum albumin) not only sensitized the glioblastoma cells to temozolomide (TMZ), the current standard chemotherapeutic agent for GBM, but also suppressed the phosphorylation of Akt, a known survival-promoting factor. Further, in T98G cells that express high levels of O6-methylguanine DNA methyltransferase (MGMT), a DNA repair protein, activation of the mAR suppressed the expression of MGMT. Our data also suggest that these mechanisms may not be mutually exclusive such that inhibition of Akt phosphorylation in and of itself led to a reduction in MGMT expression. Collectively, our data support the targeting of a putative membrane androgen receptor as complementary treatment for glioblastoma.

Sponsor: N/A
IRB/IACUC# 221

Bone Microenvironment Targeted Nanoparticles for Metastatic Prostate Cancer Treatment

The most common site of metastatic prostate cancer is the bone. These metastatic lesions are difficult to treat and often result in off target cytotoxicity from current chemotherapeutics. We hypothesize that targeted nanoparticles (NPs) designed to deliver chemotherapeutics to cancer lesions in the bone microenvironment could improve the side effect profile that results from non-discriminate action of cytotoxic agents. We have designed a novel targeted nanotherapeutic system to target the bone microenvironment in an effort to more efficiently delivery chemotherapeutics to the site of metastasis. The core of the NPs are composed of poly (D,L-lactic-co-glycolic acid) (PLGA) biodegradable polymer. The PLGA NPs have been loaded with the microtubule inhibitor, cabazitaxel. The surface of the NP has been conjugated with an amino-bisphosphonate, which has high affinity for the hydroxyapatite structure of the bone. NPs were formulated using a modified water in oil in water double emulsion solvent evaporation technique. The physiochemical properties of the NPs were characterized. Ex vivo bone binding studies were performed. Cell viability studies were performed on C4-2B and PC3 cell lines. NPs were also tested on 3D tumor spheroids. Finally, NPs were tested for efficacy in an intraosseous tumor model of metastatic prostate cancer in athymic nude male mice. NPs were made with favorable physiochemical characteristics: mean hydrodynamic diameter of 236.8 nm ± S.D. 1.19, mean polydispersity of 0.121 ± SEM 0.003, encapsulation efficiency of 57%, and drug loading of 3.74. Cellular cytotoxicity assay showed that C4-2B cells were more sensitive to the free cabazitaxel, the non-targeted NPs, and the targeted- NPs compared to PC-3 cells. We did not see an appreciable difference between the targeted-NPs and equivalent treatment of free cabazitaxel in 3D assays. In vivo analysis showed that both the non-targeted and targeted-NPs were more effective than free cabazitaxel at reducing tumor burden. Additionally, targeted-NPs improved bone morphology at tumor lesions.

In this project we have engineered a bone targeted NP formulation for metastatic prostate cancer. We have determined the chemical and physical characteristics of this system and tested the in vitro cytotoxicity. Finally, we have shown the efficacy of these targeted-NPs in an intraosseous model of bone metastatic prostate cancer.

Sponsor: American Medical Association/ American Urological Association
IRB/IACUC# 2014/15-18-A04
Angiotensin II (Ang II) has long been known to stimulate thirst by both its action peripherally as a circulating hormone, and centrally acting as a peptide neurotransmitter. Peripherally circulating Ang II can elicit thirst by stimulating the Subfornical Organ (SFO), which in turn stimulates other hypothalamic nuclei regulating blood volume homeostasis such as the Median Preoptic Nucleus (MnPO) and Paraventricular Nucleus presumably through Ang II signaling. These hypothalamic nuclei then activate higher cognitive centers resulting in thirst. Central Ang II administered via intracerebroventricular (ICV) infusion also induces thirst by directly stimulating regions such as the MnPO through the Angiotensin Type 1 receptor and following a similar signaling pathway as peripheral Ang II only ignoring the circumventricular organs.

Methods
Male Sprague-Dawley rats are microinjected in the MnPO with either a virus to knockdown AT1aR expression (shAT1a) or a scramble virus (SCR) and instrumented with radio telemetry a week later. Our lab microinjected an adeno-associated virus with short hairpin RNA matched to the Angiotensin Type 1a receptor (AT1aR) into the MnPO to test whether Ang II was necessary for thirst signaling in the MnPO. We hypothesized that Ang II was necessary for the thirst response to peripherally circulating Ang II as well as ICV injected central Ang II. Sprague Dawley rats were separated into subcutaneous (SC) and ICV administration groups. The SC group was pretested for their drinking response to 2mg/kg Ang II, and those animals that drank in response to the SC Ang II administration were utilized in the study. All animals were injected with the shAT1aR virus on Day 0, and were allowed to recover before drinking tests on day 14 and day 18. ICV animals were microinjected with the virus on Day 0 as well and instrumented with a chronic lateral ventricle cannula. These animals were administered 2ng Ang II in 1ul aCSF.

Results
Unexpectedly, we found that knockdown of AT1aR in the MnPO did not reduce drinking in the subcutaneous animals (P>0.05), but did significantly reduce drinking in the ICV animals (P

Conclusions
Peripheral generation of thirst through Ang II may be predominantly mediated through glutamatergic neurotransmission from the SFO which only uses Ang II as a co-transmitter. Mechanistic understanding of thirst generation in the hypothalamus is critical for pharmacological manipulation with currently available pharmaceuticals as well as for development of future compounds.
Contractile Differences In Left And Right Ventricles Of Healthy Human Hearts

Left ventricle (LV) and right ventricle (RV) differ in embryology, structure and function. Left ventricle originates from the primary heart field while right ventricle originates from the secondary heart field. The two heart fields express different sets of transcription factors and signaling molecules. At the molecular level, the gene expression in response to the pressure loading and failure is different in both ventricles. They also exhibit differences in response to adrenergic stimulation. Adrenergic agonist increase LV contractility but RV contractility may be reduced. Although numerous studies have been performed at macroscopic (whole organ) level previously, none (to my knowledge) address the differences at a mesoscopic level, where only a few molecules are investigated. This becomes important, as in macroscopic studies there may be differences due to basic fiber structures, differences in orientation of fibers as well as molecular crowding. These differences were investigated at the level of few molecules by sparsely labeling the myosin lever arm with SeTau 647 Maleimide. The kinetics and steady-state distribution of cross-bridges were examined in ex-vivo myofibrils isolated from the ventricles of human non-failing and failing hearts and differences were compared in LV and RV. We show that the kinetics and the steady-state distribution of orientations of myosin were different in contracting LV and RV of the non-failing human heart. In contrast, kinetics and the steady-state distribution of myosin in the failing hearts were the same. These results suggest that there is a difference in the way actin interacts with myosin cross-bridges in ventricles of non-failing hearts. We compare the clinical parameters of the failing heart with the kinetics and the distribution of the non-failing heart, and suggest molecular effectors of the function of myosin.

Sponsor
IRB/IACUC# UKY 08-0338-F2L
Occlusive arterial disease (OAD) refers to the pathological obstruction of arteries that become progressively narrowed over time and are eventually blocked due to various risk factors, such as hypertension, diabetes, and atherosclerosis. This chronic arterial damage results from vascular wall remodeling, leading to neointima formation. Store-operated Ca2+ channels (SOCs) and entry (SOCE) play a central role in the vascular smooth muscle cell (VSMC) phenotypic change from contractile to migratory and proliferative states. In the present work, we ask if Homer is a critical molecular component of VSMC SOCE and does Homer mediate VSMC migration/proliferation and neointima formation. Homer binds to transient receptor potential canonical (TRPC) channels and is required for gating of TRPCs, while stromal interacting molecule1 (STIM1) binds to and regulates TRPC and Orai channels as SOCs. We cultured rat aortic VSMCs to increase their SOCE and migration/proliferation, as seen in OAD. Studies were done using small-interfering RNA (siRNA) targeting Homer1, STIM1, and TRPCs. Scratch wound migration assays were performed, and VSMC proliferation was assessed by cell count. In our in vivo OAD model (rat carotid artery balloon injury), the arteries were treated with adeno-associated virus (AAV) encoding short-hairpin RNA (shRNA) targeting Homer1. We found that Homer1 protein expression levels increase in balloon-injured vs. intact VSMCs, similar to known increases in protein expression levels of STIM1, Orai1, and TRPCs. Furthermore, we show that Homer1 binds to Orai1 and that interactions between Homer1 & Orai1/TRPCs and between STIM1 & Orai1/TRPCs markedly increase in injured vs. intact VSMCs. Cultured VSMCs treated with siHomer1 exhibit significant reduction in SOCE (56 ± 4.0%) vs. control (scrambled siRNA), similar to the SOCE reduction seen in siSTIM1-/siTRPC-treated cells. SiHomer1-treated cells also migrate significantly less over the wound surface area (73.3 ± 5.9%), and proliferate significantly less (73.3 ± 4.2%) vs. control, similar to observations seen in siSTIM1-/siTRPC-treated cells. Finally, immunofluorescence staining shows that the increased Homer1, STIM1, and Orai1 protein expression levels are localized in the neointima of the injured carotid artery. Knockdown of Homer1 using AAV-shHomer1 reduces this neointima. These studies provide evidence that Homer is a critical component of VSMC SOCE and neointima formation.

Sponsor: NHLBI-NIH
IRB/IACUC# 2012/13-46-A05

Is Testosterone a Risk Factor for Ischemic Stroke and Neurodegeneration in Men?

In the aging population, cardiovascular disease (i.e. stroke) is a common cause of mortality that affects 1 in 3 men. An ischemic event is characterized by oxidative stress (OS) and neuroinflammation. Testosterone is an oxidative stressor, which can be protective or detrimental depending on the environment. In aging males that have high levels of OS, testosterone can increase the risk for ischemic stroke. However, it is unknown if testosterone-induced OS can increase inflammation, such as COX2, a prominent mediator of neuroinflammation and oxidative stress, leading to neuronal death. Therefore, we hypothesize that testosterone, under OS conditions, will further increase OS, induce COX2 inflammation, and increase apoptosis. To test this hypothesis, we exposed a neuronal cell line (N27 cells) to a sublethal concentration of the pro-oxidant, tert-butyl hydrogen peroxide (H2O2) for 24 hours followed by the exposure to physiological levels of testosterone to assess oxidative stress and inflammatory signaling. In addition, N27 cells were exposed to ibuprofen prior to OS (H2O2) and hormone (testosterone) treatment. Under OS conditions, testosterone increased COX2 signaling and apoptosis in neurons. Further, ibuprofen attenuated the effects of testosterone in an OS environment. Our data shows testosterone promotes COX2 inflammation, which contributes to neurodegeneration in an OS environment. Notably, ibuprofen is a common and inexpensive over the counter anti-inflammatory therapeutic. Thus, ibuprofen may be a preventative intervention against ischemic events and neurodegeneration.

Sponsor: Texas Garvey Foundation and NIH T32 AG020494
IRB/IACUC#
Results:

Accentuated Antagonism in Cold Induced Sympathetic Activation

Title: Accentuated Antagonism in Cold Induced Sympathetic Activation

Introduction:

Accentuated antagonism (AA) is a physiological phenomenon where sympathetic nerve activity (SNA) potentiates the action of the vagus nerve on heart rate slowing. This concept has been thoroughly investigated in animals but has not sufficiently been studied in humans. Exploring AA has significant public health relevance because in states when SNA is high, any given activation of the vagus may slow heart rate to a dangerous degree. Therefore, giving cardio-selective sympathetic blocking agents may have significant clinical utility in these settings. Hence, we hypothesize that R-R interval (RRI) will be higher when background SNA is high during 4 degree Celsius cold pressor test (CPT) compared to a room temperature control, and that this difference will be mitigated by giving intravenous metoprolol.

Methods

4 healthy human subjects were recruited and informed consent was obtained according to the Declaration of Helsinki. Subjects first underwent baseline -60 mm Hg neck suctions to stimulate vagal nerve-mediated heart rate slowing through the baroreflex. These suctions were repeated after submersion of the hand at wrist level in 4°C water and then 23°C water. These conditions were repeated with infusion of 10 mL saline placebo and up to 10 mg of intravenous metoprolol. We were able to differentiate between the vagal and sympathetic effects on the heart by either infusing saline or blocking the SNA with metoprolol at both temperatures.

Results:

In comparison of the placebo group with the Metoprolol group in 25°C water, we did not see a significant different in the RR interval (Difference of Means=-58.007 milliseconds; P=0.344). In addition we did not see a statistical difference when comparing the RR interval of the placebo group with the Metoprolol group in 4°C water (Difference of Means=-72.073 milliseconds; P=0.247). However, there are significant trends within the data that deserve further study.

Conclusions:

We believe the lack in statistical significance of the data presented is due to the small number of participants in the study. This study warrants further elucidation of the concept of accentuated antagonism in human subjects.

Sponsor: N/A

IRB/IACUC# 2015-090
Energy Expenditure and Substrate Utilization with Intermittent Blood Flow Restriction Aerobic Exercise

Blood flow restriction (BFR) training is characterized by the use of compressive occlusive devices proximal to the active muscle during exercise. We hypothesized that an acute bout of aerobic BFR exercise would result in equivalent caloric expenditure and substrate utilization when compared with conventional aerobic exercise (CE). Six human volunteers (3M/3F; age, 30.2±2.6 years; BMI, 23.9±1.0 kg/m²) performed 40-min of treadmill exercise at 65-70% of maximal heart rate (HR) with and without intermittent BFR (220 mmHg thigh cuff pressure applied over 4x5-min intervals followed by 5-min reperfusion periods). HR and metabolic parameters were measured and analyzed in 5-min time blocks. Oxygen consumption (VO₂) and CO₂ production (VCO₂) were used to calculate caloric expenditure between conditions, and the respiratory exchange ratio (RER) was used as an index of substrate utilization. Treadmill speed remained constant at 2.5 mph, while treadmill incline (%) was modified to elicit the target HR response. Treadmill incline was subsequently assessed to determine the absolute intensity of the exercise bouts. VO₂ and VCO₂ increased at the onset of exercise in both conditions (p2 and VCO₂ versus the BFR condition for minutes 10-40 of the exercise bout (p≤0.05 for VO₂, p≤0.09 for VCO₂). Additionally, a lower treadmill incline (%) was required to elicit the target HR response for BFR exercise compared to CE from minutes 10-40 (Range: 4.0-5.0 % for BFR vs. 5.5-6.6% for CE, ps0.025). There was no difference in overall caloric expenditure (230.3±22.8 kcal for CE vs. 204.3±22.5 kcal for BFR, P=0.44) or RER (0.87±0.01 for CE vs. 0.88±0.01 for BFR, P=0.55) between conditions. These findings suggest that aerobic exercise with intermittent BFR results in similar caloric expenditure and fuel utilization as CE. Aerobic exercise with BFR could be used as an alternative exercise modality for individuals who cannot exercise at the same absolute workloads as healthy individuals, such as those with musculoskeletal limitations.

Sponsor NIH T32 Fellowship (Sprick), UNTHSC Faculty Research Pilot Grant (Rickards)

Cardioprotective Intermittent Hypoxia Conditioning Induces Glyoxalase-1 in Rat Left Ventricle

Intermittent, normobaric hypoxia (IH) conditioning provides significant cardioprotection, including dramatically increasing myocardial resistance to ischemia-reperfusion. The cardioprotective mechanisms of IH are unknown. Myocardial ischemia-reperfusion generates methylglyoxal, a potent and toxic glycaating agent. Our previous studies demonstrated that reactive oxygen species (ROS) generated during IH cycles contribute to cardioprotection. We hypothesize that the generation of ROS during IH cycles induce the transcription factor Nrf2 to activate expression of genes encoding cytoprotective proteins. Here we evaluated IH induction of glyoxylase 1 (GLO-1), a major enzyme responsible for methylglyoxal detoxification. Sprague-Dawley rats were conditioned by a 20 day IH program consisting of 5-8 daily, 5-10 min cycles of hypoxia (9.5-10% inspired O₂) with intervening 4 min room air exposures, previously shown to produce robust cardioprotection. Control rats were sham-conditioned using 21% O₂. After completion of the conditioning protocol, the left ventricle was isolated and extracted for enzyme analysis. The activities of cytoprotective enzymes were analyzed by spectrophotometric assays. GLO-1 activity (U/mg protein) increased threefold in IH conditioned (1.05±0.16) vs. sham (0.35±0.11) rats. Glutathione reductase activity (U/mg protein) was unchanged between IH conditioned (0.015±0.0047) vs. sham rats (0.023±0.016). IH augmentation of the anti-glycation enzyme GLO-1 may contribute to the heart’s increased resistance to ischemic injury.

Sponsor NIH T32 Fellowship (Sprick), UNTHSC Faculty Research Pilot Grant (Rickards)
Changes in Gut Hormones in Relation to Cardiovascular Risk Factors One Year After Laparoscopic Gastric Banding Surgery

Title: Changes in Gut Hormones in Relation to Cardiovascular Risk Factors One Year After Laparoscopic Gastric Banding Surgery

Purpose: Obesity rates in the United States continue to rise at an alarming rate, imposing increasingly large health burdens such as cardiovascular disease and diabetes among others. Existing research on gastric bypass surgery has shown that improved gut hormone levels post-surgery are partially responsible for drastic improvements in cardiovascular health. However, similar research studying this effect in laparoscopic gastric banding surgery (LBS) is lacking. The purpose of the current study is to determine whether LBS delivers normalization of gut hormones, specifically ghrelin and GLP-1 and whether that normalization could explain improvements in cardiovascular (CV) indicators of health.

Methods: A secondary data analysis was conducted on data from a 1-year prospective study in a community bariatric surgical setting. Bariatric laparoscopic gastric banding surgery (LBS) is lacking. The purpose of the current study is to determine whether LBS delivers normalization of gut hormones, specifically ghrelin and GLP-1 as well as ApoB. Increased GLP-1 levels appear particularly related to plasma levels of lipoprotein (a) as well as ApoB which could be an indicator of GLP-1 playing an important role in lipid metabolism.

Results: The partial correlations of change scores showed that increased levels of postprandial GLP-1 correlated with a reduction in Lipo-a plasma levels (r= -0.752, p<.012). The results also showed that increased levels in fasting GLP-1 correlated with a decrease in levels of ApoB in plasma (r= -.686, p<.028).

Conclusion: Improvements in secretion patterns 12 months after LBS appears to have a significant relationship to changes in CV risk factors such as Lipoprotein (a) and ApoB. Increased GLP-1 levels appear particularly related to plasma levels of lipoprotein (a) as well as ApoB which could be an indicator of GLP-1 playing an important role in lipid metabolism.
Renal injury in the form of albuminuria (albumin excretion rate; μg/day) was increased in SLE mice compared to controls (4409±2519 vs. 4 ± 1; n=1–2/group) and had higher renal blood flow (3.0 vs. 2.5±0.1mL/min*g; n=1–2/group) and lower renal vascular resistance (21.9 vs. 23.9±1mmHg*min*g/mL; p=0.002; n =3–6/group). Albumin excretion rate was diminished in CNI-1493-treated SLE mice (420±410; p = 0.008). CNI-1493–treated SLE mice had higher renal blood flow (3.0 vs. 2.5±0.1mL/min*g; n=1–2/group) and lower renal vascular resistance (21.9 vs. 23.9±1mmHg*min*g/mL; n=1–2/group) compared to SLE mice treated with saline.

Conclusion:
These data suggest that stimulation of the vagus nerve may protect the kidney and prevent SLE hypertension; however, future studies are warranted to determine how this occurs. Taken together, our findings suggest that the vagally-mediated cholinergic anti-inflammatory pathway plays a mechanistic role in the development hypertension in the setting of chronic inflammation.

Sponsor  American Heart Association
IRB/IACUC#  2013/14-41-A04.

The Melody transcatheter pulmonary valve has been implanted successfully worldwide since its first implant in 2000. The vast majority of these valves have been implanted in pulmonary homografts. Due to surgeon preference, the most common valve used for pulmonary valve replacement at Cook Children’s is the Medtronic Freestyle stentless porcine aortic heterograft. According to review of the literature and personal contact with representatives at Medtronic, we have the largest cohort of patients with Melody implants within this type of bioprosthetic valve.

Retrospective chart review was performed. Between June 2012 and June 2015, 28 Melody valves were implanted; nineteen were placed within the Freestyle valve. The primary indication was pulmonary stenosis in 15 patients, pulmonary insufficiency in 1, and mixed stenosis and insufficiency in 3. All patients had procedural success. Mean right ventricular pressure decreased from 61.7 to 35.6 mmHg. Mean pulmonary valve gradient decreased from 38.1 to 10 mmHg. Mean degree of pulmonary insufficiency (rated 0-4) decreased from 2.3 to 0.7. Two minor procedural adverse events occurred. Three patients had some degree of elevated right ventricular pressure without significant gradient across the Melody valve (two due to moderate peripheral branch pulmonary artery stenosis and one due to pulmonary hypertension, likely secondary to obesity and obstructive sleep apnea). On follow up (2 months to 3 years), Melody valve function has been preserved and no reinterventions have been necessary.

The Melody valve can be implanted successfully within a stentless aortic bioprosthesis with good short- and mid-term longevity.

Sponsor  N/A
IRB/IACUC#  CCMC 2015-022
Changes In TRPV4 Channel Function In Vasopressin Neurons Of Rats With Hepatic Cirrhosis

Purpose: Dilutional hyponatremia associated with cardiac and hepatic failure negatively impacts morbidity and mortality of both diseases. Hyponatremia is a consequence of the dysregulation of vasopressin release but is not completely understood. In an animal model of liver failure, the membrane expression of transient receptor potential vanilloid 4 (TRPV4) channels increased in vasopressin-releasing neurons of the hypothalamus. Our hypothesis was that activation of TRPV4 channels with the specific agonist GSK 1019790A produces greater calcium influx in supraoptic nucleus (SON) vasopressin neurons collected from hyponatremic rats with liver failure induced by bile duct ligation surgery or to sham operated controls.

Methods: Adult male Sprague-Dawley rats received bile duct ligation surgery or sham ligation surgery. After two weeks, all rats were anesthetized and injected in the SON with an adeno-associated viral 2 (AAV2) vector containing a construct for green fluorescent protein (GFP) driven by a vasopressin-specific promoter. Two weeks later, the rats were anesthetized and the SONs isolated and cultured for Fura-2 ratiometric calcium imaging. Initial experiments had the cultured cells sit overnight prior to imaging; subsequent experiments imaged cells on the same day as their isolation and culturing. SON cells were tested for changes in intracellular calcium produced by the specific TRPV4 agonist GSK 1019790A (20-200 nM). Cells were also tested for its response to a calcium ionophore. In some experiments, data were collected GFP positive (vasopressin) cells. Normalized ratio responses were tested by ANOVA.

Results: In these studies using cells cultured for 24-48 hours, 1.5 nM GSK significantly increased calcium influx in GFP-positive cells from sham rats but not from BDL rats (Sham 1.53 ± 0.1, BDL 1.14 ± 0.1, P=0.03) of SLE mice compared to controls. CNI-1493 (8 mg/kg/2swk, IP) or vehicle (saline) was administered twice a week for 4 weeks, starting at 30 weeks of age in female SLE (NZBWF1) and control mice (NZW). At 34 weeks, animals were euthanized and tissues were collected in order to examine splenic and renal inflammation. The spleen and kidney were homogenized using RIPA buffer and the cytokine TNF-a was evaluated using Western blot in these tissues.

Conclusions (d): Although the results did not support our hypothesis, the data are preliminary and we suspect additional studies are needed to determine the ability of pharmacological stimulation of the vagus nerve to reduce inflammation in SLE mice. Such therapy could potentially benefit hypertensive SLE patients, since chronic inflammation has recently been linked to the development of the disease.
Effect of Pain on Cardiac Twist Mechanics: A Preliminary Study

Introduction: The sympathetic nervous system (SNS) is known to respond to various stresses that the body encounters. Stimulation of the SNS is associated with increases in heart rate, blood pressure, myocardial contractility and work of the heart. While it is universally accepted that pain causes excitation of the SNS, the relationship between the two is not completely understood due to its complicated nature. Moreover, in patients with impaired pump function, pain may further compromise pump function of the heart, yet this has not been previously investigated. As a preliminary study, we hypothesized that acute pain will increase the demand of the pump, and hence decrease myocardial strain indices, with a resultant increase in myocardial stiffness in healthy subjects.

Methods: IRB approval was obtained and each subject gave informed consent according to the Declaration of Helsinki. Each subject (N=3) underwent a standard medical history and physical prior to participation. Subjects each completed two cold pressor stimuli (CPS) by submerging a hand in two different water temperatures (4°C, and 16°C) in duplicate for a total of 4 CPS exposures. After the subject’s hand had been submerged for one minute, echocardiographic measurements were recorded. Images taken during this time included a 4-chamber, 2-chamber, and AP long axis view. A period of 20 minutes between each test was allotted to allow the subject’s physiologic variables to return to baseline values. After completion of each study, echocardiographic data, including strain and strain rate was analyzed to calculate cardiac strain indices.

Results: It was found that the 4°C CPS was associated with a decreased in cardiac strain (5% change in strain from baseline), correlating with values. After completion of each study, echocardiographic data, including strain and strain rate was analyzed to calculate cardiac strain indices. and AP long axis view. A period of 20 minutes between each test was allotted to allow the subject’s physiologic variables to return to baseline values. After completion of each study, echocardiographic data, including strain and strain rate was analyzed to calculate cardiac strain indices. and AP long axis view. A period of 20 minutes between each test was allotted to allow the subject’s physiologic variables to return to baseline values. After completion of each study, echocardiographic data, including strain and strain rate was analyzed to calculate cardiac strain indices.

Conclusions: These preliminary results suggest that perceived acute pain is at least partially responsible for increasing myocardial wall stiffness, as evidenced by cardiac strain indices. This study will be continued to fully address the hypotheses and eventually be implemented in a patient population to determine whether the effects are more significant in a diseased heart.

Sponsor N/A
IRB/IACUC# 2013-078

Role of Chronic Intermittent Hypoxia and Hypercapnia Induced Hypertension in Regulation of Blood Pressure

Role of Chronic Intermittent Hypoxia and Hypercapnia Induced Hypertension in Regulation of Blood Pressure

Purpose
Sleep apnea is a prevalent disease characterized by momentary cessations in respiration leading to sustained hypertension. The hypertension experienced can be mimicked by periodic decreases in oxygen or chronic intermittent hypoxia (CIH) in humans and animal models. More recently, CIH has been combined with hypercapnia (CIH-H) to determine if an increase in circulating carbon dioxide, which is also experienced by patients that suffer from sleep apnea, contributes to neural adaptations related to sustained hypertension. CIH has been shown to have a significant effect on increased blood pressure due to increased sympathetic outflow from initiation and maintenance of hypertension. However, it is not known if the additional hypercapnic component significantly affects blood pressure or central autonomic control.

Methods
Male Sprague-Dawley rats are instrumented with radio telemetry one week after arrival. The radio telemetry provides information regarding cardiovascular variables continuously over a specified period of time. Animals were monitored for recovery for one week and then acclimated to the CIH or CIH-H rooms for 6 days, and monitored during this period for baseline data before experiencing 7 days of CIH, CIH-H or normoxic conditions. The CIH exposure is applied for 8 hours during the light (nocturnal) period from 8:00 AM to 4:00 PM, during which time hypoxia is produced using 3 min on-3 min off cycles that reduces oxygen from 21% to 10% to then being flushed with room air, so the inspired oxygen rises back to 21% before the cycle repeats. During CIH-H, rats are exposed to the same conditions with the addition of carbon dioxide that is raised from 0% to 8% during hypoxia to also produce hypercapnia.

Results
Rodents exposed to hypoxic and hypercapnic conditions did exhibit a greater increase in blood pressure than rodents exposed to only hypoxic conditions in the light period. The difference was not sustained during the return to normoxic conditions.

Conclusions
The results are consistent with previous studies which showed periods where there were greater increases in blood pressure in CIH-H animals than those exposed to hypoxia alone. Both CIH and CIH-H produced a greater increase in blood pressure during the light period. The difference did not appear to be sustained when rats were breathing room air.

Sponsor P01 HL088052
IRB/IACUC# 2014/15-28
Cytoprotective and Anti-Glycation Defenses in Porcine Brain after Cardiac Arrest and Cardiocerebral Resuscitation

Cardiac arrest (CA) is often lethal, and survivors often face sequelae that greatly impact quality of life due to brain injury inflicted by ischemia-reperfusion. Effective cardiocerebral resuscitation (CCR) is essential for survival and recovery from CA. The complexity of the injury cascades ignited by CA and the presence of the blood-brain barrier challenge the development of pharmacological interventions to protect the brain. Our goal is to identify a blood-brain barrier-permeable intervention that mitigates CA-induced brain damage and, thus, fosters neurological recovery. Pyruvate, a cellular metabolite, energy substrate and antioxidant, has been found to be neuroprotective in a rat stroke model via induction of the cytoprotective cytokine erythropoietin (EPO).

Hypothesis: Pyruvate treatment during CCR and post resuscitation decreases brain injury by upregulating cellular defense mechanisms including hypoxia inducible factor-1α (HIF-1α), EPO, the product of HIF-1α’s gene program, and glyoxalase-1, the principal component of the brain’s defenses against the powerful glycat ing agent and glycolytic byproduct, methylglyoxal.

Methods: Yorkshire swine (25-35 kg, both genders) were subjected to sham protocol (n = 6) or pacing-induced CA (n = 12). CCR was administered by precordial chest compressions (100/min) at 10-14 min CA, and transthoracic countershocks were applied to restore sinus rhythm. NaCl (n = 6) or Na-pyruvate (n = 6) was infused iv (0.1 mmol/kg/min) during CCR and the first 60 min recovery. At 4 h recovery, brain was cross-perfused with 0.9% NaCl, and then brain biopsies were freeze-clamped for biochemical analysis or fixed in 10% formalin for immunohistochemistry. Results: In hippocampus, activity of the oxyradical-sensitive TCA cycle enzyme aconitase fell by 50% (P < 0.05) during CA + CPR with NaCl and Na-pyruvate treatment, while no appreciable difference was detected in the cerebellum. There were no statistically significant differences in HIF-1α or EPO contents in the hippocampus among the sham and CA groups. Similar trends were observed in the cerebellum except for EPO content, which fell by 40% (PConclusion: Cardiac arrest inactivates aconitase and depletes cytoprotective EPO in ischemia-sensitive brain regions. Although pyruvate intervention during CPR and the initial 60 min recovery did not produce sustained protection or upregulation of aconitase or EPO, it produced robust augmentation of glyoxalase-1, thereby bolstering the brain’s defenses against the glycat ing metabolite methylglyoxal.

Sponsor NINDS Support: NS076975
IRB/IACUC# 2012/13-29-A10
Low-dose Aspirin During Gestation Promotes Vascular Dysfunction and does not Ameliorate Maternal Hypertension in Rats Exposed to Innate Immune System Activation

Background: Daily low-dose aspirin after 12 weeks of gestation is recommended as a preventive intervention for women at high risk for preeclampsia, a hypertensive disorder of pregnancy with high rates of maternal and fetal mortality and morbidity. Activation of the innate immune system during pregnancy is implicated in the development of preeclampsia. Maternal exposure to synthetic CpG oligonucleotides (CpG ODN, specific ligand of the innate immune receptor Toll-like receptor 9) induces maternal hypertension, vascular dysfunction, and upregulation of cyclooxygenase enzymes in pregnant rats. Hypothesis: We hypothesized that maternal treatment with low-dose aspirin during gestation would ameliorate TLR9-induced hypertension and vascular dysfunction in pregnant rats. Methods: Pregnant Sprague-Dawley rats were treated with a synthetic CpG ODN (ODN2395) or vehicle on gestational day (GD) 14, 16, and 18. Aspirin treatment (or control) started on GD10 and continued throughout gestation for all groups [control (no treatment), ODN2395 (300 μg), aspirin (1.5 mg/kgBW), aspirin+ODN2395]. Blood pressure was measured on GD19 using the tail cuff method and mesenteric resistance artery (MES) function was assessed on GD21 using wire myography. Results: ODN2395-treated rats had higher blood pressure on GD19 compared to vehicle-treated dams and aspirin did not ameliorate ODN2395-induced hypertension (control: 97 ± 0.4 mmHg, ODN2395: 121 ± 7 mmHg, aspirin: 101 ± 5 mmHg, aspirin+ODN2395: 121 ± 7 mmHg, p<0.05). Aspirin treatment increased MES sensitivity to PE (pEC50, ODN2395: 5.6 ± 0.1 vs. aspirin+ODN2395: 5.9 ± 0.1, ppEC50, ODN2395: 7.6 ± 0.1 vs. aspirin+ODN2395: 7.0 ± 0.1. pConclusion: Treatment with low-dose aspirin throughout gestation did not prevent the development of TLR9-induced maternal hypertension, augmented vascular sensitivity to α1-adrenergic receptor activation and attenuated endothelium-dependent dilation in rats exposed to innate immune system activation. The use of aspirin during gestation should be considered with caution in clinical cases associated with innate immune system-induced pregnancy complications.

Sponsor American Heart Association

IRB/IACUC# 2013/14-40-A05

Uterine Perivascular Adipose Tissue Potentiates Contractile Responses in Uterine Arteries from Pregnant rats

Background: Perivascular adipose tissue (PVAT) is the fourth and outer layer of the vascular wall. PVAT has vasoactive effects, mostly via paracrine actions. The effects of PVAT vary with anatomic location; PVAT has anti-contractile effects in peripheral vascular beds in animals and in humans but it potentiates contractions in coronary vascular smooth muscle. Pregnancy is characterized by adipose tissue expansion as well as structural and functional changes in the uterine vasculature. However, the effects of PVAT on uterine artery reactivity during pregnancy are not understood.

Hypothesis: We hypothesized that uterine PVAT has a functional role in uterine artery contractile and dilatory responses and this role is modified by pregnancy.

Methods: Pregnant Sprague-Dawley rats were sacrificed on gestational day 16 (term=21-22 days). Uterine arteries and their surrounding PVAT were harvested and cleaned for study. Concentration response curves (CRCs) to potassium chloride (KCl, 4.7 – 80 mM) and phenylephrine (PE, 10-9 – 3x10-5 M) were performed using wire myography. CRCs were performed in the presence and absence of the surrounding PVAT (0.1 g) or PVAT-conditioned media. Arteries were incubated with PVAT or PVAT-conditioned media for 30 minutes. To make the media, we incubated 0.4 g of PVAT in 15 ml physiological salt solution for 90 min (37°C - 5% CO2, 95% O2).

Results: Uterine arteries incubated with PVAT (+PVAT) had greater contractile responses to KCl compared to control vessels [KCl (30 mM), control: 4.0 ± 0.81 mN vs. +PVAT: 14.7 ± 1.68 mN; KCl (40 mM), control: 14.4 ± 0.68 mN vs. +PVAT: 19.6 ± 0.88 mN, p50, control: 6.0 ± 0.08 vs. +PVAT: 6.3 ± 0.10, p50), control: 6.1 ± 0.08 vs. +PVAT-media: 6.4 ± 0.10, p<0.07].

Conclusions: Our data show that uterine PVAT has a pro-contractive effect on uterine arteries from pregnant rats. We propose that uterine PVAT provides signaling from the outer layer to the inner layers of the vascular wall that determines uteroplacental vascular adaptations to pregnancy.

Sponsor N/A

IRB/IACUC# 2013/14-40-A05
A Vital role for Median Preoptic AT1a Receptors in the Sustained Hypertension of Chronic Intermittent Hypoxia

Purpose
The hypoxemia from Sleep Apnea (SA) results in hypertension during both the hypoxic sleeping period and the normoxic waking period. This pathophysiological sustained hypertension persists during waking hours and is a source of numerous cardiovascular sequelae. In order to better understand the neurological changes that underlie this disease state, our lab utilizes Chronic Intermittent Hypoxia (CIH) to model the hypoxemia and generate the hypertension of SA sufferers. Previously, our lab has shown that the Median Preoptic Nucleus increases in both neuronal activity and Angiotensin Type 1a Receptor (AT1aR) RNA expression in response to CIH. The MnPO is situated in a critical location that allows it to receive inputs from nuclei outside of the blood brain barrier and provide inputs to regions that control sympathetic outflow, and therefore blood pressure. The ability to modulate sympathetics based upon peripheral inputs coupled with increased activity and AT1aR expression leads us to hypothesize that increased Angiotensin signaling to the MnPO is essential for the sustained component of hypertension from CIH.

Methods
Male Sprague-Dawley rats were microinjected in the MnPO with either a virus to knockdown AT1aR expression (shAT1a) or a scramble virus (SCR) and instrumented with radio telemetry a week later. Radio telemetry provides continuous recording of cardiovascular variables. After a week of surgery recovery the animals were monitored for a 5 day baseline period before experiencing 7 days of CIH. The morning of the final day, the animals were either perfused with formaldehyde for immunohistochemistry (IHC) or their brains were snap frozen for quantitative PCR. Results
Rodents injected in the MnPO with the shAT1a did not exhibit the sustained component of hypertension compared to SCR animals (P

Conclusions
Overall, this data indicates that the increase in AT1aR expression in the MnPO is essential for the development of the sustained component of CIH hypertension. The shAT1a virus successfully prevents the increase in AT1aR expression and this leads to normal waking blood pressure in the CIH exposed rodents. IHC results indicate that there is less activity in the MnPO and RVLM of the rodents most likely related to reduced sympathetic outflow. This data lends support to optimizing our current treatment regiment through blood brain barrier AT1aR blockers and ACE inhibitors. Future treatment methods could focus solely on preventing Angiotensin as a peptide neurotransmitter in the MnPO to ameliorate neurogenic hypertension.

Sponsor N/A
IRB/IACUC# 2014/15-28
Buschke-Lowenstein Tumor Requiring Extensive Genitourinary Reconstruction

Contemporary Management of Buschke-Lowenstein Tumor Requiring Extensive Genitourinary Reconstruction

Slit Ventricle Syndrome: A Case Report

Sponsor

IRB/IACUC# 2016-024
**Novel Approach to Skydiving after Right Hemipelvectomy and Left Hip Disarticulation**

This is a highly unusual case of a patient with a hemipelvectomy on the right with a hip disarticulation on the left who desired to skydive. The goal for this case was to design a protective seating orthosis, that would be 1. lightweight, 2. dissipate impact forces to protect against dynamic overshoot. 3. It would also need to be relatively compact to allow for aerodynamic stability and not create too much drag. 4. We also desired the prosthesis to be affordable (i.e., cost $300 or less). These criteria could be directly opposed to one another and costly. We believe this seating orthosis has broad applications to many patients with severe lower extremity trauma and spinal abnormalities, who wish to have the thrill of a completely solo parachute jump. This technology may have potential to be modified to protect our paralympic athletes who participate in high impact sports.

This is a 24 year old Caucasian male who presented for evaluation for a right hemipelvectomy with a left hip disarticulation and a large amount of heterotrophic ossification in the soft tissue surrounding his pelvis. He sustained a career ending, near fatal, blast injury, while serving in Afghanistan in 2012. Once he became healthy enough to return to his activities of daily living, he had a strong desire to start skydiving. He made an initial attempt to skydive with uni-density foam from a commercial furniture store. This resulted in soft tissue injury that was significant enough to required hospitalization. He was very determined to continue skydiving, therefore, his military contacts helped establish a relationship with Dr. Dombroski. Dr. Dombroski has expertise in blast impact helmet technology, along with having served as a flight surgeon for the US army. A team with Dr. Dombroski, his prosthetist and sports medicine doctor worked together to help him achieve his dream of a completely solo parachute flight.

**Physical examination:**

He is a pleasant, goal directed 24 year old male. He has normal vital signs. His height is 37 inches and he weighs 66 lbs. He appears alert and oriented. His HEENT, cardiovascular, respiratory, abdominal exams, spine, and upper extremity exam are all within normal limits. On MSK exam his pelvis demonstrates the absence of an ischial tuberosity on the right. In addition to this he has multiple painful pelvic soft tissue masses that represent his underlying heterotrophic ossification. His GU exam is significant for the absence of testicles. His psychiatric exam demonstrates a normal affect. He is intelligent and actively involved in online college classes. He is hopeful that he can be a role model for others with disabilities.

**DDX**

n/a

**TEST RESULTS**

3D reconstruction of Pelvis

**FINAL DIAGNOSIS**

Right hemipelvectomy Left hip disarticulation with heterotrophic bone formation

**DISCUSSION**

There have been no case reports to our knowledge that report on solo sky diving after right hemipelvectomy and left hip disarticulation, although tandem jumps have been completed, this is felt to not be as thrilling. This is important as there are many individuals with congenital and acquired lower extremity disabilities that desire to live an active life and this may include solo sky diving. Our goal is to allow them to share in the thrill of solo free fall.

Initially, he did provide us with consent to help design this seating orthoses, write this case report and waived all liabilities to all parties involved. He is well aware of the risk involved with skydiving. Dr. Dombroski than attempted to adapt his knowledge of helmet technology to create a helmet for our patients pelvis. The orthoses was made from a multi density foam and placed at a distance of no greater than 5/8ths of an inch from the skin surface. Several trial seating orthoses were produced in the process. These prototypes included a chair with lumbar support and 4 motorcycle springs, a circular snow-sled lined with the multi-density foam, 3D printed ABS plastic shell lined with multi-density foam and finally a 50/50 weave carbon-fiber shell lined with multi-density foam. These seating orthoses were tested using a 40lb sand bag dropped from a height of 7 feet, which represents 60% of our patient’s body weight. Prototype 1 did not work secondary to failure to control landing trajectories and being too heavy. Prototype 2 created two much drag and would lead to unsafe parachute deployment. Prototype 3 worked but the plastic failed after multiple drops. Prototype 4 was successful and allowed to be tested as a live jump. Our patient then tested this technology with a successful live jump.

**Follow up:**

Our patient has since completed 19 jumps, and he has video-recorded some of them. He continues to encourage and support others with lower extremity disabilities. We are thankful for his service and his willingness to participate in this case report. We were able to meet all 4 of our initial criteria. We believe this technology can be adapted to a wide range of skydiving application to allow patients with severe lower limb injuries, cerebral palsy, spina bifida, and spinal injuries to experience the thrill of solo parachute jumps. It also has the potential to be adapted for our paralympic athletes who participate in high impact sports. More research is needed in these area as we encourage our amputees to become more active.

**Sponsor**

IRB/IACUC# 2016-031
Mucolipidosis Type II (I-Cell Disease)

1. Our case is unusual because ML II does not generally present with fractures. This case demonstrates the importance of considering ML II in infants presenting with in-utero fractures.
2. Athena was used to access the patient’s medical chart to collect information on this case presentation.
3. We describe a 10-month-old, Hispanic male of non-consanguineous parents with a history of in-utero fractures. In addition to multiple fractures, osteopenia, congenital heart defect, and jaundice were also present. The infant’s clinical presentation initially suggested osteogenesis imperfecta (OI), however genetic testing found no evidence of known mutations of OI. A careful review of the skeletal survey was suspicious for ML II, and further genetic sequencing at approximately 5 months of age confirmed the diagnosis.
4. Currently, there is no cure for ML II. Treatment focuses on palliative care including physical therapy to alleviate joint stiffness, speech therapy to assist in language acquisition, and surgery to correct conductive deafness. Continued research is needed to reduce morbidity and improve mortality.

Sponsor  N/A
IRB/IACUC#  CCMCIRB
Growth Hormone Treatment in Rapadilino/Rothmund-Thomson Syndrome

INTRODUCTION/CASE PRESENTATION
We describe two female Caucasian siblings with compound heterozygous mutations in the RECQL4 gene. Both were referred to the Endocrine clinic for severe short stature. The 4 year old has talipes equinovarus, bilateral radial reduction defects, small palpebral fissures, small mouth, and skin changes. She was found to be growth hormone (GH) deficient, with a small pituitary gland on MRI scan, and was treated with biosynthetic GH. Her 22 month old sibling was born with bilaterally absence of her tibias, bilateral radial ray reduction defects, small mouth, and small palpebral fissures, but normal GH.

DISCUSSION
The RECQL4 gene encodes helicases that are important in DNA replication and repair. Clinically RECQL4 mutations are found in three rare conditions: 1) Rapadilino syndrome (RS), 2) Rothmund Thomson syndrome (RTS) and 3) Baller Gerold syndrome (BGS). These three autosomal recessive conditions have similar characteristics of skeletal abnormalities, and an increase prevalence of cancer, such as osteosarcoma, particularly in RTS and RS. Osteosarcoma development has been reported in growth hormone treated RS and RTS patients. The DNA helicase activity of RECQL4 has been shown to be critical in skeletal development. Animal models of mutated RECQL4 deregulate p53 activity that can possibly explain the predisposition to osteosarcoma.

CONCLUSION
We report two sibling with a rare disorder due to the RECQL4 gene mutation associated with multiple skeletal abnormalities and predisposition cancer, such as osteosarcoma. In individuals who are deficient, GH has been shown to significantly improve linear growth and quality of life. Although the older sibling has shown a favorable response, because of its mitogenic effects GH should be used with caution in children predisposed to cancer. A better understanding of the pathophysiology of the diseases associated with mutations in the RECQL4 gene is needed to help develop a more effective treatment program.

The Management of a Pediatric Patient Under General Anesthesia with Undiagnosed Primary Hypothyroidism: A Case Study

Hypothyroidism is a common endocrine disorder known to produce major metabolic and physiologic disturbances in an individual under general anesthesia. This case deals with the perioperative management of a pediatric patient with undiagnosed primary hypothyroidism, and illustrates the successful use of high dose epinephrine during an acute decompensation of a pediatric patient with significantly depressed thyroid function. During an elective tracheocutaneous fistula closure, the patient suffered an acute hypotensive event with hypoxemia, shortly following intubation. He initially received a 100mL lactated ringer (LR) bolus and 2 micrograms (mcg) of intravenous epinephrine, but his condition continued to deteriorate. Multiple additional LR boluses, a high dose corticosteroid, and exponential doses of epinephrine (totaling 150 mcg) were then given, which successfully elevated and sustained the patient’s blood pressure. The patient’s condition was initially attributed to a pulmonary hypertensive crisis and a viral pneumonia secondary to rhinovirus. However, the healthcare team later discovered the decompensation was connected to an undiagnosed primary hypothyroidism, and with proper management and use of hydrocortisone and synthetic thyroid hormone, the young boy made a full recovery. To our knowledge this is the first published report of a pediatric patient surviving general anesthesia with a TSH greater than 500 U/mL, and brings to note the importance of primary hypothyroidism being a possible etiology in an acute decompensation of the pediatric patient after the exclusion of alternate causes.
The Urgent Management of T-Cell Acute Lymphoblastic Leukemia (T-ALL) in Children

Purpose:
Children with T-ALL often have aggressive disease with life-threatening problems at the time of diagnosis. This presentation of three cases describes the diagnostic process of T-ALL, discusses the clinical options involved in initial management, and delineates expectations for patients prior to discharge. This descriptive study highlights the most important steps in managing a patient with T-ALL and its associated complications.

Method:
Three recently diagnosed cases (late 2015) were available for study. Patient records were reviewed to gather information regarding history, physical exam, laboratory data, imaging, and management.

Results:
Each of these patients, ages 18 months, 3 years, and 10 years of age, had a different clinical presentation. They were referred to Cook Children’s Medical Center (CCMC) after evaluation by a primary care or urgent care provider. The suspicion of leukemia was confirmed with peripheral blood smears and flow cytometry. Two of the three patients had a mediastinal mass present. All patients presented with severe leukocytosis with white blood cell counts ranging from 425,000 to 781,000/mm3. Due to the concerns of leukostasis, they each underwent leukapheresis to decrease their white cell counts. Concerns addressed during admission included respiratory distress, cerebral leukostasis, and tumor lysis syndrome.

These patients spent an average of eleven days in the hospital with each patient spending five days in the Pediatric Intensive Care Unit. Two were enrolled in a randomized clinical trial assessing the efficacy of investigational drug bortezomib in T-ALL. The patient that was not enrolled in the trial received the current standard of care.

Conclusion:
T-ALL (with or without mediastinal mass) can be the underlying cause of life threatening clinical problems. Although protocols are the backbone of treatment, there may be differences in the initial management, including the decision to utilize leukapheresis to bring WBC levels from initially dangerous elevations to values that are safer before beginning anti-leukemic therapy, as well as steroid preconditioning. Patients were discharged after evidence of clinical stability, treatment progress, and improvement in hematological lab values. In addition, each of these patients had family demonstrating commitment to follow up for additional treatment.

Atherogenic Cholesterol in 2 Siblings with Congenital Generalized Lipodystrophy

Congenital generalized lipodystrophy (CGL) is a rare autosomal recessive disorder characterized by near total absence of body fat from birth, with predisposition to insulin resistance, diabetes, hypertriglyceridemia and hepatic steatosis. This clustering of risk factors is often associated with increased atherogenic cholesterol, increasing risk of premature atherosclerotic cardiovascular disease (ASCVD)-related events. We describe two Mexican-American siblings, a 17 yr old male and a 6 yr old female, with congenital generalized lipodystrophy type 4, a variant of CGL, due to null mutations in polymerase I and transcript release factor (PTRF). Both siblings had characteristic findings of near lack of total body fat with very low levels of serum leptin, insulin resistance, hepatic steatosis, dyslipidemia and myopathy with elevated CPK. Leptin (ref range 1.4-16.5): 0.8 ng/mL. Measurement of fasting lipid and lipoproteins revealed severe hypertriglyceridemia and low HDL-C. Elevated levels of atherogenic cholesterol (non-HDL-C and LDL-C) are causally related to the development of atherosclerosis, the key underlying process contributing to most clinical ASCVD events. Measurements of atherogenic cholesterol in our two siblings with CGL-4, appeared to increase with age. Lipid profiles in children with CGL-4 are similar to those described in metabolic syndrome, i.e. moderate to severe hypertriglyceridemia with low HDL-C and increased small dense LDL-C. Although CVD risk is increased, children with CGL-4 are prone to sudden cardiac death, the latter most likely a result of the cardiomyocyte dysfunction.
Hyperinsulinism Secondary to Congenital Disorder of Glycosylation Type 1a

Purpose
Congenital disorders of glycosylation (CDG) are a group of rare genetic disorders caused by defects in enzymes responsible for a series of post-transcriptional glycosylation reactions. The most well known subtype of these disorders is CDG type 1a. More than 700 cases have been reported worldwide. Its clinical spectrum and severity are widely variable; common symptoms include seizure, ataxia, hypotonia, developmental delay, liver dysfunction, and cardiomegaly, but hypoglycemia secondary to hyperinsulinism has rarely been reported. A closely related subtype of CDG is CDG type 1b. CDG type 1b is characterized by protein-losing enteropathy and diarrhea, as well as endocrine-related symptoms, such as hypoglycemia.

Methods
A 2-month-old male was admitted for severe hypoglycemia and liver dysfunction. Because of his concomitant liver disease, enzymatic testing and gene sequencing for a disorder of glycosylation were requested. He was found to have a mutation of the gene for CDG type 1a. Over the subsequent 2 years, the child was noted to have ataxia and hypotonia. An MRI scan of the brain demonstrated a hypoplastic cerebellum and vermis. He experienced multiple seizures. Hypoglycemia, secondarily to hyperinsulinism, was controlled with diazoxide. The hypoglycemia resolved by 2 yrs of age when he was able to fast for >24 hours while maintaining a glucose >50mg/dL and beta-hydroxybutyrate>3mmol/L. Therefore, the diazoxide was discontinued.

Results
The most common presenting symptoms of CDG type 1a are neurological. In addition to hypotonia and seizures, our patient has persistent hypoglycemia associated with hyperinsulinemia, an unusual presentation of CDG type 1a as opposed to CDG type 1b. The proposed mechanism hyperinsulinemia is secondary to constitutively closed ATP-sensitive K+ channel, producing unregulated release of insulin. Given its ability to open the ATP-sensitive K+ channel, diazoxide is a reasonable treatment option. Our patient's hypoglycemia responded well to diazoxide.

Conclusion
Currently, there is no cure for disorders of glycosylation. Mortality within the first year of life is as high as 20%. Treatment options are being explored to facilitate glycosylation with either a membrane-permeable mannose-1-phosphate treatment or enzyme replacement therapy. Additional research is needed to find more effective treatments to improve morbidity and reduce mortality in affected patients.

Movement Disorder, Suicidal Ideation and Depression Related to Streptococcal Infection

Purpose: Following streptococcal infections, children appear to develop neurologic and psychiatric symptoms. We describe two cases of pediatric patients who developed a wide array of neurologic symptoms during or just after streptococcal infections, as measured by elevated ASO titers.

Materials and Methods: The medical history and clinical outcomes of the patients were obtained. Patient 1 is a ten year old who presented at age 8 with anxiety and core muscle spasms that culminated in bilateral ballismus and tremors on the right side. He was seen by Neurology and Infectious Disease. Patient 2 is a 10 year old male with one month of insomnia and suicidal thoughts that were beyond his control. Evaluation included CXR, ESR, CBC, CMP and ASO titer and urgent outpatient psychology evaluation.

Results: An elevated ASO titer was the only abnormal lab for Patient 1. He improved in 36 hours on oral Cefdinir. Neurology and Infectious Disease were unable to establish a definitive diagnosis. He has had two relapses of chorea like abdominal movements associated with anxiety that both improved with Cefdinir. He improved in 72 hours after starting treatment with Cefdinir and to date is symptom free. Patient 2 had an elevated ASO. He improved in 72 hours after starting treatment with Cefdinir and to date is symptom free.

Conclusion: These cases demonstrate that clinicians should consider prior streptococcal infections in the differential of acute neurologic or psychiatric symptoms.
Methamphetamine-induced activation of trace amine associated receptor (TAAR) 1 regulates astrocyte excitatory amino acid transporter (EAAT)-2 via differential CREB phosphorylation during HIV-associated neurocognitive disorders (HAND)

Objective: Methamphetamine (METH) abuse commonly results in neurocognitive decline, a characteristic shared with HIV-associated neurocognitive disorders. METH abuse exacerbates HAND partly through glutamate dysregulation. Astrocyte excitatory amino acid transporter (EAAT)-2 is responsible for >90% of glutamate uptake from the synaptic environment and is significantly decreased with METH and HIV-1. Our previous work demonstrated astrocyte trace amine associated receptor (TAAR) 1 to be involved in EAAT-2 regulation. Astrocyte EAAT-2 is regulated at the transcriptional level by cAMP responsive element binding (CREB) protein and NF-κB, transcription factors activated by cAMP, calcium and IL-1β. Of these, cAMP and calcium are second messengers initiated via activation of TAAR1, that is upregulated by IL-1β. METH-mediated increases in these second messengers and signal transduction pathways have not been shown to directly decrease astrocyte EAAT-2.

Hypothesis: We propose CREB activation serves as a master regulator of EAAT-2 transcription, downstream of METH-induced TAAR1 activation.

Materials and Methods: To investigate the temporal order of events culminating in CREB activation, genetically encoded calcium indicators, GCaMP6s, were used to visualize METH-induced calcium signaling in primary human astrocytes. RNA interference targeting cAMP-dependent protein kinase A and calcium/calmodulin kinase II confirmed METH-induced regulation of EAAT-2 and resultant glutamate clearance. Furthermore, we investigated METH-mediated CREB phosphorylation at both serine 133 and 142, the co-activator and co-repressor forms, respectively.

Conclusions: Overall, this work revealed METH-induced differential CREB phosphorylation is critical for EAAT-2 regulation, and may serve as a mechanistic target for the attenuation of METH-induced excitotoxicity in the context of HAND.

Polymeric Nanoparticles for Gene Delivery to Human Astrocytes

Purpose: Currently available therapies for the treatment of neurodegenerative disorders (NDD) are inadequate. Challenges include low blood-brain barrier (BBB) permeability, brain structure complexity. Nanoparticles (NPs) and gene therapy are the two suggested approaches to overcome these problems. Small diameter of NPs (100-200 nm) may allow them to cross the BBB and gene therapy can target specific type of cells to alter gene regulation and cellular function. In this study, we combined both approaches and tested gene delivery to astrocytes, the principal type of glial cells in the brain, via two NPs formulations.

Methods: A5P50, an Arginine-based polyethylenimine (PEI) polymer and poly-lactic-co-glycolic-acid (PLGA) NPs were tested for their gene delivery potential in primary human neural cells and cell lines. AFM imaging was carried out to determine A5P50 and PLGA NP dimensions. CMV-or GFAP-promoter-driven luciferase reporter plasmids (pGL3) served as test genes. Cytotoxicity was measured using MTT, LDH, and DNA fragmentation assays. Luciferase assay and Yoyo-dye labeling was used to evaluate the efficiency of gene delivery.

Results: FDA-approved, biodegradable PLGA NPs were able to deliver pGL3 across the cell membrane in astrocytes. However, pGL3 expression was negligible or absent. In parallel, A5P50 successfully delivered and expressed the pGL3 in all tested cell types including astrocytes. AFM imaging showed that the size of NPs remained similar when combined indicating absence of direct interaction. Live imaging with Yoyo-labeled pGL3 indicated that presence of A5P50 facilitated PLGA-mediated pGL3 delivery across the nuclear membrane by an unknown mechanism.

Conclusions: A5P50-PLGA-combination system was successfully used for gene delivery to astrocytes as well as other cell types. Low A5P50 concentration in the combination eliminated biocompatibility issues in human neurons. Further in vivo testing is necessary to establish this system for future therapeutic use. Presented in vitro results are promising to progress in that direction.
IL-1beta autocrine loop differentially regulates astrocyte inflammatory responses in HAND

Hypothesis: HIV-1 infection of the central nervous system (CNS) impairs brain function and leads to HIV associated neurocognitive disorders (HAND). Astrocytes are the most abundant cell type in CNS and provide structural and metabolic support under homeostasis and in diseases including HAND. It is well established that IL-1beta is regulated in an autocrine fashion. Given our prior work on astrocyte inflammatory responses in HAND, we sought to investigate the role of IL-1beta autocrine loop in differential outcomes.

Materials and Methods: Successfully knocking down new synthesis of IL-1beta by RNAi, changes in levels of CXCL-8, TNF-alpha, AEG-1, EAAT-2, TAAR-1 and TIMP-1 were measured in response to IL-1beta stimulation. Astrocytes were infected with the help of doubly fluorescent labelled pseudotyped HIV-1, and latently infected ones were sorted.

Results: As expected, RT2-PCR data confirmed that there was an increased mRNA expression of CXCL-8, TNF-alpha, TAAR-1 and TIMP-1 and no changes in EAAT-2 and AEG-1 levels.

Conclusions and Future Directions: This suggests that IL-1beta autocrine loop likely plays a differential role in astrocyte inflammatory responses. Furthermore, we are particularly interested in differential response of healthy versus latently HIV-1-infected astrocytes that act as viral reservoir in CNS. Our long term goal is to delineate the specific role of IL-1beta autocrine loop in differential regulation of inflammatory responses in latently infected astrocytes. These studies are highly significant to address CNS reservoir issues in post ART HAND.

Sponsor
IRB/IACUC# 2007-121

Potassium: a fifth "element" for the regulation of pluripotency and the cellular state in human pluripotent stem cells

Many inorganic elements are critically involved in the modulation of biochemical reactions and cell signaling pathways, suggesting that cells in unique states may display distinct elemental profiles and have specific requirements for different elements. Using X-ray fluorescence (XRF) spectrometry and inductively coupled plasma mass spectrometry (ICPMS) techniques, we measured the amounts of 56 major and trace inorganic elements in undifferentiated human pluripotent stem cells (hPSCs), their isogenic differentiated derivatives, and somatic cells used for cell reprogramming. While the amounts of most elements analyzed did not appear correlated with the pluripotent state of cells, the amount of potassium cation in undifferentiated hPSCs was significantly lower than that in multiple types of non-pluripotent cells. This phenomenon was reproducibly and consistently shown by both XRF spectrometry and ICPMS analyses in multiple hPSC lines and differentiated cells. Flow cytometry analysis using a cell-permeable fluorescence indicator for potassium, APG2-AM, also suggested that higher percentages of cells in pluripotent populations have a low level of intracellular potassium than those in non-pluripotent populations. To test whether the cellular pluripotency could be influenced by the manipulation of intracellular potassium, we used pharmacological tools to alter the permeability and intracellular concentration of potassium in hPSCs. The treatment with two potassium channel blockers, tetraethylammonium and 4-aminopyridine, increased intracellular potassium in human embryonic stem cells (hESCs) and induced pluripotent stem cells (hiPSCs), accompanied by the dose- and time-dependent downregulation of pluripotency markers POU5F1 and NANOG. In contrast, treatment with two types of potassium channel activators led to a decrease in intracellular potassium and the upregulation of POU5F1 and NANOG. Via 4-aminopyridine, we further exploited the link between cellular states and potassium thresholds, selectively eliminating hPSCs from differentiated derivatives within a dose window. Collectively, our data indicates that the amount of intracellular potassium is associated with the cellular states of hPSCs, and that the manipulation of intracellular potassium with pharmacological tools has functional impact on the regulation of pluripotency signaling in hPSCs. Potassium-altering agents may therefore be utilized in regenerative medicine for one of several purposes, including cellular purification and changing cellular identity. We demonstrate the first evidence that at the most basic level, a periodic element can be manipulated and have physiological, and potentially, therapeutic consequences.

Sponsor
Stem Cell Start-up Fund (UNT System School of Pharmacy); NIA T32AG020494
IRB/IACUC# 2014-101
601 Poster Classification: Staff (Not For Competition)
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**MedStar Mobile Healthcare Programs Improve Patient Health While Reducing ED Utilization and Hospital Costs**

Purpose: Locally, over 50% of Emergency Department (ED) visits in Tarrant County are associated with inappropriate ED use totaling ~$2 billion. To help mitigate inappropriate local ED use, the county’s primary 9-1-1 emergency response team, MedStar Mobile Healthcare, introduced several Mobile Health Program (MHP) interventions. Here, we evaluated outcomes from a high utilizer group (HUG) and a congestive heart failure (CHF) group to determine whether or not the MedStar MHP intervention would reduce ED transports and overutilization, inpatient admissions, and hospitalization costs. Hypothesis: Patients participating in the MedStar MHP intervention will experience a significant reduction in ED transports, utilization, inpatient admissions, and generate less hospitalization costs than before they participated in the MedStar MHP.

Methods: Pre- and post-program data of patients who participated in the HUG or CHF Readmission Avoidance program from July 2009 to October 2015 were evaluated retrospectively. Hospitalization costs were determined using data from 2013-2015. Data were analyzed using SPSS (version 21) and included descriptive statistics, frequency distributions, paired t-tests, ANOVA, and regression modeling, as appropriate. All analyses were conducted using a 95% confidence level and an alpha level of 0.05 was used to determine statistical significance.

Results: A total of 629 participants participated in the HUG (n = 406) or CHF (n = 223) Medstar programs. Those in the HUG program experienced an overall reduction in ED encounters of 72.5% resulting in a cost avoidance of over $ 6 million for ED transports. They also self-reported a 22% decrease in pain/discomfort and a 26% reduction in anxiety and depression. Participants in the CHF program had 48% fewer ED visits and experienced a 56% drop in inpatient encounters resulting in a total of $378,741 cost avoidance for ED transports during the program.

Conclusion: The HUG and CHF MedStar MHP interventions appear highly effective at reducing ED transports, utilization, and inpatient admissions while improving patient health outcomes. Reducing ED overutilization and inpatient admissions also resulted in a significant reduction in hospitalization costs. MedStar MHP interventions appear to promote substantial health improvements in chronically ill patients which frees emergency transport and hospital teams to provide acute crisis treatment to high-acuity patients community-wide.

Sponsor MedStar Mobile Healthcare
IRB/IACUC# 2014-171 N/A

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602 Poster Classification: Resident
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**Epidemiology of Hip Fractures, a Retrospective Review**

Purpose: To determine the epidemiology and fracture characteristics of hip fractures at a level two trauma center. To establish a hip fracture database to further research on the subject.

Methods: An IRB exempt retrospective chart review was undertaken on consecutive patients 55 years of age and greater from December, 2010 through July, 2013 who sustained a proximal femur fracture from a ground level fall. All of these patients underwent operative fixation at a single, urban, level two trauma center. X-rays were reviewed by three Orthopedic surgeons blinded to patient identification and were characterized using the AO/OTA classification system into fractures of the femoral neck (FN), intertrochanteric region (IT), and subtrochanteric region (ST). Fracture classification and fixation method were recorded and combined with clinical information from the hip fracture database.

Results: There were 986 patients that met study characteristics including 281 (28.5%) males and 705 (71.5%) females, the average age was 79.5 years old. Fracture characteristics included 91 (9.2%) non displaced FN, 332 (33.7%) displaced FN, 275 (27.9%) stable IT, 169 (17.1%) unstable IT, 82 (8.3%) reverse obliquity IT, 28 (2.8%) ST, and 9 (0.1%) peri-prosthetic fractures. The average length of stay was 5.9 days (range 1-36 days), and the most common discharge destinations were 526 (53.35%) patients to a skilled nursing facility and 303 (30.7%) to a rehabilitation facility. Only 76 (7.7%) of patients were discharged home. The in hospital mortality rate was 1.6% (16 patients).

Conclusion: Hip fractures in the geriatric population are very common and lead to significant morbidity, mortality, and loss of pre-injury functional level. Understanding the epidemiology of these fractures will better guide patient care and allow us to formulate treatment protocols to best serve this vulnerable patient population. Further research should continue on, among other things, the appropriate types of fixation for these fractures, factors that influence length of stay, and ways to improve function after hip fracture. The aim of this research should be to reduce the physical, psychological, financial, and social burden that hip fractures have on both patients and society as a whole.

Sponsor N/A
IRB/IACUC# 2016-036
suggest that factors other than stigmas influence help-seeking attitudes. Exploring these factors would help inform interventions to address social barriers to help-seeking. Further work could assess the following factors' influences on attitudes towards help-seeking: perceptions of attitude towards professional mental health help-seeking and personal and perceived stigmas towards depression among rural central Texas residents.

Conclusion: Our results show that minimally invasive sacroiliac joint fusion can be used as an alternate therapy for long term control of sacroiliitis when conservative methods fail. The results also show that careful selection of patients who will benefit from this surgery is warranted and more studies are needed in this area as not all the participants were able to benefit from this procedure. IRB for this study was approved by Chesapeake IRB.

Sponsor N/A
IRB/IACUC# cIRB Pro00015844

Objective: Stigma about depression may be perceived stigma or personal stigma (negative attitudes about oneself as a result of internalization of stigmatizing ideas held by society). Both types may inhibit help-seeking. Few researchers have reported on these constructs in rural samples despite higher prevalence and completion rates of suicide among rural residents. The current study investigated the relationship between attitude towards professional mental health help-seeking and personal and perceived stigmas towards depression among rural central Texas residents. Methods: This analytical, cross-sectional study used the Stigma and Attitudes towards Depression Questionnaire (SAD-Q) to determine a) contact with help-seeking, b) personal stigma and perceived stigma, c) attitudes toward seeking help from a mental health professional, and d) depression status of 273 residents of the towns and surrounding areas of Eastland, Dublin, and Gatesville, Texas. Through factor analysis, factors were identified that attribute to personal stigma and perceived stigma. After adjusting socio-demographic variables, multiple linear regression was fitted on help-seeking attitude to understand the relationship of history of seeking help from a mental health professional for depression, current depression status, and personal stigma and perceived stigma factors. Results: Personal stigma and perceived stigma factors were distinguished with Cronbach alpha coefficients of 0.90 and 0.94, respectively. Female gender and having a history of help-seeking for depression were found to be significantly related to an attitude favorable towards help-seeking for depression. Participants with possible depression status were found to have significantly more personal help-seeking contact than participants who screened negative for depression. Depression status was not significantly related to either perceived stigma or personal stigma. Contrary to the authors’ expectations and the findings of previous studies, personal and perceived stigmas were not significantly related to help-seeking attitudes in these samples. Conclusion: Some of these results are reassuring: many rural Texas residents who have symptoms of major depression are seeking help from mental health professionals and b) many rural Texas residents who have sought mental health help in the past seem to maintain a positive attitude towards help-seeking. However, the question remains: for those who are depressed but do not seek help, why not? These results suggest that factors other than stigmas influence help-seeking attitudes. Exploring these factors would help inform interventions to address social barriers to help-seeking. Further work could assess the following factors’ influences on attitudes towards help-seeking: perceptions of a) effectiveness of mental health services and b) barriers to obtaining them.

Sponsor N/A
IRB/IACUC# 2015-097
Services Available for Homeless Veterans

Many factors contribute to homelessness, including shortage of affordable housing, inability to access health care, less than adequate income and a lack family and social support networks. For veterans, the effects of post-traumatic stress disorder and substance abuse can compound these issues. (National Coalition for Homeless Veterans, 2014). The objective of this search was to determine what resources are available to homeless veterans in Tarrant County. Methods were to search public databases for resources and determine common obstacles in accessing those resources. It was discovered that there are multiple resources available for veterans who are faced with homelessness in Tarrant County, although the need and requisition of appropriate paperwork is a consistent barrier. It can be concluded that although there are a variety of resources available, there are several barriers to accessing the appropriate help that should be addressed by organizations intending to serve the veteran population.

Combination of Positive Airway Pressure Compliance and Efficacy Improves Subjective Sleepiness Compared to Compliance Alone

INTRODUCTION: Purpose of this study was to evaluate whether high PAP compliance and PAP efficacy produces decreased subjective sleepiness compared to high compliance alone and compliance as measured by the Medicare standard.

HYPOTHESIS: We hypothesized that (1) higher compliance will result in lower Epworth Sleepiness Scale (ESS) scores, (2) that higher PAP efficacy will also result in lower ESS scores, (3) that OSA patients with high PAP compliance but low PAP efficacy will exhibit higher ESS scores, and (4) OSA patients who exhibit very high PAP compliance and efficacy will have lower ESS scores than OSA patients who merely meet the Medicare threshold.

METHODS: Patients were included if they had a diagnosis of OSA made by overnight polysomnography and in-lab PAP titration studies according to AASM criteria. In study 1, patients were arranged into quartiles of PAP compliance. In study 2, patients were arranged into tertiles of PAP effectiveness. In study 3, patients were arranged into two groups, one group with high compliance and low efficacy, and the other group with high compliance and high efficacy. In study 4, patients with high compliance compared with current Medicare standard. One-way ANOVA was used to test differences in study 1-2 and unpaired Student’s t-tests were used in study 3-4.

RESULTS: In study 1, patients in the first and second quartile of compliance had higher subjective mean ESS (P

CONCLUSIONS: We conclude that patients who are highly PAP compliant, but have relatively poor PAP effectiveness, are sleepier than patients who are highly compliant and effective with PAP treatment.
Nutritional Barriers in Geriatrics

There are many factors that contribute to weight loss and malnutrition in older adults and this is directly correlated with increased morbidity and mortality. We believe that Tarrant county has in place many programs that would be of benefit to our geriatric population in relation to their nutritional health.

We first indicated the most important factors that contribute to the nutritional health in a geriatric population and then identified specific community programs and resources that could cater to improving each of these aspects.

There are many factors that lend to alterations in nutritional health as patients age. Some of the factors discussed in this overview include socioeconomic factors, psychological factors, and physiological factors including oral and dental health, gastrointestinal health, and the frequent presence of multiple disease processes.

We identified community resources to address each of these contributing factors including socioeconomic factors, psychological factors, and physiological factors including oral and dental health, gastrointestinal health, and the frequent presence of multiple disease processes. We concluded that many of these programs are easily accessible to every patient in the geriatric patient.

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Vision is a sense that often goes underappreciated among the many sighted members of our community. Everyday activities such as commuting to and from one’s home, participating in classroom learning, or finding appropriate employment would be drastically hindered by loss of sight. Diseases like glaucoma, macular degeneration, and cataracts affect people in our own community every day. Thankfully, Tarrant County has a variety of resources available for those with vision disabilities. Some of these organizations provide clinical services to prevent and treat blindness, while others provide economic, social, and emotional support to help those with vision disabilities regain important aspects of their daily lives. Others still, provide our county’s indigent children with routine eye exams and glasses that may make all the difference in their school and home lives. In this Poster, we provide a summary of the resources available in Tarrant County to meet the needs of those with vision disabilities.
GLP-1 and its implications for neuroprotection in diabetes-associated neurodegenerative diseases

Background: There is growing evidence linking type 2 diabetes (T2D) with dementia and neurodegenerative diseases such as Alzheimer’s disease (AD). The incretin hormone glucagon-like peptide 1 (GLP-1), utilized for its insulinotropic properties in the treatment of T2D, is also synthesized in the CNS as a neuropeptide and has been demonstrated to have neuroprotective effects. We studied the effects of GLP-1 on insulin signaling in astrocytes, the only type of brain cells that store glycogen, which is utilized in learning and memory.

Hypothesis: Our hypothesis was that GLP-1 would act on astrocytes and mimic insulin action at baseline conditions. In the presence of insulin, we expected GLP-1 to enhance insulin action, exhibiting a mechanism by which astrocytic glycogen storage could ultimately be augmented.

Methods: We first treated astrocytes with GLP-1 and used a cAMP assay to determine if there was a functional GLP-1 receptor (GLP-1R) on the astrocytes. We then treated astrocytes with insulin alone, insulin and GLP-1 added 18 hours prior, insulin and GLP-1 added 30 minutes prior, and GLP-1 alone and determined expression of pAKT and pGSK-3B with Western Blot analysis.

Results: Astrocytes appear to express a functional GLP-1R, suggesting the possibility that previously studied neuroprotective effects of GLP-1 occur via an astrocytic mechanism. GLP-1 was shown to mimic astrocytic insulin signaling at baseline conditions and enhance the phosphorylation of both AKT and GSK-3B when astrocytes are treated acutely at 30 min. as well as at 18 hours. GLP-1’s effects on insulin signaling suggest it can ultimately increase glycogen synthesis. The enhancement of insulin signaling by GLP-1 is most apparent at 10nM insulin, inducing a near maximal response.

Summary: Our results suggest GLP-1 may have a role in attenuating insulin resistance and decreased glycogen storage, providing a mechanism by which GLP-1 analogs can offer neuroprotection to patients with diabetes-associated neurodegenerative disease such as Alzheimer’s.

Redox imbalance and aberrant mitochondrial enzymatic activities in diabetic lung

The lung is a known target of diabetic injury, but the underlying mechanisms of damage remains poorly understood. We hypothesized that pulmonary cellular redox imbalance and mitochondrial abnormalities contribute to diabetic lung injury. To test this hypothesis, we induced diabetes in rats by streptozotocin and measured redox imbalance parameters including aldehyde reductase activity, poly ADP ribose polymerase (PARP) activation, NAD+ and NADPH contents along with mitochondrial functional parameters represented by the enzymatic activities of complexes I to IV. Results indicate that aldose reductase activity was elevated and PARP was upregulated in diabetic lung, while the contents of both NAD+ and NADPH were decreased in diabetic lung, demonstrating an excess NADH-linked redox imbalance problem in diabetic lung. Consequently, the enzymatic activities of complexes I to IV were all elevated in diabetic lung mitochondria due to an NADH oversupply. We also found that the enzymatic activities of dihydrolipoamide dehydrogenase (DLDH) and mitochondrial sirtuin 3 (Sirt3), both of which are inducible enzymes and are NAD+-dependent, were impaired in diabetic lung, and such an impairment was due to a decreased level of protein expression for both DLDH and Sirt3. For DLDH functional impairment in diabetic lung, protein acetylation also appeared to play a role as DLDH acetylation was increased. Additionally, we found that an increased complex I activity in diabetic pulmonary mitochondria was partly due to hyperglycemia-induced upregulation of nicotinamide N-methyltransferase (NNMT) and a concomitant increase in the expression of NDUFS3, a complex I subunit that is responsible for complex I assembly. The overall outcome of this NADH-driven redox imbalance and aberrant mitochondrial enzyme functions were a decreased ATP content, an increased NAD(P)H dehydrogenase, quinone 1 (NQO1) activity, and an elevated hydrogen peroxide concentration that reflects an aggravated oxidative stress. These findings demonstrate that diabetic lung exhibits NADH/NAD+–linked redox imbalance and abnormal mitochondrial function that likely contribute to energy deficiency and oxidative damage involved in diabetic lung injury.
HbA1c vs FPG and 2-Hour OGTT Glucose in Identifying Dysglycemia in Youth

INTRODUCTION
In recent years, there has been an increased incidence of pre-diabetes and type 2 diabetes mellitus in youth 10 years of age and older.1 Dysglycemia has been shown to be a continuous risk factor for cardiovascular disease and thus offers a compelling reason for evidence-based screening and management.2 Current ADA guidelines for the diagnosis and management of pre-diabetes in youth are based upon extrapolation from adult studies and may not be valid in the pediatric population.1, 3

EXPERIMENTAL METHODS
To evaluate the utility of HbA1c in identifying dysglycemia in youth, results of the HbA1c, fasting plasma glucose (FPG), and 2-h oral glucose tolerance test (OGTT) were collected retrospectively from a multiethnic cohort of 390 youth seen in a preventive cardiology clinic from 2012 to 2015. Results of the HbA1c were compared to the FPG and 2-h glucose following a standard OGTT.

RESULTS
Table 1. Comparison between HbA1c and FPG values
Table 2. Comparison between HbA1c and OGTT 2-h glucose values
Of the patients with a HbA1c

DISCUSSION
HbA1c is frequently used to identify dysglycemia in at-risk youth. Although it is a convenient screening tool, the results may be discordant with other measures of dysglycemia. Results from the 2005-2010 Yale Pathophysiology of Type 2 Diabetes in Obese Youth Study indicate that the optimal A1c threshold for identifying T2DM was 5.8% and that the best predictor of 2-h glucose at a 2-year follow-up was the combination of the subject’s baseline A1c and 2-h glucose.4 A cross-sectional study compared results of OGTT and HbA1c to measurement of glycemia via continuous glucose monitoring. The OGTT and HbA1c each predicted different patterns of dysglycemia, with the former providing a greater correlation with peak glucose and variability and the latter providing a greater correlation with average and overnight glucose values.5

CONCLUSION
Diagnostic tests for pre-diabetes and diabetes in youth are often discrepant. It would appear that HbA1c is a convenient but imperfect screening tool in youth. The cutoff for the different categories of glycemia may need to be modified, and the HbA1c may need to be paired with the OGTT to increase the sensitivity of pre-diabetes screening in at-risk youth. More studies are needed to evaluate diagnostic markers of dysglycemia and effective management of pre-diabetes in this vulnerable population.
Analysis of Comorbid Depression and Diabetes among Males 30–50 Years of Age

Introduction: Depression and diabetes are among the most prevalent chronic diseases in the United States and are common comorbid conditions. The purpose of this study was to assess whether diabetes is a risk factor for depression in a representative sample of males ages 30-50.

Methods: This cross-sectional analysis used 2013 data from the Behavioral Risk Factor Surveillance System for Mississippi males ages 30-50, N=712. Chi-square analyses and multiple linear regression were used to determine the association between diabetes and depression.

Results: Significant relations between diabetes and depression were observed at the bivariate level (p=.02, 95% CI=1.06, 4.23); however, the relationship was insignificant after controlling for number of chronic health problems, physical activity level, weight, tobacco use, alcohol use, educational level, marital status, age, and ethnicity/race. The relations between number of chronic health problems and depression were significant at the multivariate level.

Conclusions: Overall, depression and diabetes were not related in this age group. However, number of chronic health problems was significant for this age group, and thus having multiple comorbidities such as diabetes seems to be a key factor impacting depression risk for males 30-50. Consequently, clinicians should be cognizant of the relationship between comorbidities and depression and provide screening to patients with multiple comorbidities in addition to resources or referrals as necessary.

Sponsor N/A
IRB/IACUC# 2015-105

Effect of Body Mass Index and Menopausal Status on Lipid Levels in African American Women

Background: Lipid levels are negatively impacted by menopause. Total cholesterol (TC), low density lipoproteins (LDL), and triglyceride levels have been shown to increase due to menopause, increasing risk of cardiovascular disease (CVD). Limited research indicates this relationship may be independent of weight status. This study aims to examine lipid levels (TC, LDL-C, fasting glucose) by menopausal and weight status (Body Mass Index [BMI] > 25) in African American (AA) women to better understand this relationship.

Methods: Lipid profile, BMI, and menopausal status were obtained from AA women enrolled in a NIH-funded study, Better Me Within, to evaluate a faith-based diabetes prevention program. This study included overweight and obese AA women with an absence of hysterectomy. Lipid profile (TC, LDL-C, fasting glucose) was obtained after a 12-hour fast via finger stick (Alere Cholestech LDX Analyzer). BMI was calculated with objectively collected height and weight data, and menopausal status through self-report.

Results: 56 AA female participants with a mean age of 46.7 (SD=12.4) years were included. LDL, TC, and fasting glucose were all significantly higher in postmenopausal as compared to premenopausal women (all p values <.05). When evaluating obese women, mean lipid levels were higher for postmenopausal women as compared to premenopausal women (LDL p=0.01, TC p=0.05); however, this difference was not seen in overweight postmenopausal as compared to premenopausal women.

Conclusion: In this study of AA women, TC, LDL, and fasting glucose were higher for postmenopausal women compared to premenopausal, and in obese postmenopausal women compared to obese premenopausal women. This study indicates greater levels of BMI worsen the effect of menopausal status on lipid levels. Future research is needed to evaluate the relationship between excess weight, menopause, and lipid levels in larger samples, particularly since AA women are at higher risk for chronic conditions including diabetes and CVD.

Sponsor N/A
IRB/IACUC# 2011-164
Regulation of TGF β1 signaling pathway by Store Operated Calcium Entry in Mesangial Cells: A mechanism for controlling Extracellular Matrix Protein Expression in Kidney

Excessive extracellular matrix (ECM) proteins accumulation in glomerulus is one of the consistent pathological changes seen in kidney diseases, such as diabetic nephropathy. The Orai1-mediated store operated Ca2+ entry (SOCE) is associated with many physiological and pathological processes in a variety of cells, including glomerular mesangial cells (MCs) which are a major source of ECM proteins. Previously, we demonstrated in vivo and in vitro that SOCE is enhanced in MCs in diabetes. Also, in cultured human MCs, activation of store-operated Ca2+ channels significantly decreased fibronectin protein expression and collagen IV mRNA expression while inhibition of the channels significantly increased the expression of fibronectin and collagen IV. In vivo knockdown of Orai1 in MCs in mice using the targeted nanoparticle siRNA delivery system resulted in increased expression of glomerular fibronectin and collagen IV. However, the downstream mechanism underlying the SOCE effect is not known. Transforming growth factor-β1 (TGFβ1)-Smad3 pathway plays a critical role in ECM protein expression and renal fibrosis. The present study was conducted to test the hypothesis that SOCE suppressed ECM protein expression by inhibiting TGF β1-Smad3 pathway in MCs. In cultured human MCs, TGFβ1-induced activation of Smad3 in terms of its phosphorylation and translocation was examined in presence and absence of thapsigargin (TG, 1 µM), a classical activator of store-operated Ca2+ channel. We found that treatment with TGFβ1 (5 ng/ml for 15 hours) significantly increased the expression level of Phospho-Smad3 (p-Smad3) evaluated by Western blot. However, this response was markedly inhibited by TG treatment. Consistently, immunocytochemistry and Western blot showed that TGF β1 significantly increased the expression of nuclear Smad3. Again, this TGFβ1-induced nuclear translocation of Smad3 was prevented by pre-treatment with TG. Importantly, the TG effect was reversed by La3+ (5 µM) and GSK-7975A (10 µM), both of which are selective blockers of store-operated Ca2+ channel. Furthermore, knockdown of Orai1 using siRNA approach significantly augmented TGFβ1-induced p-Smad3 expression. Taken together, our results indicate that SOCE in MCs negatively regulates the TGFβ1/Smad3 signaling pathway which may in turn suppress the ECM proteins and thus could be a potential therapeutic target of kidney disease with glomerular fibrosis like diabetic nephropathy.

Plasma Water T2 as a Biomarker for Early Insulin Resistance Syndrome

Insulin resistance is defined as a blunted response to insulin by tissues. It is thought to be the body’s response to energy imbalance and is exacerbated by over-nutrition, physical inactivity, obesity and/or genetic factors. Early-stage insulin resistance does not occur in isolation, but is part of a broader syndrome that includes four main components: (1) compensatory hyperinsulinemia, (2) dyslipidemia, (3) subclinical inflammation with shifts in plasma protein levels, and (4) subclinical acid-base abnormalities. Individuals with insulin resistance are at higher risk for developing type 2 diabetes. Yet, insulin resistance is often undetected by the tests used to diagnose and screen for type 2 diabetes, namely fasting serum glucose and hemoglobin A1c. There is an unmet need for practical screening tools for early insulin resistance syndrome. Water mobility can be measured as plasma water T2 using a simple benchtop implementation of nuclear magnetic resonance. To test this hypothesis, we conducted an observational cross-sectional study of 51 asymptomatic, non-diabetic human subjects, ages 24-80, and quantified the association of plasma water T2 values with over 100 established metabolic biomarkers and diagnostic tests. Plasma water T2 exhibited bivariate correlations with markers of each of the four components of the insulin resistance syndrome. Multiple regression models revealed independent associations of plasma water T2 with fasting insulin levels, total serum protein concentration or viscosity, white blood cell or neutrophil count, and total cholesterol. Analysis using receiver operator characteristic curves demonstrated that plasma water T2 can diagnose insulin resistance (as defined by the McAuley Index) with a sensitivity of 86%. By comparison, the sensitivities of fasting glucose and hemoglobin A1c were 14 and 47%, respectively. This discovery provides a foundation for developing a new diagnostic test for early insulin resistance syndrome and a practical screening tool for the early identification of individuals at risk for type 2 diabetes.
Does Physical Health Differ by Physical Activity in Diabetic Middle-aged Males?

Introduction: The purpose of the study was to assess the relationship between physical activity and physical health in diabetic middle aged males.

Method: This cross sectional analysis used 2013 BRFSS data from South Carolina, West Virginia, Tennessee, Alabama, and Mississippi in multiple linear regression analysis.

Results: The results indicated that middle aged males reported higher days of physical health for all levels of physical activity after controlling for alcohol use, tobacco use, educational level, employment status, weight, age, and race/ethnicity.

Conclusion: Providers should assess levels of physical activity in their middle aged diabetic male patients and, if needed, provide patient education for the importance of physical activity for their physical health.

IRB/IACUC# 2015-105

The Association between Child Health Status and Family Functioning with Risk for Type 2 Diabetes among 10-14 Year Olds

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Abstract

Introduction: Obesity is a risk factor for type 2 diabetes (DM2), and family environment stressors can increase risk of obesity among children and adolescents. Family factors such as parental divorce, cohabitation, and remarried family relationships are among these stressors. For example, living in a single-parent family is positively associated with BMI and greater risk of obesity. Poor family functioning has also been linked to overweight and obesity in children. Research, however, has not assessed associations between these stressors and risk for DM2. The purpose of this study was to assess whether child health status and family functioning are associated with being high risk for DM2 among Mexican American children aged 10-14 years.

Methods: This cross-sectional study included 298 children and a parent/caregiver. High risk for DM2 was determined by having ≥ 3 of these 5 risk factors: first or second degree relative with DM2, BMI ≥ 95th percentile, blood pressure ≥ 95th percentile, elevated glucose, positive for Acanthosis Nigricans. Logistic regression was used to estimate odds ratio (ORs) and 95% confidence intervals (CIs) for the association between child’s health status and family functioning with being high risk for DM2. Multiple regression controlled for child factors (age, ethnicity, gender), parent/legal guardian’s factors (marital status, health status, relationship to child), and household factors (primary language spoken in the household and highest household education).

Results: Of 298 children, 91 (31%) were high risk for DM2. Parents rated the child’s health as poor/fair/good for 105 (35%) of child participants. Children with poor/fair/good health status were over 5 times (OR: 5.37; 95% CI: 2.84-10.14) more likely to be high risk for DM2 compared to children with very good/excellent health status. None of the family functioning predictors (sharing ideas about things that matter, relationship to child, making decisions together, and coping with demands of parenting) were significantly associated with being high risk for DM2.

Conclusions: Our research shows that a parent’s assessment of their child’s health predicts risk for DM2. This may be important for clinical visits, such as well child visits, or for programs aimed at reducing DM2 in children. While our research did not demonstrate an association between family functioning and risk for DM2, these factors should be explored further with questions obtained from validated measures.

IRB/IACUC# 2012-151
Results: Student survey responses demonstrate clearly that student question creation holds promise as an active learning tool with Pharmacy subject matter.

To test this hypothesis, we conducted an observational, cross-sectional study of over 30 asymptomatic, non-diabetic human subjects who were recruited though an approved IRB protocol. Antecubital venous blood was drawn into lavender-top tubes containing EDTA as the anticoagulant. The blood samples, prior to NMR measurements, were allowed to spontaneously settle in the tube thereby creating two phases: a liquid supernatant (plasma) and blood cell pellet. The NMR relaxation constants T1 and T2 were determined using a Bruker mq20 Minispec NMR instrument operating at 20MHz. The data were collected using inversion recovery and modified Carr-Purcell-Meiboom-Gill pulse sequences, respectively. The NMR time-decay curves were transformed using an inverse-Laplace algorithm in order to extract T2 values. In addition, we measured over 100 diagnostic biomarkers on each subject and correlated the NMR measurements with established markers of metabolic function. The supernatant water T2 values from whole blood were compared to those obtained from fractionated plasma samples and to the other 100-plus biomarkers. The associations were quantified using parametric and non-parametric correlations and the Student t-test. Statistically-significant bivariate correlations were observed between whole blood water T2 and and lipid biomarkers, which are associated with insulin resistance and metabolic disease.

Whole Blood NMR Relaxometry for the Detection of Insulin Resistance

Time-domain nuclear magnetic resonance relaxometry (TD-NMR) is a practical method for measuring the physical and dynamical properties of complex, heterogeneous samples. In prior work, we showed that TD-NMR measurements of human plasma or serum report on an individual’s metabolic status, particularly with respect to insulin resistance. The relationship between plasma water transverse relaxation time (T2) and insulin resistance is mediated by subtle subclinical shifts in protein and lipoprotein levels in the circulation. The previous test required separation of blood cells in order to conduct T2 measurements on isolated plasma or serum. We hypothesized that this separation may not be required, as it is conceivable that similar metabolic relationships could be gleaned from T2 measurements on water in whole blood.

To test this hypothesis, we conducted an observational, cross-sectional study of over 30 asymptomatic, non-diabetic human subjects who were recruited through an approved IRB protocol. Antecubital venous blood was drawn into lavender-top tubes containing EDTA as the anticoagulant. The blood samples, prior to NMR measurements, were allowed to spontaneously settle in the tube thereby creating two phases: a liquid supernatant (plasma) and blood cell pellet. The NMR relaxation constants T1 and T2 were determined using a Bruker mq20 Minispec NMR instrument operating at 20MHz. The data were collected using inversion recovery and modified Carr-Purcell-Meiboom-Gill pulse sequences, respectively. The NMR time-decay curves were transformed using an inverse-Laplace algorithm in order to extract T2 values. In addition, we measured over 100 diagnostic biomarkers on each subject and correlated the NMR measurements with established markers of metabolic function. The supernatant water T2 values from whole blood were compared to those obtained from fractionated plasma samples and to the other 100-plus biomarkers. The associations were quantified using parametric and non-parametric correlations and the Student t-test. Statistically-significant bivariate correlations were observed between whole blood water T2 and lipid biomarkers, which are associated with insulin resistance and metabolic disease.

Comparing Traditional Case-Based Application and Student Question Creation Exercise on Student Performance and Perceptions

Objective: To compare impact of traditional case-based application exercise to student question creation exercise on a) student exam performance, b) student perceptions of enjoyment, competence, understanding, effort, interest in continuing participation and interest in subject.

Methods: Subjects were 84 second-year pharmacy students in fall 2015 pharmacotherapy course. Research focus was active learning dealing with chronic kidney disease-mineral bone disorder (CKD-MBD). Students formed 12 teams with 6-7 students each. Teams were randomly assigned to either case-based or student question creation exercises using PeerWise. Four multiple choice questions related to CKD-MBD assessed student performance prior to and after participation. After completion an online survey assessed perceptions of enjoyment, competence, understanding, effort, interest in continuing participation, and interest in the subject matter. The UNTHSC Institutional Review Board approved the study protocol.

Data Analysis: Two sample t tests assuming equal variances were used to compare the group experiencing student question creation with the group experiencing the case-based exercise on a) enjoyment, competence, understanding, effort, interest in continuing participation, and interest in the subject matter and b) gain scores on four multiple choice test questions administered prior to and after introduction of the subject.

Results: Student survey responses demonstrate clearly that student question creation holds promise as an active learning tool with Pharmacy students. Two sample t tests assuming unequal variances found statistically significant differences in favor of the student question creation group on enjoyment and interest in the subject matter although other differences between the two groups on the survey questions were not significant. A two sample t test comparing the traditional case-based group to the student question creation group on gain score from pretest to posttest on the four questions related to CKD-MBD found statistically insignificant differences between the groups.

Conclusions: Based upon student perceptions, student question creation has demonstrated potential as a useful learning tool. Insignificant differences on some measures of student perception as well as pretest-posttest gain scores may be due to a relatively small sample size and a very small number of test questions. The researchers expect that larger samples and repeated applications will confirm and extend positive findings in support of student question creation.
802  Poster  Classification:  Staff (Not For Competition)
Presenter:  Jeffrey Mott, DHSc, PA-C  Department:  <-- Please Select Department -->
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Humeral Head Intravenous Access: Filling the Military Training Gap

Purpose: Traumatic life-threatening injuries often require immediate intravenous access for the delivery of lifesaving fluids and medications. When intravenous access is difficult or impossible to achieve, alternate methods of fluid and medication administration are essential. One method is intravenous infusion, which is the process of delivering fluids directly into the bone marrow space to provide non-collapsible entry into the circulatory system. Although the U.S. Army has spearheaded the initiative of treating wounded service members on the battlefield by using the humeral head needle, it is at a disadvantage by not having a realistic human anatomical model to train on the device. Military medical providers use live tissue models in the absence of a realistic simulations trainer. Despite the limitations of anatomical variations of live tissue, the U.S. Army weighed the risks and benefits of fielding the humeral head intraosseous needle and placed them into the medical equipment sets worldwide in 2015.

Description:
The U.S. Army Research Laboratory assessed the scientific and technical feasibility of using a low-cost medical simulator for training military medical personnel and developed a Partial Task Trainer to train the procedure. The research involved performing a comprehensive requirements analysis, identifying current gaps in training and prioritizing capabilities.

Results:
The research team followed a user-centric structured system engineering approach allowing for collaboration between stake holders and the development team to facilitate transitioning the technology. Military and civilian subject matter experts identified training gaps. Research was conducted to define technology requirements that would support training. After conceptual design and prototype development, usability evaluations were conducted at various stages of development to refine the final prototype.

Conclusions: Usability evaluations and subject matter expertise support the continuation of phase II prototype production of a partial task trainer for the insertion of a humeral head intraosseous needle.

Sponsor  Department of Defense
IRB/IACUC#  N/A N/A

803  Poster  Classification:  TCOM DO Student
Presenter:  Grace Rovner  Department:  Pediatrics
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Assessment of health literacy and potential barriers regarding Human Papillomavirus (HPV) and the HPV vaccine among parents/guardians

Purpose: As the number of epidemics that are currently threatening the health of Americans and the associated health consequences continue to grow, protecting future generations from sexually infected viruses has become a concern. With the recent release of Human Papillomavirus (HPV) vaccines, children have the chance to be protected from some of the more common and symptomatic types of the virus. However, vaccine uptake has remained low, leaving many children and adolescents at risk for contracting HPV once they become sexually active. This research study aims at increasing the uptake of the HPV vaccine by identifying potential barriers in completing the three-dose regimen. Information gained will provide the basis for developing a new health literacy intervention within the department of Pediatrics at UNT Health Science Center (UNTHSC).

Methods: Parents/guardians of pediatric patients at the department of Pediatrics at UNTHSC will be asked to participate in the study. There are two parts to this study: the initial interview used to establish a baseline, and a follow-up interview to estimate efficacy of the health literacy intervention. The multiple choice questionnaire evaluates the parent’s/guardian’s general perception of vaccinations, knowledge of HPV and the HPV vaccine, and potential obstacles that parents may face when obtaining immunizations for their child. After the initial interview, there will be a short 5 to 10 minute education session about HPV and the HPV vaccine, and the parent/guardian will be given a handout to take home. Additionally, a different questionnaire will be given to pediatricians to help assess their thoughts and perceptions behind the low uptake of the HPV vaccine among adolescents and recommendations of better ways to improve uptake of the vaccine.

Projected goals/findings: The goal is to increase parent/guardian understanding about HPV and the HPV vaccine and to determine barriers to receiving the vaccination. By assessing parent/guardian retention of the information regarding HPV and the HPV vaccine and changes in their perception and/or opinions about HPV and the HPV vaccine, this project will gauge the effectiveness of the education session and handout method. If parents/guardians are made aware of HPV and the HPV vaccine, we predict that more children would receive the vaccine and complete all three doses of the vaccine. Moreover, since the population being evaluated in this study tends to have lower levels of education and income, identifying barriers will help increase our understanding of how to get the HPV vaccine to these individuals and be affordable for them. This project is ongoing and the protocol will be adjusted according to the study results.

Sponsor  IRB/IACUC#  2015-148
Improving Communication Skills in Orthopedic Residents: Dale Carnegie Experience

Background: Professionalism and communication skills have often been described as essential to quality patient care. In 1999, the ACGME introduced six areas of residency competency, one of which was communication skills. There have been many different approaches to implementing and improving residents’ communication skills by residency programs since that time. In this study we propose another possible approach for improving Orthopedic surgery residents’ communication skills through the Dale Carnegie Training Course.

Methods: Six Orthopedic Surgery residents were randomly selected over a four-year period to attend the Dale Carnegie interpersonal communication skills training course. 360-degree (based on Clinical/Nursing/Admin Staff) and Faculty evaluations were collected for all residents, including those that did not attend the course, before and after the course. The results of the evaluations were then compared using analysis of variance (ANOVA) and analysis of covariance (ANCOVA) statistical test for continuous variables. Regression analysis was also performed to identify independent outcome predictors. P values generated with P < 0.05 were considered statistically significant.

Results: There was a statistically significant improvement in the 360-degree evaluations of residents that attended the course as compared with those that did not, p = 0.0015. There was no statistically significant improvement in faculty evaluation scores of residents that attended the course over those that did not, p = 0.1583. However, it appears that some residents that attended improved more than others, p = 0.0097, and perhaps gained more from the experience.

Conclusions: Communication skills and professionalism are essential components of quality patient care and should be emphasized during medical education. The Dale Carnegie course could be considered as a possible effective tool for improving residents’ communication skills. Our study revealed a statistically significant improvement in the residents evaluations completed by nursing staff, clinic staff and other departments. This course is a time tested program with expansion to multiple franchises around the world, with consistent and reliable results. It may not be financially reasonable for residency programs to send every resident for this training, however, it might be utilized as an alternative for residents identified as “at risk” or those with noted poor communication skills by their program directors.

Sponsor: UNT
IRB/IACUC#: 2010-155

The Impact of Guided Reflection in the Professional Development of Medical Students in the Context of Death and Dying.

Statement of the Hypothesis

Medical students often struggle with end-of-life issues. To address this need, two educational sessions about death and dying were introduced to fourth year medical students during their Core Geriatric Clerkship. The curriculum included the use of guided reflection, which involves facilitated discussion and reflective writing, to help students identify and cope with their feelings about death and dying. Many students had reported struggling to identify their role as a health professional related to the topic of death and dying. This study explores the impact of helping students reflect on their understanding of a medical professionals role in death and dying.

Brief Summary of Materials and Methods

The idea for this project originated from the results of a previous study conducted by the Reynolds Geriatric Education and Training in Texas (GET-IT) program. A pre- and post-survey was administered to fourth year students (n=805) prior to the start and again at the end of the 4 week Core Geriatric Clerkship. The survey found that students felt less comfortable discussing palliative care and end-of-life issues after exposure during the rotation (pre-test mean: 4.20, post-test mean: 3.59, p)

A Summary of the most pertinent, significant results

As part of their core geriatrics clerkship, fourth year medical students were required to attend two sessions on end-of-life care that included lecture, guided discussion, community resources and a reflective writing assignment. The follow-up self-assessment survey greatest improvement in competency was end-of-life care. In the pre-test students had reported 1.96 average mean in their comfort level related to End of Life Care; and, after participation in the revised curriculum, students reported an average mean score of 3.02. This findings indicate that the average student now feels they have “significant ability” to talk about end-of-life issues.

Conclusions derived from the presented data

Fourth year medical students at UNTHSC were found to have struggled with communication related to palliative care and end-of-life issues. By providing a safe platform for review and communication on end of life issues, the study found that students reported improved confidence in the ability to cope with death and dying. While 150 minutes of instruction cannot fully prepare students to cope with these difficult and sensitive issues, students can gain confidence in this area of their professional role as future physicians. Through peer support and faculty feedback, the guided reflection increased students’ belief in their own competence, freeing them to use their unique life experiences and skills to cope with death and dying.

Sponsor: Donald W Reynolds Foundation
IRB/IACUC#: IRB 2009-076
Role of Service Learning in Medical Students' Clinical and Professionalism Competencies

The role of service learning in students’ acquisition of knowledge, skills and professional attitudes is poorly understood. Osteopathic medical students perform service during the first two years as one of the required elements of their ‘doctoring’ course. The availability of this data provides the first opportunity to more systematically examine the role of service learning in students’ acquisition of clinical and professional attitudes.

Self-report data from osteopathic medical students’ required service is required for each activity or event and is now collected electronically. Starting in Fall 2015 semester, this data is now collected electronically. Data includes the type of service, and Likert scale ratings of students overall satisfaction with the experience, and the extent to which each activity meets certain learning objectives and promotes professional values such as service, integrity, respect and collaboration.

Data from 458 students with a total of 1569 service learning evaluation reports are available for preliminary analysis. The most common type of service is assisting at indigent clinics, n=498 events, followed by health fairs n= 310, sporting events=203, health education and safety for children n=154 and direct health services including OMM n=120. 65.0% of students strongly agreed and 31.8% agreed the overall experience of a specific event was good for of them. 89.7% strongly agreed health career promotions was an overall good experience, followed by 88.7% for homeless services and 83.3% for school and sports physicals. 94.3% strongly agreed clinical skills objectives were met during homeless services events and 81.3% for school and sports physicals. Basic descriptive statistics facilitate understanding of students’ attitudes toward various types of service activities and generate additional hypotheses regarding satisfaction, learning objectives and professional values.

Service learning is designed to provide opportunities to engage in experiential learning which is task and problem specific, improve clinical skills, and experience the benefits of altruistic behavior. The model of learning applied here originated with John Dewey (1938) and more recent elaborations by Kolb (1984) and Boyatzis (2000) who addresses issues of emotional intelligence in professional competencies. This is a step in understanding the impact of service learning in meeting specific I objectives in medical education.

Sponsor: N/A
IRB/IACUC#: 2015-159

Genetic and pharmacological inhibition of ER stress-induced ATF4/CHOP pro-death pathway prevents myocilin misfolding and rescues mouse models of glaucoma

Purpose: We recently demonstrated that ER stress-induced pro-death markers including ATF4 and CHOP are significantly increased in human post-mortem glaucomatous trabecular meshwork (TM) tissues. The purpose of this study was to further explore the role of ATF4/CHOP in myocilin misfolding in TM and IOP elevation.

Methods: ATF4 and CHOP levels were analyzed in the TM of Tg-MYO437H and dexamethasone (Dex)-treated mice by Western blotting (n=3). Conscious IOP was monitored by rebound tonometer in C57BL/6 mice injected intravitreally with Ad5 Null or ATF4 virus. IOP was measured in Chop-/Tg-MYO437H mice and compared to Chop+/Tg-MYO437H and WT mice. The effects of CRISPR-Cas9 mediated knockdown of ATF4/CHOP on myocilin accumulation was studied in TM-5 cells expressing mutant myocilin. Myocilin accumulation and ER stress was examined in TM cells treated with pharmacological inhibition of the ATF4/CHOP pathway with 100 and 200nM of ISRIB (an inhibitor of the integrated stress response) for 48 hours. Furthermore, ocular hypertensive Tg-MYO437H mice were treated with an intravitreal injection of ISRIB (2ul, 2mM) and IOP was measured 4 days post-injections.

Results: Western blot analysis demonstrated increased ATF4 and CHOP levels in the iridocorneal angle tissues of Tg-MYO437H and Dex-treated mice. Forced expression of Ad5.ATF4 led to significant IOP elevation in WT mice (16mmHg in null vs 23mmHg in Ad5.ATF4-injected mice; p+/+Tg-MYO437H mice (22mmHg, n=16) had significantly elevated IOP compared to WT Chop+/+ littermates (16.5mmHg, n=4), while Chop-/ Tg-MYO437H mice (19mmHg, n=8) did not elevate IOP compared to Chop-/- littermates (18mmHg, n=6) indicating that deletion of Chop rescues ocular hypertension in Tg-MYO437H mice. In addition, Cas9 targeting of ATF4 or CHOP dramatically reduced ATF-4 and CHOP levels and also reduced myocilin accumulation and ER stress in TM-5 cells. Treatment of TM cells with ISRIB (100nM) dramatically reduced myocilin accumulation and also prevented ER stress. Pharmacological inhibition of the ATF4/CHOP pathway with ISRIB (2mM) significantly reduced elevated IOP in Tg-MYO437H mice (14.5mmHg in vehicle vs 10mmHg in ISRIB treated Tg-MYO437Hmice, p

Conclusion: These studies indicate that genetic or pharmacological inhibition of the ATF4/CHOP pathway may provide a novel approach to glaucoma treatment.

Sponsor: NIH EY022077
IRB/IACUC#: 2015-002
Phosphoproteomic changes in the retina following optic nerve crush

Purpose: Phosphorylation is a major type of protein post-translational modification. In this study, we evaluated the phosphoproteomic changes in the retina induced by optic nerve crush (ONC) in the mouse, an acute model of central nervous system (CNS) axonal injury. The functional role of an identified major phosphoprotein was further studied.

Methods: Intraorbital ONC was performed in adult C57BL/6J mice. Retinas were collected at 0, 6, and 12 h following optic nerve injury. Retinal proteins labeled with CyDye-C2 were subjected to 2D-PAGE. 2D gel phosphoprotein staining was performed, followed by in-gel and cross-gel image analysis. The ratio change of protein differential phosphorylation following ONC was obtained. Proteins with significant changes in phosphorylation (ratios ≥ 1.5) in retinas of the injured eyes compared to the control eyes were spot-picked, tryptic digested, and peptide fragments were analyzed by MALDI-TOF (MS) and TOF/TOF (tandem MS/MS). Proteins identity was based on 10 or more peptides. Identified proteins were validated by western blotting and immunofluorescence staining in separate experiments (n ≥ 3). Cell migration assay and flow cytometry-based phagocytosis assay were performed using primary cultured mouse optic nerve astrocytes.

Results: Intraorbital ONC increased phosphorylation of many retinal proteins. Among them, 53 significantly phosphorylated proteins were identified. Significantly phosphorylated proteins in optic nerve crushed retinas include protein kinase C alpha, glycogen phosphorylase, tubulin-folding cofactor B, among others. One of the identified phosphoproteins, PEA-15, was confirmed by western blot analysis; ONC increased phosphorylation of this protein without affecting its basal protein expression level. Immunofluorescence staining using phospho-PEA-15-specific antibody demonstrated that increased phosphorylated PEA-15 co-localized with GFAP, a marker for Müller cells and astroglia in the retina and optic nerve. PEA-15 knockdown significantly promoted optic nerve astrocyte migration and suppressed phagocytosis.

Conclusions: Our novel approach identified specific proteins whose phosphorylation was increased by ONC. One of these proteins, PEA-15, mediates major optic nerve astrocytic functions, which likely affect retinal neuronal survival and regeneration after injury. These new insights will lead to novel therapeutic targets for retinal and CNS neurodegeneration.

Sponsor: N/A
IRB/IACUC#: 2015-0002

Epigenetic regulation of TGFβ2 in the pathogenesis of glaucoma

Primary open angle glaucoma (POAG) is a leading cause of blindness worldwide. The primary risk factor for the development and progression of this optic neuropathy is increased intraocular pressure (IOP) caused by glaucomatous damage to the trabecular meshwork (TM). The glaucoma-associated factor, transforming growth factor beta 2 (TGFβ2) is increased in the TM of POAG patients. TGFβ2 elevates IOP in perfusion cultured human eyes and in rodents. We hypothesize that histone acetylation plays a role in dysregulated TGFβ2 expression. To test our hypothesis, we treated primary non-glaucomatous human TM (NTM) cells as well as perfusion cultured bovine eyes with 10 nM thailandepsin-A (TDP-A), a potent histone deacetylase inhibitor. We found that TDP-A increased protein acetylation in the TM using Western immunoblotting. Chromatin immunoprecipitation showed that TDP-A induced histone hyperacetylation associated with the TGFβ2 promoter. This change of acetylation significantly increased TGFβ2 expression in NTM cells as shown by quantitative PCR (n=6, p
The role of canonical Wnt signaling and K cadherin in the regulation of intraocular pressure

Purpose: Primary open angle glaucoma (POAG) is the most prevalent form of glaucoma and has been associated with pathological changes in the trabecular meshwork (TM), the primary site of aqueous humor outflow in the eye. We have found that inhibition of canonical Wnt signaling in the TM raises intraocular pressure (IOP), and restoration of Wnt signaling normalizes IOP, though the mechanisms by which Wnt signaling maintains TM homeostasis are unknown. We hypothesize that the canonical Wnt signaling pathway in the TM regulates IOP via caderhins junctions.

Materials and methods: We studied five cadherin isoforms abundant in the TM as shown by exome sequencing of normal and glaucomatous human TM (NTM and GTM, respectively) tissues. For in vitro studies, NTM cells (gift from Novartis) were treated with or without recombinant 100ng/ml Wnt3a or 1ug/ml sFRP-1 or both for 4-48 hours. Membrane protein fractions were isolated for western immunoblotting (WB) and probed for the cadherin isoforms. TM cells were also immunostained for cadherin isoforms or β-catenin. RNA was extracted from TM cells for cDNA synthesis and qPCR analysis of cadherins. Ad5.CMV recombinant adenoviruses encoding E cadherin, K cadherin, and/or sFRP-1 were injected unilaterally into the eyes of 4-6 month old female BALB/cj mice (n=6). Conscious IOP of both eyes was then non-invasively measured for up to 35 days.

Results: WB showed that Wnt3a TM cell membrane associated K-cadherin, which was inhibited with the addition of the Wnt antagonist sFRP-1. Immunostaining showed that β-catenin accumulated on TM cell membrane upon Wnt3a treatment, and filopodia-like connections formed between TM cells. qPCR showed that Wnt3a also significantly increased K cadherin expression (n=3, p<0.05).

Conclusion: Our results suggested that cadherins play a role in the regulation of TM homeostasis and IOP via the Wnt signaling pathway.

Sponsor
IRB/IACUC# 2015-0002

GRα and GRβ expression levels in trabecular meshwork determines steroid responsiveness upon glucocorticoid treatment

Purpose
Glucocorticoid (GC) induced ocular hypertension (OHT) is a serious side effect of prolonged GC therapy with patients showing elevated intraocular pressure (IOP). Two major isoforms of glucocorticoid receptor (GRα and GRβ) regulate GCs sensitivity and specificity in various tissues. GRβ acts as a dominant negative regulator of GC activities and has been shown to regulate GC responsiveness in trabecular meshwork (TM). We evaluated GRα and GRβ expression levels in two mouse strains and studied how expression levels regulate GC and GC-induced OHT.

Methods
TM cells from C57BL/6J and BALB/cj mice strains were isolated and characterized. RNA was isolated from TM cells and evaluated for GRα and GRβ expression levels using quantitative (Q)-PCR. To study how both TM cell lines respond to Dexamethasone (DEX) (100nM) and myocilin (MYOC) expression in TM cells was determined by Q-PCR analysis. Three month old C57BL/6J and BALB/cj mice strains were used to evaluate changes in IOP upon DEX treatment. Mice were peri-ocularly injected with DEX-Acetate (100ug/eye) in both eyes. Conscious IOP measurements were taken using a TonoLab tonometer. Two-tailed Student’s t-test and One-way ANOVA were used for statistical analysis.

Results
MTM cells from both strains (C57BL/6J and BALB/cj) expressed TM markers, including collagen IV, laminin and α-smooth muscle actin. GRα expression levels between both strains were similar. TM cells from BALB/cj mice expressed significantly higher levels of GRβ compared to TM cells from C57BL/6J. When TM cells were treated with 100nM DEX, TM cells from C57BL/6J showed induction of myocilin expression compared to untreated controls whereas, TM cells from BALB/cj did not show myocilin induction. IOP measurements upon DEX-Acetate treatment showed significant IOP elevation in C57BL/6J mice (ΔIOP of 3.5mmHg, p<0.05).

Conclusions
In mouse, GRα and GRβ expression levels determines GC responsiveness. Higher GRβ expression levels leads to GC resistance. The current findings provide an important foundation for comparisons of GRα and GRβ expression levels in the TM among different strains. Also, manipulating GRα to GRβ expression levels holds a promise for desensitizing cells and tissues to GCs effects.

Sponsor
2R01EY016242
IRB/IACUC# 2015-0002
Purpose: The endothelin system has been shown to play a causative role in the neurodegenerative effects seen in animal models of glaucoma. However, the mechanisms leading to neurodegeneration need to be examined further. The goal of this study was to investigate the endothelin signaling pathway to determine the contribution of extracellular signal-regulated kinases 1 and 2 (ERK1/2) to endothelin-mediated cell death.

Methods: Male retired breeder Brown Norway rats were subjected to IOP elevation by the Morrison’s method and maintained for 2 and 4 weeks. Retinal sections obtained from the rats were subjected to immunohistochemical analysis of ETA receptor expression. In a separate set of experiments, Western blots were performed on transformed 661W cells transiently transfected with either the ETA receptor or ETB receptor cDNA expression vector. Another set of experiments was performed with stable clones overexpressing the ETA receptor. The cells were grown on 100 mm dishes and treated for 24 hr with 100nM endothelin-1 (ET-1) or endothelin-3 (ET-3). Immunoblot analysis of levels of endothelin receptor and ERK1/2 phosphorylation was carried out. Results: An increase in immunostaining for ETA receptors was observed mainly in the inner plexiform layer and a modest increase was also observed in the RGC layer which was significant at 4 weeks of IOP elevation. Cell culture experiments showed an appreciable upregulation of ETB receptors following overexpression of ETA receptors and a reciprocal upregulation of ETA receptors following overexpression of ETB receptors. A 1.8-fold increase in ERK1/2 phosphorylation was observed in stable clones overexpressing ETA receptors, which was further elevated 2-3 fold after treating cells with either endothelin-1 or endothelin-3, compared to empty vector transfected cells. Conclusions: While the two endothelin receptors may have distinct functions, there is a significant overlap of the ETA and ETB receptor mediated signal transduction pathways and there appears to be some level of cross-talk between the two receptors. While there is a substantial body of evidence for the pro-survival role of ERKs, prolonged activation of ERK1/2 has been shown to be associated with cell death. While the mechanisms are not completely clear, the current study points to an association of ERK1/2 with cell death following overexpression of ETA and ETB receptors.

Sponsor: NBA Training Grant - T32 AG020494
IRB/IACUC#: 2013/14-44-A05
Tissue transglutaminase causes intraocular pressure elevation in mice

Purpose: The profibrotic cytokine TGF-β2 increases expression of the crosslinking enzyme tissue transglutaminase (TGM2). In the trabecular meshwork (TM), excessive crosslinking of ECM proteins mediated by TGM2 could increase extracellular matrix (ECM) protein deposition, thereby decreasing the aqueous humor outflow facility. We hypothesize that increased expression of TGM2 increased ECM crosslinking in TM cells, and increases aqueous humor outflow resistance leading to elevated intraocular pressure (IOP) in mice.

Methods: MTM cells were grown to confluency and transduced with Ad5.TGM2 (MOI of 75). On Day 5, MTM cells were fixed with 4% PFA for immunocytochemistry (ICC). Ad5.TGM2 (1.28 \times 10^6 pfu in 2ml) was injected intravitreally into the left eye of female BALBc/J retired breeder mice (n = 18). The uninjected (right) eye served as a control. Daytime conscious IOP measurements were taken twice a week using a TonoLab rebound tonometer for approximately 3 weeks. Aqueous humor outflow facilities (C) was studied on day 23 (n = 6) using our published constant flow infusion method.

Results: In cultured MTM cells, treatment with Ad5.TGM2 increased immunostaining of ε-(γ-glutamyl)lysine (GGEL) bonds, demonstrating increased TGM2 crosslinking activity after treatment with Ad5.TGM2. In BALBc/J mice, injection of Ad5.TGM2 significantly increased IOP from day 14 to 22, with the maximum difference elevation at Day 19, (15.86 +/- 1.06 mmHg (injected) versus 10.7 +/- 0.48 mmHg (control) (p < 0.05).

Conclusion: Increased expression of TGM2 in mouse TM cells increases the ECM cross-linking activity of TGM2. Increased expression of TGM2 in the TM of the living mouse increases aqueous outflow resistance and elevates IOP. In the future, we will study whether TGM2 is responsible for TGF-β2 induced ocular hypertension.

Sponsor N/A
IRB/IACUC# 2015-0002

Validate Grx2 gene knockout mice as a new model for age-related retinal degeneration

Purpose: Age-related macular degeneration (AMD) is a leading cause of blindness worldwide. The poorly understood pathogenesis has greatly hindered our progress in therapeutic development. To address this shortcoming, this project was designed to examine how retinal redox dysregulation leads to AMD and characterize glutaredoxin 2 (Grx2), a mitochondrial thiol redox regulating enzyme, knockout mice as a new animal model for AMD.

Methods: The retinal pigment epithelium (RPE) layers were isolated from healthy and AMD donor eyes. Grx2 protein levels were measured by Western blot analysis. Primary RPE cells were isolated from wild-type (WT) and Grx2 knockout (KO) mice for the in vitro study. The visual function of WT and Grx2 KO mice were examined by fundus photography and scotopic electrotinography (ERG). H&E staining was used for histological exams. RPE structural changes were assessed by immunostaining of tight junction protein ZO-1. Lipofuscin autofluorescence was examined on cryostat sections. The level of protein glutathionylation (PSSG) was measured by immunoblotting using anti-PSSG antibody.

Results: Grx2 protein level and enzyme activities were decreased by approximately 30% in AMD donor eyes. Primary RPE cells isolated from Grx2 KO mice were more sensitive to H2O2-induced oxidative damage than WT RPE cells. Grx2 KO mice developed age-dependent retinal degenerative pathology. By 12 months of age, Grx2 null mice showed ~50% decrease in a-wave and ~30% decline in b-wave amplitudes (n=8, P < 0.05).

Conclusions: Grx2 plays a critical role in maintaining the mitochondrial redox homeostasis in the aging retina. Grx2 deficiency causes PSSG accumulation and sensitizes RPE cells to age-related oxidative damage, leading to RPE degeneration and photoreceptor damage. As a new animal model for AMD, Grx2 KO mice will provide new insights into the pathogenesis and therapeutics of AMD.

Sponsor Biofocus Foundation
IRB/IACUC# 2012/13-18
Risk-based Exposure Evaluation Process: Protecting Worker Exposure to Active Pharmaceutical Ingredients

The purpose of this project is to support Alcon’s Risk-based Exposure Evaluation Process (REEP). The objective of REEP is to transfer Novartis’s decision-making process from a hazard-based approach to a risk-based, data driven approach in order to protect their pharmaceutical workers’ exposure to active pharmaceutical ingredients (APIs) during the manufacturing process. Personal breathing zone air sampling was conducted for the high risk APIs to determine personal exposure during different unit operations. Sampling results were compared to Novartis Internal Occupational Exposure Limits (IOEL). Bayesian statistical analysis was performed to determine if a change in control is necessary and to interpret findings. While REEP is a continuous process, these preliminary results revealed the first set of risk-based API exposure data for Alcon’s six pharmaceutical sites. Based on the results, improvements to multiple levels of control such as engineering, administrative, and respiratory protection equipment (RPE) are currently in the process of implementation.

Effect of BAMBI expression on intraocular pressure and aqueous humor outflow facility in mice

Purpose: Elevated intraocular pressure (IOP) is an important risk factor in the development of glaucoma. TGFβ2 is well known to be involved in regulating both the extracellular matrix in the trabecular meshwork (TM) as well as ocular hypertension. BAMBI (BMP and activin membrane-bound inhibitor), a TGF-β pseudoreceptor, has been shown to be a negative regulator of TGF-β2. However, the role of BAMBI in regulating IOP is unknown. We investigated whether knockdown of BAMBI results in ocular hypertension in mice due to uninhibited TGFβ2 signaling.

Methods: B6;129S1-Bambitm1Jian/J mice were injected intravitreally with 2.5x10⁷ pfu of either Ad5.TGFβ2 (n=10), Ad5.Cre (n=9), or Ad5.TGFβ2 + Ad5.Cre (n=10), in one eye of each animal. The contralateral uninjected eyes were used as negative controls. IOP was measured using a TonoLab rebound tonometer. Aqueous humor outflow facility was assessed using a constant flow infusion method. Student’s t-test was used to compare between vector-treated and control uninjected eyes.

Results: Injection with either Ad5.Cre, Ad5.TGFβ2, or Ad5.TGFβ2 + Ad5.Cre each induced ocular hypertension starting at day 7 post-injection and maintained significant IOP elevation throughout the 56 day time course compared to uninjected control eyes (p Conclusions: Here we show for the first time that conditional knockdown of BAMBI in the TM with Ad5.Cre induces ocular hypertension by reducing aqueous humor outflow facility. These data further explain the mechanisms involved in the development of glaucomatous TM damage and provide potential new targets to lower IOP.
Glutaredoxin 2 (Grx2) Protects Retinal Pigment Epithelial Cells from Oxidative Damage by Regulating Autophagy

Purpose: Glutaredoxin 2 (Grx2) is an oxidoreductase present in the mitochondria where it protects the organelle from oxidative damage and maintains its redox homeostasis. The purpose of this study is to evaluate the cytoprotective effects of Grx2 in human retinal pigment epithelial (RPE) cells and characterize its potential function in regulating autophagy.

Methods: Primary RPE cells were isolated from Grx2 knockout (KO) mice and treated with or without 400 µM H2O2 for 4 h. Human retinal pigment epithelial (ARPE-19) cells were transfected with either human Grx2 cDNA-containing plasmid (pCR3.1-hGrx2) or an empty vector pCR3.1. Cells were treated with or without 200 µM H2O2 for 16 h. Grx2 protein expression was detected by western blot analysis. Cell viability was measured by a colorimetric assay with WST8. The morphology of nuclear chromatin was assessed by staining with Hoechst 33342. Apoptosis was quantitatively analyzed by flow cytometry. The level of protein glutathionylation (PSSG) and autophagy pathway proteins were measured by immunoblotting.

Results: Primary RPE cells that lack Grx2 were more sensitive to oxidative damage. On the other hand, Grx2 overexpression protected RPE cells from H2O2-induced cell viability loss. Assessment of apoptosis indicated that cells transfected with Grx2 were more resistant to H2O2 with fewer cells undergoing apoptosis compared to vector control cells. PSSG accumulation was also attenuated by Grx2 overexpression with acute H2O2 challenge. Furthermore, protein levels of LC3II and Beclin-1, which are key molecules to initiate autophagy, were inhibited in Grx2 overexpressed cells with H2O2 treatment. Conversely, primary Grx2 KO RPE cells showed higher levels of LC3II and Beclin-1 under oxidative stress.

Conclusion: Grx2 rescues RPE cells from lethal oxidative damage, possibly through alleviation of ROS-related neurodegeneration. Moreover, Grx2 overexpression increases the autophagy process, protecting RPE cells from oxidative damage.

Sponsor: BrightFocus Foundation
IRB/IACUC#: 2012/13-18-A04

Overexpression of Endothelin A and B Receptors Enhances Calcium Mobilization in Ocular Astrocytes and Ciliary Epithelial Cells

Purpose: Endothelin-1 (ET-1), a vasoactive peptide, binds ETA receptor and ETB receptor to exert its role in multiple cellular processes. A growing body of evidence suggests that elevated levels of ET-1 and activation of its receptors contribute to neurodegeneration in glaucoma, where reactive astrocytes are found to induce damage of retinal ganglion cells. Overexpression of c-Jun, a transcription factor, has been shown to increase levels of ETB receptor, suggesting that the expression of ETB receptor is regulated by c-Jun. This study aims to determine if overexpression of ET-1 receptors affects calcium influx in response to ET-1 treatment.

Methods: Primary astrocytes were isolated from retina and optic nerve of rat pups postnatal 4–7 days. Calcium imaging using Fura-2-AM fluorescent dye was used to determine calcium influx following treatment of ET-1, in the presence and absence of BQ610 (ETA selective antagonist), or BQ788 (ETB selective antagonist) or no treatment (control). ETA, ETB and c-Jun were also overexpressed in Human Non-Pigmented Epithelial (HNPE) cells using DNA transfection and calcium mobilization was measured.

Results: Overexpression of ETA or ETB in HNPE cells significantly increased [Ca2+]i levels compared to control following ET-1 treatment at p2+ in primary astrocytes. Treatment with either BQ610 or BQ788 in primary astrocytes significantly (p2+) levels compared to control following ET-1 treatment.

Conclusion: This study demonstrated that ETA and ETB can mediate calcium influx in HPNE cells and primary astrocytes. ETA receptor stimulation produced a similar calcium influx in HPNE cells as ETB receptor activation, suggesting that both receptors may be involved in [Ca2+]i signaling. The increase in calcium can result in activation of cell death pathways that may explain the ET-1 neurodegenerative actions.

Sponsor: N/A
IRB/IACUC#: 2010/11-11-A05
RGC death in a mouse model of congenital glaucoma

Purpose: Mutation in the podosomal adaptor protein SH3PXD2B (nee) causes anterior segment dysgenesis, elevated intraocular pressure (IOP), and congenital glaucoma, as previously described in B10.A(H-2h)(4R)SgDvEg mice. We investigated the effect of the nee mutation in C57BL/6J mice with respect to IOP, total retinal ganglion cell (RGC) death, and RGC subtype specific death in nee mice containing the Trhr-GFP transgene (selectively expresses GFP in ON-OFF direction selective RGCs).

Methods: IOP and RGC death were measured in B6.Sh3pxd2bnee mutant (MUT) and wild type (WT) mice at post-natal days 30, 60, 75, and 90. C57BL/6J mice containing the Trhr-GFP transgene were crossed with B6.Sh3pxd2bnee to obtain nee mutant mice expressing GFP in ON-OFF direction selective RGCs. IOP was measured using a TonoLab tonometer. RGC damage was assessed by immunofluorescence of labeled retinal flat mounts using the GFP biomarker and NeuN.

Results: Significant IOP elevation was observed in MUT mice at days 30, 60, 75, and 90 compared to WT mice (p<value of 0.742. Significant differences in the percent cell survival of GFP positive RGCs was observed in MUT mice containing the Trhr-GFP transgene at 30 days (55.1±15%; n=4-6; p=0.0017), 60 days (16.5±4.6%; n=4-6; p

Conclusions: These studies characterized the nee glaucoma phenotype in C57BL/6J mice and demonstrate the specific susceptibility of ON-OFF direction selective RGCs. Future studies will identify susceptibility to additional subtypes of RGCs using this model system. These data are important to determine timing and onset of disease as well as identifying novel therapeutic targets.

Sponsor: Knights Templar foundation

IRB/IACUC#: 2015-0002
Conclusion: Our studies which involved the expression of σ1r were aimed to investigating the mechanisms by which ET-1 promotes the reactivation of primary rat ocular astrocytes. This reactivation could lead to dysfunction in the optic nerve and affect RGC survival.

Results: RGC death was accelerated in σ1r k/o ONC mice when compared with wild-type mice. σ1r k/o ONC mice injected with AAV2-CAG-α-SMA-GFP vector demonstrated significant increases in RGC numbers and activity when compared with α-SMA-k/o ONC mice injected with empty vector or non-injected α-S1 k/o ONC animals.

Conclusion: Our studies which involved the expression of σ1r in a system devoid of σ1rs, provided direct evidence of neuroprotective role of σ1r in RGCs when they are challenged by neurodegenerative insults.

Financial Disclosure: Supported by a grant from DOD (W81XWH-10-2-0003)
Anxiety in Obese Individuals is Associated With Leptin Concentration

Background: Obese individuals suffer from increased incidence of depression and anxiety. Recently research has suggested that appetite regulating hormones may modulate emotions. Although contradictory thus far, some studies suggest that leptin may play a role in mediating anxiety. Obese individuals have higher leptin concentrations primarily due to augmentation of adipose tissue. In addition to leptin’s role in regulating appetite, leptin receptors are also present in non-hypothalamic regions such as the amygdala and hippocampus that modulate emotional function. Obesity is well-known to confer leptin resistance, bringing into question its potential to contribute to emotional dysregulation.

Hypothesis: The following hypotheses were examined: (1) Obese subjects (OB) will have higher anxiety than normal weight controls (NW); (2) Leptin will be positively associated with anxiety independent of obesity status.

Methods: Bariatric candidates (OB) (n=71) (Mean age = 44.6 years and Mean BMI = 43 kg/m2) underwent pre-surgical assessment. Normal weight controls (NW) (n=30) were assessed for comparison. State anxiety was measured using the State-Trait Anxiety Inventory. Fasting blood samples were taken to analyze serum leptin. Difference in anxiety between OB and NW was analyzed using ANOVA. Logistic regressions were performed to ascertain the effects of leptin with and without obesity status on the likelihood that subjects would have high anxiety.

Results: There was a significant correlation between anxiety and leptin (r=.202, p=.004). Anxiety was higher for OB compared to NW (F=7.446, p=.008). Logistic regression for fasting leptin was statistically significant (X2=8.600, p=.003); explaining 12% of the variance in anxiety and correctly classifying 65.3% of the cases. Increasing leptin was significantly associated with increasing likelihood of anxiety. The model for leptin and obesity status was statistically significant (X2=9.566, p=.008). When leptin was adjusted for, the association between the anxiety and obesity was no longer significant. This shows that the relationship between obesity, leptin and anxiety was present in the obese, bariatric candidate sample but not in the NM control group.

Conclusion: Bariatric candidates have higher anxiety compared to NW counterparts. The association between leptin and anxiety is not independent of obesity status as it was observed in the obese, bariatric candidate group only. While the cause of anxiety is likely multifactorial further, the association between anxiety and leptin should be further explored.

Acknowledgements: This study was supported by NIH grants H75/CCH224064, HL04297 and HL64913 and approved by the IRB at the University of North Texas Health Science Center.

Sponsor: NIH grants H75/CCH224064, HL04297 and HL64913
IRB/IACUC#: 2007-053

Internet Accessibility and Perceptions for Possible Online Interventions

BACKGROUND: Healthcare costs are a serious escalating burden, especially within Medicare/Medicaid populations. The Internet and social media have made the flow of information cheaper and more efficient. Previous studies have shown increasing internet penetration into lower social economic households creating a potential opportunity to improve health outcomes.

HYPOTHESIS: The primary aim was to evaluate internet accessibility of patients of an urban clinic with large Medicare/Medicaid populations. The secondary aim was to evaluate racial/ethnic differences in preferences for using various formats with healthcare information.

METHODS: Patients in a family medicine clinic completed a 25-item survey. Logistic regression was performed to assess the association between race/ethnicity (Caucasian, Hispanic, African American, and Other) and likeliness to use selected formats for healthcare information (very unlikely/unlikely, likely/very likely) while controlling for gender, age, and income. A regression model was run for the following formats: online video, 3-4 page handout, and online chat/forum. Odds ratios and 95% confidence intervals were calculated.

RESULTS: A total 107 participants with the mean age of 45 (SD=16) completed the survey. Approximately 67% were females, 85% had internet access, 61% were on Medicare/Medicaid. Racial/ethnic distributions were 32% Hispanic, 33% Caucasian, 25% African-American, and 10% Other. All racial/ethnic groups connected to the internet using a phone more than a laptop, desktop, or tablet. Caucasians (70.0%) and Hispanics (59.3%) selected online video more often than other formats. African-Americans (57.1%) and Others (66.7%) were more likely to select handout than other formats. Adjusted analyses showed racial/ethnic differences in the likelihood of using selected formats to receive healthcare information. African-Americans were less likely than Caucasians to select online video (OR=0.18: 95% CI:0.05-0.69). Hispanics were less likely than Caucasians to select handout (OR=0.15: 95% CI:0.04-0.56) and online chat/forum (OR=0.14: 95% CI:0.03-0.61).

CONCLUSIONS: Medicaid/Medicare patients are interested in online interventions, but it is best individualized towards each patient in consideration of culturally related preferences. Future studies should further explore sociocultural differences in format preference given equal accessibility, and compare online interventions directly to traditional resources.

ACKNOWLEDGEMENTS: Material cost of the survey was funded by UNTHSC. This study was approved by the IRB at UNTHSC. IRB # 2015-125
Hypothesis: Obese subjects (OB) will have greater deficits in executive cognitive function (EXE) than normal weight controls (NW). Common psychological and biological markers that may predict EXE were explored.

Methods: Secondary data analysis of a one-year prospective study in a community bariatric surgical setting. OB (n=71) (Mean age=44.6 years, Mean BMI=43 kg/m2) underwent pre- and post-surgical assessments. NW matched for age and gender (n=30) were assessed for comparison. Self-report survey-assessed indicators of psychological dysfunction. Fasting blood samples were taken to analyze common clinical indicators. The Stroop test was used to determine EXE. Independent t-tests were used to analyze EXE between OB and NW. Relationships between EXE with biological and psychological indicators were explored using Pearson correlation. Significantly correlated variables were used in logistic regression to ascertain their ability to predict high or low EXE. Repeated measure t-tests were used to compare changes for OB in EXE at one-year post-surgery.

Results: OB had significantly lower EXE than NW at baseline (t=-2.491, p=.017). EXE was significantly correlated with Total Protein (r=-.279, p=.015) and Total Bilirubin (r=.327, p=.004). Logistic regression for Protein and Bilirubin was significant in predicting cognitive status (X2=8.117, p=.004). EXE was improved for OB at one year post-surgery (EXE (t=-2.491, p=.017)).

Conclusion: Increases in Total Protein and decreases in Total Bilirubin may be early biomarkers of executive dysfunction in severe obesity. These associations may represent distal markers of higher inflammation and lower antioxidant status and are consistent with other work on possible mechanisms for neuropsychiatric sequelae of obesity. Weight loss may ameliorate cognitive risk.
Does Alcohol Misuse Differ by Gender & Veteran Status in Adults Age 25+?

Introduction: Alcohol misuse has been reported as one of the most common and persistent mental health problems in veterans; however, female veterans may be at less risk than male veterans. Therefore, the purpose of this study was to determine whether alcohol misuse differs by gender and veteran status in a representative sample of adults 25 years and older.

Methods: This cross-sectional analysis used 2013 BRFSS data for adults 25 and older from the states of California, Florida, Texas, Virginia, and Washington. The relationship among gender, veteran status, and alcohol misuse (any drinking, binge drinking, and heavy drinking) was assessed using multiple logistic regression while controlling for demographic and psychosocial variables.

Results: About 54-58% of female and male veterans reported any drinking, 10-12% reported binge drinking, and 6-7% reported heavy drinking. In adjusted analyses, gender and veteran status were significantly related to alcohol misuse, but differently by type of drinking.

Conclusions: This study found that gender and veteran status are related to alcohol misuse, and female veterans may be at similar risk for heavy drinking as male veterans. Providers should continue to monitor male and female veterans for alcohol misuse.

Sponsor: N/A
IRB/IACUC#: 2015-105
Emergency Room Patient Presenting with Severe Hematuria

The purpose of this case study is to describe a patient who presented with hematuria and significant anemia secondary to a renal mass and stone complicated with hydronephrosis. In addition to highlighting the clinical features and medical management for this patient, our aim is to stress the importance of exploring and managing multiple causes for hematuria.

Methods:
History and physical information were obtained by medical staff on a 64 year old Hispanic male with a history of HTN, BPH, HLD, & prior bladder surgery (1985) who presented with sudden onset of gross hematuria, dysuria, and decreased urine output with red heavy clots for one day. The patient had similar episodes 6 months prior however the incident was milder and resolved on its own. PT also noted 10 lbs weight loss. PT is a retired police officer, fireman, and denied smoking, alcohol, or illicit drugs. Positive findings on physical included a reducible mid-epigastric hernia. There was a urinary catheter in place with gross blood in the Foley bag.

Results:
The patient's lab results indicated severe anemia with a hemoglobin/hematocrit as low as 7.9/26.7g/dL. Urine analysis showed large amounts of blood and few bacteria. BUN and creatinine were elevated. A non-contrast CT scan of the ABD/Pelvis showed right sided hydronephrosis secondary to obstructing mid ureteral stone, abnormal right perinephric stranding, abnormal 10 cm heterogeneous exophytic mass of the inferior right kidney, and gallstones. Work up for pre-op required MRV and Head CT to rule out IVC thrombus and metastasis. PT underwent stent placement for the stone prior to the radical nephrectomy. PT was also consented to have a prophylactic cholecystectomy for the gallstones. During the surgical removal, a lesion was identified on the pancreas suspicious for metastasis or inflammation and was later ruled out with EUS.

Conclusion:
Although most cases of hematuria are due to a urinary tract infection or urethral stone, it is important to do a thorough evaluation to rule out other significant life threatening causes of hematuria. A biopsy of the kidney done later identified the mass as stage T3 Clear Cell Renal Cell Carcinoma (CCRCC) extending to the renal sinus and major vein. Biopsy also showed glomerulosclerosis, urinary calculus, and chronic interstitial nephritis. This case illustrates and stresses the importance of thorough evaluation of the multiple causes of a patient presenting with hematuria.

Sponsor
IRB/IACUC#  2016-029
Mechanism of Supination External Rotation Short Oblique Ankle Fractures Revisited: A Cadaveric Study

PURPOSE: The Lauge-Hansen classification system for ankle fractures has been the most commonly used system because it explained mechanism of injury of several common fracture patterns. However, there are limitations to the original Lauge-Hansen experiments and we have chosen to focus our central objective of this study on the biomechanical mechanisms behind stage 1 & 2 supination-external rotation (SER) ankle fractures in a cadaveric model.

METHODS: 5 Fresh frozen cadaveric specimens were mounted into a custom made ankle rig with the tibia held rigid using half pins while allowing free movement of the fibula. The foot was secured to a wheel with a torque sensor attached to record examiner external rotational stress application. An electromagnetic tracking system was used to track the motion of the specimen with 6 degrees of freedom at each segment. A control arm was used to hold the foot in dorsiflexion while all other rotations were held in neutral. An ultrasound probe was used to monitor tibiofibular space as the examiner applied a controlled 100N maximal external rotational torque. Specimens were first tested with all ligaments intact prior to incremental resection of the anterior inferior tibiofibular ligament (AITFL) with repeat stress examination after each change.

RESULTS: All specimens withstood the normal state testing of up to 100N of external rotational force without any injury. However, 4 out of 5 specimens received short oblique fracture patterns to the distal fibula after partial (75%) or full AITFL resection. Comparison of pre and post radiographs, visual observation via dissection, and live ultrasound video confirmed these results. 3D kinematics were recorded and analyzed as well to determine bone movement and fracture timing and compared to ultrasound video of the tibiofibular space.

CONCLUSION: Prior studies have used unmeasured forces, non-physiological ligament strain rates, and poor alignment techniques. We sought to exclude the ligament strain rate and other design issues from our study by performing incremental resection of the AITFL as a synthetic mechanism for stage 1 SER ankle injuries and focusing on the reproducibility of the stage 2 fibula fracture in an SER injury. Our study demonstrated: 1. A 100N external rotational force did not result in an AITFL injury 2. Partial sectioning of the AITFL alongside a 100N external rotational force led to a reproducible oblique distal fibula fracture in a cadaveric ankle model.

Health Behaviors of Medical Students During the First Year of Medical School

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. However, the high stress of the academic environment of medical training makes students vulnerable to poor health behaviors. Research has shown that there is an association between high stress environments and poor health behaviors, thus this study is a follow-up on our previous studies to study this relation further.

Hypothesis: We hypothesized that the number of days per week spent exercising decreases, and that consumption of alcoholic drinks and energy drinks increases early in medical school and remain changed during the first year of medical school.

Methods: This study was approved by the UNTHSC IRB. The study involved the administration of a health behavior survey via Qualtrics to medical students on three different occasions during the first year of medical school. The survey was administered the week before beginning of medical school (n=191), during the 3rd week of classes (n=104) and during the last 2 weeks of the semester (n=99). Data analyses of the three surveys only included the students who completed all three surveys (n=90). Repeated measures ANOVA was used to compare number days per week of exercise, number of alcoholic drinks consumed per week, and the number of 8oz servings of energy drinks consumed per day. An alpha level of less than .05 was considered significant.

Results: Results: Of the participants, 46.9% of the students were male and 53.3% were females ranging from ages 21-38. There was a significant increase in the number of alcohol drinks consumed/week (p<0.05).

Conclusion: Consistent with the proposed hypotheses, we found that within the first 3 weeks of medical school, students significantly decreased their participation in exercise activities and increased their alcohol consumption. There was also a modest increase in the number of energy drinks consumed per day. In order to decrease these behaviors in first medical students, we must build awareness. The healthier the future doctors of America are, the better role models they become for their patients.

Sponsor N/A
IRB/IACUC# 2013-151
Preconception Care and Reproductive Life Planning: Engaging Primary Care Providers

Purpose: In the United States, about 51% of pregnancies are unplanned (Guttmacher Institute, 2015). Preconception care (PCC) provides patients with the resources and knowledge to prepare for pregnancy and improve birth outcomes. By utilizing PCC, physicians can advise patients on numerous behavioral and lifestyle changes to help prevent complications from occurring. The usage of preconception care is a strong candidate to decrease the amount of unplanned pregnancies for women in their child bearing years. The objective of this project is to identify primary care providers educational and behavioral needs in preconception care screening practice.

Materials and Methods: Participants were recruited from NorTex members “by-invitation only” recruitment. The preconception care surveys were administered on-line via email to clinicians, including primary care providers, pediatricians, OB-GYNs, nurse practitioners, and physician assistants to assess the essential role of clinicians in reproductive life planning. The survey contains approximately 12 questions and takes approximately 10 minutes to complete. The on-line responses were exported in a database and analyzed using Excel.

Results: Of the 500 expected surveys, 149 have been completed by family practice physicians (28%), OB/GYNs (10%), pediatricians (2%), physician assistants (5%), nurse practitioners (22%), and nurses (33%). Survey results revealed providers’ obstacles to providing reproductive life planning in their practice included factors such as lack of time with patients (37%) and inadequate/ insufficient information (brochures, Posters, flyers, etc.) to provide to the patient (31%). Additionally, providers indicated the need of educational materials on Reproductive Life Planning (57%) and believed inclusion of Reproductive Life Planning questions into the EMR (47%) would help implement Reproductive Life Planning in their practice. Of the participating providers, 83% were unaware of the Texas Department of State Health Services “Someday Starts Now” public awareness campaign.

Conclusions: Integrating preconception health into routine primary care encounters with patients of reproductive age should be a significant driver in the reduction of infant mortality rates and increase in healthy families. Future studies should investigate PCC’s integration into providers’ care with the most effect tool, educational material or inclusion of Reproductive Life Planning questions into the EMR.

Sponsor Tarrant County Public Health and Texas Department of State Health Services
IRB/IACUC# 2015-146
Individualized Education Programs and their Effects on Preventive Medical, Dental and Vision Care

Abstract

Purpose:
Individualized Education Programs (IEPs) are designed to help children with disabilities to progress through general education and transition into adulthood. The IEP is an opportunity to increase health awareness and advocate for preventive health for the child who is at an increased risk for multiple health problems such as obesity and oral health problems. The aim of this study is to examine the exposure to IEP and its association with three preventive health outcomes—preventive medical care, preventive dental care, and preventive vision care—for disabled youth from 6-17 years of age.

Methods:
Using the National Survey of Children’s Health 2011-2012 dataset, we conducted a cross-sectional study of children ages 6-17. 65,480 children were categorized into two categories: those with an IEP and those without. We then compared the association between IEP exposure and the three preventive health outcomes in three separate models utilizing logistic regression.

Results:
At a significance of α=0.05, children with an IEP are 31% more likely to receive preventive medical care and 35% more likely to receive preventive vision care when compared to children without an IEP. In contrast, children with an IEP are 8% less likely to receive preventive dental care, though this was not significant at α=0.05.

Conclusion:
The results of this study appear to justify the role of IEPs in improving health outcomes for children with disabilities. The continuation of these programs and further integration of health education could prove to be pivotal in shaping the life-course of children with disabilities as they transition to more independent roles after exiting the school system.

Sponsor  N/A
IRB/IACUC#  2015-177
Effect of Having a Quality Medical Home on School Attendance for Children with Asthma

Purpose:
Understanding the concept of a quality medical home is important when it comes to ensuring the health of those with asthma. Previous studies have not examined the relationship between having a quality medical home and school absenteeism in children with asthma. The objective of this study it to estimate the effect of having a medical home on missing more than 11 days of school among children with asthma.

Methods:
Secondary data analysis of the 2011-12 National Survey of Children’s Health (NSCH) was conducted. A total of 95,677 child-level interviews were completed. However, 6,623 surveys were analyzed for children ages 6-17 with current asthma. We estimated the frequencies of potential confounders (individual, family, and clinical measures) by missed school days. We used SAS Proc Surveylogistic to model the (1) effect of having a quality medical home; and (2) individual medical home subcomponents on missing 11 or more school days, adjusting for confounding variables.

Results:
Our key result is that children who did not have a quality medical home were 1.7 times more likely (95% CI: 1.2-2.3) to miss 11 or more school days than the children who had a quality medical home. We also found that children who did not have a usual source of sick care, which was a subcomponent of having a quality medical home, were 2.2 times more likely (95% CI: 1.2-4.0) to miss 11 or more school days than the children who had a usual source of sick care.

Conclusions:
From statistical analysis, it can be inferred that having a quality medical home will significantly decrease the chances of missing 11 or more school days. Interventions should be implemented to educate parents of children with asthma on the importance of having a quality medical home. Quality healthcare is essential to adequate asthma management which in turn can affect a child’s ability to regularly attend school.

Do Depression Rates Differ by SES Factors in Females Ages 25-45 from States with Varying Income Equality?

Introduction: Research shows that depression is related to socioeconomic status (SES); however, few studies have focused specifically on depression and SES in females during young- to mid-adulthood, which would have important ramifications on parenting, work productivity, and interpersonal relationships. Therefore, the purpose of this study was to assess whether depression rates differ by SES factors in representative samples of females ages 25 to 44 years from states with varying levels of income inequality.

Methods: This cross-sectional analysis used 2013 BRFSS data for females ages 25 to 44 years from Louisiana, New Hampshire, New York, and Utah. The relationship between SES variables (income, education, and employment) and depression was assessed using multiple logistic regression while controlling for demographic and psychosocial variables.

Results: About 19-31% of females reported depression across all four states. In adjusted analyses, none of the SES variables were related to depression across all four states. However, after adjusting for all variables in the model, both low general health and being a smoker were related to depression in each state.

Conclusions: This study found that SES was not related to depression in representative samples of females ages 25 to 44 years across four states after controlling for other demographic and psychosocial variables. However, health status and smoking status were related to depression in all four states. Practitioners should assess mental health status in patients from this target group who have low general health and/or are smokers, and vice versa.
Is Our Community Trauma-Informed?

Purpose: The Mental Health Connection (MHC) of Tarrant County supports the incorporation of Trauma-Informed Care (TIC) practices for all organizations serving trauma survivors. Trauma-informed organizations are able to respond to signs of trauma using specific policies, practices, procedures, and knowledge aimed at preventing re-traumatization (SAMHSA, 2015). The MHC conducted a survey regarding the current state of TIC incorporation within various organizations in order to gauge the community's current ability to provide comprehensive trauma-informed care. The purpose of this study was to determine how effectively the principles of TIC were implemented in the MHC's organizations.

Methods: The MHC TIC survey was administered to 495 participants, representing over 60 organizations. The survey prompted employees to report the level of TIC implementation in various areas of their organization. Response frequencies were determined and composite variables were created for five key areas: policy, leadership, organization structure, training, and finance. Within each category, the top, moderate, and lowest progress items were identified to determine which aspects of TIC were implemented effectively and which could be improved. Responses relating to the participants' confidence levels and most recent TIC trainings were further analyzed.

Results: The results indicated that the top policy, organizational structure, and training items were better implemented than the top leadership and finance items. Within policy, 64% of respondents reported that confidentiality measures were effectively implemented. Furthermore, the difference in the mean response for policy items was significant at the 90% confidence level between those who did and did not participate in TIC training. Those who participated in TIC training were also significantly (95% confidence level) more confident in their ability to provide TIC than those who did not participate.

Conclusions: The results demonstrated that employees who participated in TIC training were more confident in their ability to provide trauma-informed care than those who did not receive training. Apart from highlighting the importance of TIC training, the respondents reported areas where participating organizations were excelling, as well as areas of improvement. Overall, the study reinforces the importance of TIC training and avenues for further item implementation that will aid organizations in becoming fully trauma-informed.

Sponsor: Mental Health Connection
IRB/IACUC#: 2015-205
**Internalizing Behaviors in Hispanic Boys Predict Overweight/Obese Status**

Background: Obesity has been a troubling trend among Hispanic youth. Emotional eating has been described as the consumption of comfort food to cope with negative emotions, which in turn can contribute to weight gain. Negative emotions can lead to internalizing (feeling worthless, sad, withdrawn) and externalizing (bullying, arguing, disobeying, stubbornness) behaviors. Studies suggest these may precede obesity in children with poor socioeconomic status. The aim of this study was to examine these behaviors in relation to weight in under served Hispanic children.

Hypotheses: Overweight children (OW) will have higher internalizing or externalizing behaviors as compared to normal weight children (NW).

Methods: Subjects included Hispanic youths (117 males, 116 females) ages 10-14. Subjects were classified into NW (n=85) and OW (n=148) based on BMI percentile. Parents completed a 1-5 Likert scale survey of social-emotional behaviors. Responses were summed to arrive at scores for Internalizing (INT) and Externalizing (EXT) behaviors. Relationships between INT, EXT, age, and BMI percentile were examined for boys and girls separately using Spearman correlation. Logistic regressions were conducted to ascertain the effects of significantly associated variables on the likelihood that subjects would be OW.

Results: For boys, BMI percentile was associated with INT (rs=.180, p=.053) and age (rs=.215, p=.020). Girls showed no significant correlations. Logistic regression for boys using INT and age was significant (X2=10.570, p=.005). Increasing age in boys was significantly associated with an increased likelihood of being OW (OR= 1.439, CI=1.056 – 1.961). The Wald criterion indicated that increases in INT approached significance in predicting OW (p=.069). EXT was not significant for boys. Regression models for girls were not significant.

Conclusion: Internalizing behaviors increased for boys who were overweight or obese, especially with increasing age. This trend was not significant in girls. These data contradict previous literature suggesting Hispanic girls are at higher risk for obesity due to increased internalizing behaviors. Future research should broaden the scope of internalizing behaviors that may place children at risk for obesity.

Acknowledgments: This study was supported by intramural grants, and the study was approved by the IRB at the University of North Texas Health Science Center.

Sponsor: N/A

IRB/IACUC#: 2015-076
A Comparison of Three Screening Tests in Detecting the Prevalence of Latent Tuberculosis Infection in Refugees by History of Residence in Refugee Camps

Purpose: The purpose of this study was to examine residence in a refugee camp as a predictor of testing positive for latent tuberculosis infection (LTBI) according to each of three LTBI screening tests.

Methods: Data were obtained from a study funded by the Centers of Disease Control and Prevention (CDC) through the Tuberculosis Epidemiologic Studies Consortium. Refugees presenting at Tarrant County Public Health in Fort Worth, Texas, from countries classified by CDC as having a medium or high risk of tuberculosis (TB) were eligible to participate. Participants were interviewed to obtain data on variables associated with LTBI and received three LTBI screening tests: QuantiFERON-TB Gold In-Tube (QFT), T-SPOT TB, and the tuberculin skin test (TST). The results of each screening test were used as the indicator variable for LTBI. Data analysis was conducted for each screening test result independently using logistic regression to adjust for potential confounders including age, gender, birth country, education, income, smoking, alcohol use, history of incarceration, and being a close contact to a TB case.

Results: Of the 994 participants, twenty-six percent originated from medium-risk countries, 22% from high-risk countries in Africa, and 52% from high-risk countries in Asia. The odds of having LTBI for those who lived in a refugee camp compared to those who did not differ according to the screening test used, but was not significant for any of the three tests (QFT OR 0.843, 95% CI 0.568–1.252; T-SPOT OR 0.819, 95% CI 0.548–1.226; and TST OR 1.121, 95% CI 0.791–1.590).

Conclusions: Among participants in our study, living in a refugee camp conferred no significantly increased risk of LTBI when adjusted for other predictive variables, independent of the type of screening test utilized.

Sponsor N/A
IRB/IACUC# 2012-139
Introduction: The purpose of this study was to investigate risk factors of metabolic biomarkers of allostatic load in African-American women in the Better Me Within (BMW) program, a community-based participatory research study testing a faith-enhanced diabetes prevention program.

Methods: Baseline health measures, psychosocial and demographic survey data were collected in 136 African-American women with a mean age of 49.3 years and mean body mass index (BMI) of 37.8 during baseline measurement for the BMW study at 7 churches in Dallas County over a period of 2 years. The metabolic biomarkers of high density lipoprotein (HDL), total cholesterol/HDL ratio, systolic blood pressure, diastolic blood pressure, glycylated hemoglobin (HbA1C), triglycerides, and BMI were collected. The highest risk quartile of each biomarker was assigned a value of “1,” while all other values were assigned a “0.” All biomarker scores for each participant were summed for a maximum allostatic score of 7. A Poisson Regression was used to assess the relationship between allostatic load score and behavioral determinants of health (perceived stress, depression, and spiritual locus of health), controlling for age, income, and education level.

Results: Regression model that included perceived stress, income, education, depression, spiritual locus of health, and age, found the main risk factor for higher allostatic load was low income level.

Discussion: Although no statistical significance was found in the relationship of the tested behavioral determinants of health and allostatic load, the significant association between low income and high allostatic load in this study of African-American women reinforces the known relationship of poverty and poor health outcomes in health disparities. Further investigation is needed to discover whether poverty mediates poor health or whether it is a proxy for experiences of poverty-related adversity, like childhood trauma, neighborhood poverty, and chronic stress.

Sponsor National Institute for Minority Health and Health Disparities
IRB/IACUC# 2011-164
Exploring Compassion Fatigue and Satisfaction Among Refugee Leaders in the DFW Area

Compassion fatigue describes the secondary traumatic stress seen in those working with others that have experienced trauma. It can lead to chronic fatigue, anxiety, irritability, and eventually burnout. Compassion fatigue has been studied in numerous helper and caregiver roles, such as social workers, nurses, and child protection caseworkers. However, research has not been conducted to investigate the presence of compassion fatigue within refugee populations or to understand how compassion fatigue may affect community leaders in this high-risk population. This study will explore the behavioral, emotional and physical effects of working with refugees among refugee leaders.

In-depth qualitative interviews were conducted with refugee leaders working with refugees in the DFW area. Each participant completed a demographic questionnaire, a comprehensive interview and Professional Quality of Life Scale: Compassion Satisfaction and Compassion Fatigue Version 5 (ProQOL). The ProQOL questionnaire is a validated tool used to assess compassion fatigue.

Nine refugee leaders, representing six refugee groups, completed the demographic questionnaire, interview and ProQOL questionnaire. Participants reported a high level of compassion satisfaction (mean = 44.2), a low level of burnout (mean = 18.9), and a varied level of secondary traumatic stress. Refugee leaders reported a reliance on faith and a compulsion to help others due to their refugee experience as factors that outweighed the cost to their family wellbeing, physical and emotional health.

Refugee leaders are highly resilient. They are often recruited by health care organizations, researchers and resettlement agencies to provide services and information to other refugees. These findings have implications for organizations to provide training on self-care practices and support services.

Sponsor: CPRIT
IRB/IACUC#: 2015-197

Exploring the Relationship between Socioeconomic status and C-Reactive protein levels in the US population using NHANES Survey Data

Several studies have examined the impact of socioeconomic status on health and its overall quality. Low socioeconomic status has been associated with a higher prevalence of chronic health conditions, mortality from coronary heart disease, stroke, diabetes and subclinical markers of disease risk. An elevated Plasma C-Reactive Protein (CRP) is one of such markers, signaling an increased risk for atherosclerotic cardiovascular disease and sub clinical stages of pulmonary dysfunction. Various studies have been carried out on the association between CRP levels and socioeconomic status. However, most studies did not consider how factors like acute and chronic health conditions along with health behaviors relates with the socioeconomic difference in CRP levels. In addition, many of the study samples in the previous studies were not representative of the socioeconomic diversity of the United States. In this study, we explored the relationship between socioeconomic status and C-Reactive protein levels in the US population, taking account of health indicators and behavioral factors.

We used the National Health and Nutrition Examination Survey (NHANES) dataset from 2001 to 2006. The survey includes interviews, clinical examinations and laboratory test data. Demographic factors (age, ethnicity and poverty), health/immunity indicators (recent illness, leucocyte count, asthma, chronic bronchitis and rheumatoid arthritis) and behavioral risk factors (obesity, current smoker, heavy drinking and exercise) were examined in this study to see how they predict the socio economic variation in CRP levels. Blood samples from a total of 13,708 adults who were over 20 years were assayed for CRP. Pregnant women (888) and participants who did not have income data (1006) were excluded from the study. For our analysis, CRP were divided into three categories: moderate (1.01 – 3.0 mg/L), high (3.01 – 10.0 mg/L) and very high (> 10 mg/L).

First, bivariate analysis was done to display the characteristics of the study population by poverty status. T-tests and Chi-square tests were used for continuous and categorical variables respectively. Multinomial logistic regression was then used to obtain the relative odds of having a CRP level that is above normal in relation to poverty.

The mean levels of CRP and blood leucocyte count were higher for subjects in poverty. Subjects in poverty were more likely to be female and of a younger age. People in poverty had a higher prevalence of recent illness, asthma, chronic bronchitis, and rheumatoid arthritis. They also reported a higher prevalence of obesity, current smoking, heavy drinking and as well as less exercise. As age increased, the odds of all CRP levels compared to the normal increased. Obesity had the highest odds ratio (Moderate 2.81; 95% CI: 2.41 – 3.29; High 5.88; 95% CI: 4.96 – 6.96; Very high 8.51; 95% CI: 7.03 – 10.30) for CRP above normal levels. The odds of having very high CRP level was also increased for people with chronic bronchitis and rheumatoid arthritis. Controlling for the demographic factors, health indicators and behavioral factors, living in poverty increased the odds of very high CRP levels by 36% when compared to those not living in poverty.

Socioeconomic status is related to higher CRP levels, and this relationship is noteworthy at very high CRP levels. People who have low indicators of health and immunity are more likely to be in poverty and to have a very high CRP level. We found that the line depicting CRP level for those in poverty and above poverty crossed as age increased. Further studies need to be carried out on this subject to examine if there is an interaction effect between CRP levels and poverty at different age groups.

Sponsor: N/A
IRB/IACUC#: 2016-039
Purpose:
Adolescent obesity is a major public health concern in the United States. According to the CDC, more than 33% of children and adolescents are either overweight or obese. A major known risk factor for changes in BMI status is stress. Multiple risk factors, such as living in a food desert, race, and exposure to family and neighborhood stressors cause various emotional and physiological changes in the body, which can increase the risk of adolescent obesity. Due to this, we use the socio-ecological model to understand intertwined risk factors of adolescent obesity. Based on biological and scientific evidence we hypothesized that adverse childhood experiences (ACEs) are associated with body mass index (BMI) status among adolescents aged 10-17 years.

Methods:
The secondary data analysis was done using the 2011-2012 National Survey of Children's Health and conducted univariate, bivariate, and polytomous logistic regression to assess the relationship between ACEs and BMI while controlling for gender, federal poverty level, health insurance status, learning disabilities, and how often the studied family eats meals together. The estimation of adjusted odds ratio represents an adolescent having undergone at least one or more ACEs and its effect on BMI measured in three categories: underweight, normal weight, overweight and obese.

Results:
The odds of being overweight are 1.10 times higher (95% CI 0.94-1.30) for adolescents who are exposed to 1 ACE, while the odds of being overweight are 1.26 times higher (95% CI 1.08-1.47) for adolescents with 2 or more ACEs, with both odds ratios being compared to adolescents with normal BMI and no ACEs. The odds of being obese are 1.13 times higher (95% CI 0.96-1.33) for adolescents who are exposed to 1 ACE, while the odds of being obese are 1.43 times higher (95% CI 1.20-1.71) for adolescents with 2 or more ACEs, with both odds ratios being compared to adolescents with normal BMI and no ACEs.

Conclusion:
The study observed that increasing the number of ACEs adolescent experiences increases the odds of being overweight or obese. These results indicate that public health professionals should intervene at each level of the socio-ecological model in order prevent major fluctuations in adolescent BMI status.

Sponsor: N/A
IRB/IACUC#: 2015-177
Research Gap in Identifying the Relationship Between Breastfeeding and Early Childhood Caries in The United States: A Systematic Review

Objective: To demonstrate the current research deficit, involving the association between breastfeeding and early childhood caries in the United States (U.S), as compared to other countries through a systematic review.

Method: The PubMed database was searched for previously conducted studies relating to the effect of breastfeeding on occurrence of early childhood caries (ECC). Keywords used included “Breastfeeding” “Dental caries” and “dental decay”. Results were further narrowed by searching keywords “Breastfeeding” and “Early childhood caries”. PubMed search resulted in 355 articles published from 1890-2015, and of that 59 articles were selected for the review. References cited in the articles were also selected. Articles were retrieved and categorized according to the country where research study was conducted.

Results: Studies conducted in U.S. contributed to only 5% (n=3) in comparison to Brazil, which led the research marathon at 17% (n=10). Research studies conducted in Asia (n=22), Europe (n=12), and Africa (n=7), contributed approximately 67% collectively. 53% of the studies found significant relationship between either prolonged breastfeeding (>12 months) or nocturnal breastfeeding and early childhood caries, while 15% were inconclusive.

Conclusion: Study results indicate a clear gap in the research conducted in the U.S. investigating association between breastfeeding and early childhood caries when compared internationally. Although many studies have found significant association, it is a highly complex relationship and additional research needs to be done for the U.S. population involving children from different racial, ethnic, educational and socioeconomic background to reach definitive conclusions and decrease the burden of dental caries.

Sponsor: N/A

IRB/IACUC# 2014-091; 2015-045

The Challenges of a Second Chance: Exploring the Role of Social Support among Females who were Previously Incarcerated

Objective: The incarceration rate for women in the United States has increased by 31% in the last decade (Minton, 2012). Community reentry following incarceration is a complex process, leading to approximately 45% of women recidivating (Brown, 2010). Upon release, women are in need of comprehensive services including empowerment programs with opportunities to achieve self-sufficiency (Richie, 2001). However, studies show providing housing, employment and treatment alone are not sufficient in addressing recidivism, fortifying the need for additional support systems (Adritti & Few, 2008; Makarios, Steiner, & Travis, 2010). The Second Chance Mentoring program (SCM) coordinated by Family Pathfinders of Tarrant County provides re-entry mentoring services for formerly incarcerated females. Volunteer mentors focus on providing support during this integral transition. This study aimed to evaluate the effectiveness of the social support triangular relationship between mentors, mentees, and the SCM staff members.

Methods: This study utilized a mixed method design using secondary data from 58 women enrolled in the SCM program between 2010-2015. Individual case notes, risk scores, and data related to recidivism were analyzed using qualitative and quantitative methods. Textual data were coded using content analysis procedures to investigate key themes from progress notes. Data associated with recidivism were analyzed using SPSS. Qualitative and quantitative findings were triangulated in iterative cycles to develop an understanding of variable/theme interactions.

Results: Using the Ohio Risk Assessment System (ORAS), the level of family/social support and their attitudes towards crime reflect that 44.6% of the participants reported low social support with criminal activity, 37.5% had moderate levels of social support, and 18% had high social support with criminal activity. Additionally, ORAS yielded a score based on peer associations and their attitudes towards crime, resulting in: 53.8% with high peer association risk, 46.2% of moderate risk, none of the sample had positive associations. Through qualitative data analysis, the triangular relationship between the participants, mentors, and staff members was examined to assess supportive influences associated with varying levels of risks and needs.

Conclusion: The results indicate that the triangular relationship serves an important role in addressing the needs of reintegrating women, and staff members provide a strong scaffolding influence. Navigating a complex system of internal and external barriers requires both strong social support and tangible resources.

Sponsor: Bureau of Justice Assistance (BJA)

IRB/IACUC# 2014-091; 2015-045
What’s the Agreement between Self-Reported and Biochemical Verification of Drug Use? A Look at Permanent Supportive Housing Residents in Ft. Worth

People who are chronically homeless are nearly seven times as likely to use illicit drugs, compared to the general population. We evaluated the validity of self-reported drug use in a sample of previously homeless people housed in permanent supportive housing programs in Ft. Worth. We used data from 345 clients who completed a baseline assessment prior to participating in a health coaching intervention. Self-reported drug use and saliva drug tests were compared to determine the positive predictive value for amphetamines/methamphetamines (47.1% agreement), cocaine (43.8% agreement), and marijuana (69.7% agreement) drug tests. Exclusively relying on self-reported drug use may not be a valid measure of drug use in this population. However, we also found instances where people self-reported recent drug use that was not captured by the saliva drug test. In general, amphetamine/methamphetamine and cocaine use was adequately captured by the biological test, while marijuana use was best captured by a combination of self-report and biological data. Assessments of drug use among permanent supportive housing residents should not rely exclusively on self-reported measurements of drug use.

Sponsor
IRB/IACUC# 2014-125

Effect of Low Birth Weight and Preterm Birth on Incidence of Autism Spectrum Disorder

Effect of Low Birth Weight and Preterm Birth on Incidence of Autism Spectrum Disorder

Purpose:
Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that affects the social, communication, and developmental abilities of a person (CDC, 2015). There are still a lot of unknowns regarding ASD, however it is hypothesized that low birth weight and preterm birth are risk factors for ASD. This study was done to assess if there was any association between low birth weight (LBW) and preterm birth on the presence of ASD in children 2-17 years old.

Methods:
Secondary data analysis was done on the 2011-2012 NSCH survey, which had 95,677 child-level NSCH interviews completed nationally. 1,850 individual interviews were collected per state and the results were weighted to represent a national population of children ages 0-17 in each state. The sample was restricted to exclude children below the age of 2. A multivariable logistic regression model was done to see if there was a relationship between the presence of ASD and preterm birth and LBW. A second multivariate logistic regression model was done examining the presence of ASD with only preterm birth. Both models were statistically adjusted for gender, age of the child, maternal physical health, maternal mental health, race/ethnicity, health insurance, household income and type of insurance.

Results:
The key findings from this study were that preterm birth had a significant association with the presence of ASD, but LBW did not have any statistical significance. Children who were born preterm had a 2.045 [95% CI 1.491-2.806] greater odds of being diagnosed with ASD than children who were not born preterm. The covariate gender was also shown to be highly associated with ASD. Males had 4.529 [95% CI 3.464-5.923] times greater odds of being diagnosed with ASD than females.

Conclusion:
The results show that preterm birth was associated with the manifestation of ASD. There was no correlation between LBW and ASD found. The results also indicate that males are more frequently diagnosed with ASD than females. These results can be used to help show the importance of adequate prenatal care to help reduce the prevalence of preterm births, which can hopefully help to reduce the prevalence of ASD.

Sponsor
IRB/IACUC# 2015-182
Efficacy in Relation to Access to a Health Provider

Background: Obesity is one of the most predominant health concerns within the African American community, particularly among women. It is heavily associated with diseases such as type II diabetes and high blood pressure in addition to other weight related health complications. It is perceived that patients who have access to a healthcare provider have better self-efficacy concerning health behaviors and therefore more likely to have improved health outcomes.

Methods: Cross-sectional data was used to review a survey administered at baseline to participants in the Better Me Within program. The relationship between provider access, dietary habits, and confidence (measured with the PANSE survey) were evaluated. Further, these relationships were evaluated in regards to indicators of chronic diseases such as body mass index (BMI), fasting glucose level, and cholesterol to determine whether there was a relationship between access to a provider and these health markers.

Results: A total of 145 African American women with a BMI at or over 25 participated in the surveys. Data showed a positive relationship between provider access and lower glucose levels. There was no significant difference in the mean confidence (PANSE) scores between those who identified as having access to a health provider and those that did not. Data also showed no significant difference in the BMI of participants with and without access to a healthcare provider.

Conclusions: In our sample, self-efficacy for health behaviors was not different for individuals with and without access to a healthcare provider. However, glucose levels were healthier when individuals had access to a health care provider. Future research should explore what psychosocial variables are related to provider access to determine strategies to motivate individuals to find a medical home, which is linked to more positive health outcomes.

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Why did Mrs. X Die? Multi-Level Influences on Health and Healthcare among a Refugee Woman following Resettlement in Tarrant County

Purpose Hepatitis B virus infection (HBV) is a significant global health problem. Two billion people around the world have contracted the disease, and almost four million cases are a part of the refugee population. Although screening is mandatory before and after resettlement in the U.S., HBV status can still go undetected. There are several challenges working against the refugee population when it comes to health that result in increasing rates of HBV-related morbidity and mortality. The present study examines the case of a refugee woman who died from liver cancer less than four years after resettlement in Tarrant County. The case study illustrates how multi-level influences prevented her from receiving adequate and timely care.

Methods The patient's medical records, UNTHSC Building Bridges Initiative’s case files, and medical case management files were reviewed for the study. The Building Bridges Initiative (BBI) is a UNTHSC program funded by the Cancer Prevention and Research Institute of Texas (CPRIT). The program uses lay health educators from the refugee community to conduct free educational workshops, health screenings, and connect medical case management to the community.

Results Analysis of the patient’s records revealed missed opportunities to address the patient’s liver cancer and HBV status. Upon initial entry into the medical system, the patient had a 7.3 cm mass in her liver and tested positive for Hepatitis B. Despite subsequent appointments and numerous visits to the E.R. for abdomen pain, two years passed before doctors addressed the mass again. At this time, she was near the end of her pregnancy and the mass had grown. Following pregnancy, a surgery was scheduled. Lack of insurance and community members advising the patient against chemotherapy may have impacted her decision to miss multiple oncology consultations and follow-up appointments after the surgery. She enrolled in BBI four months before she passed way. In those months, she attended Hepatitis B educational sessions which helped bring her into care again. She then agreed to chemotherapy for comfort, and started palliative care.

Conclusion Each source of evidence provided a unique perspective to the experience of Mrs. X in the U.S. health system. Though records supported a gap in the health care system, the case also revealed a possible lack of understanding of the severity of the illness, or the patient’s inability to advocate for herself in the system. Had BBI, or similar advocacy and navigation services, been in place and accessed at the time of initial diagnosis, perhaps the outcome might have been different for Mrs. X. In this case, medical case management was necessary to navigate the health care system, improve Mrs. X’s understanding of her condition, and improve communication between Mrs. X and the system. Without personnel to advocate on their behalf, refugees like Mrs. X get lost in the health care system.

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Sponsor Cancer Prevention and Research Institute of Texas (CPRIT)
IRB/IACUC# 2016-027

Sponsor National Institute for Minority Health and Health Disparities
IRB/IACUC# 2011-164
Improving Lives of Most Vulnerable: The Relationship between Diet, Physical Activity, and Quality of Life among Permanent Supportive Housing Residents

Background: Chronic homelessness is a complex public health concern in the United States. People experiencing chronic homelessness are much more likely to suffer from mental illness and substance use, and to be overweight or obese (Tsai & Rosenheck, 2013; Tsemberis, Kent, & Respress, 2012). Housing First is an approach to place people who are chronically homeless into Permanent Supportive Housing (PSH) (Rog et al., 2014). There is clear evidence PSH programs increase housing retention and, reduce healthcare and criminal justice costs (Tsemberis & Eisenberg, 2014; McLaughlin, 2010). However, becoming housed does not necessarily improve a person’s overall quality of life (QOL) (Wolf et al., 2001). Improvement in diet and physical activity may be one way to improve QOL among vulnerable populations (Blissmer et al., 2006). However, this association has not been explored among PSH residents. The purpose of this study was to explore the patterns of change and relationship between diet, physical activity and QOL among PSH residents enrolled in a health coaching program.

Method: We used data collected during baseline and follow up interviews from m.chat—a health coaching program for PSH residents in Fort Worth. The program utilizes motivational interviewing and wellness incentives to help people achieve health goals. Specifically, we examined demographic characteristics, diet, physical activity and overall QOL from 230 participants enrolled in the m.chat program. Paired t-test and mixed model analysis was performed utilizing SPSS software.

Results: We found a significant improvement in the total QOL scores from baseline to follow-up. A random intercept model showed a positive association between change in diet and the improvement in QOL. Physical activity was not significantly related to improved QOL; however, there was large variation in the physical activity data.

Conclusion: This study is the first to look at changes in QOL among PSH residents enrolled in a health coaching program. Interventions that encourage diet and physical activity may improve overall QOL among PSH residents.

The Association of Low-Income and Food Insecurity on Chronic Disease: NHANES 2005-2012

Purpose: Food insecurity is a household level economic and social condition of limited or uncertain access to adequate food leading to hunger. It is estimated that 14% of the U.S population will experience food insecurity at any given point during the year. Between 5-6% of Americans are severely food insecure in which meals are skipped with disruptions in eating patterns. The purpose of this study is to evaluate the association of food insecurity and chronic disease among low-income individuals who are particularly at risk for food insecurity.

Methods: Data from four NHANES cohorts from 2005-2012 combining eight years of data collection (n = 40,790). The sample was restricted to adults between the ages of 18-65, with income levels below 200% of the federal poverty level guidelines (FPL). The NHANES survey utilizes the Food Security Survey Module (FSSM) which is a validated questionnaire developed by the USDA to measure food security. The dependent variables consisted of a self-reported measures and clinical/laboratory indicators of three forms of chronic disease: hypertension, hyperlipidemia and diabetes. All analyses were conducted in SAS 9.3 for complex survey analysis.

Results: Food insecurity was significantly associated with age, race, education level, income, health insurance, and current health status. Crude adjusted models found a significant positive association between food insecurity and hypertension (OR = 1.62, 95% CI 1.40, 1.86), hyperlipidemia (OR = 1.26, 95% CI 1.06, 1.49), and diabetes (OR = 1.92, 95% CI 1.55, 2.37). Additionally, among the most severely food insecure there was a highly significant association between food insecurity and both self-reported and clinical hypertension, (OR = 1.84, 95% CI 1.52, 2.22 and OR = 1.69, 95% CI 1.39, 2.05 respectively). Among adults already diagnosed with disease, food insecurity was associated with inadequate control of diabetes (OR = 1.57, 95% CI 1.14, 2.15) but not hypertension or hyperlipidemia.

Conclusion: Food insecure adults were associated with increased cardiovascular risk factors. Given the importance for a healthy diet for disease prevention and health promotion it will be important for policymakers to increase access to affordable, nutritious foods in low-income neighborhoods. Additionally, increased access and utilization of federal food assistance programs such as SNAP (Supplemental Nutrition Assistance Program) can also address the large number of food insecure Americans.
A comparative study of groundwater quality in Texas was performed to assess the impact of oil drilling, unconventional shale gas horizontal drilling and hydraulic fracturing (fracking) technology on groundwater quality during years 2000-2007 and 2008-2015 given the increased number of fracking wells and production in the last eight years. This study analyzed whether anthropogenic activities from natural gas extraction has affected the salinity of groundwater using accepted brines ratio (Na+ to & Cl-) to Total Dissolved Solids (TDS) commonly used in evaluating brine impact from oil extraction.

2. Material and Methods

The data was from the United States Geological Society (USGS) Water Quality Samples for the Nations: Discrete Water Quality Samples database of historical conductivity field readings. The dataset is a comprehensive set of water constituents comprising decades of collections. Specific ratios of chemical constituents have been determined to reflect impact of energy extraction on water quality. In line with this determination, we analyzed chloride and sodium (mg/L), dissolved solids or TDS, and strontium (mg/L). The ratios of (Na+ + Cl-) to TDS, lithium to bromide, sodium to chloride, sodium to bromide, or bromide to chloride individually or collectively were analyzed, as they are indicators of water pollution by brines when exceeding a corresponding threshold.

3. Results

If a ratio of (Na+ + Cl-) / TDS is greater than or equal to 0.64, it is an indicator of pollution of water by brines. A total of 11,786 wells were statistically analyzed. Chi square (X2) statistical test was used for the unadjusted data, and logistic regression was used for the adjusted variable to assess the groundwater and fracking brines’ pollution. For the unadjusted analysis, the P-value (0.005) is significant, as it shows a negative association. When controlling for wells used for public supply and irrigation use, the result is statistically significant, with a negative association (-0.0014). These results suggest that groundwater wells from 2008 to 2015 have a lower level of brines despite the increase in fracked wells in Texas. The decrease in brines does not imply that the quality of groundwater has improved.

4. Conclusion

The brine ratio used to assess the impact of oil extraction on water quality indicated that the salinity of groundwater wells seems to improve as years pass. The (Na+ + Cl-) to TDS ratio may not be an appropriate predictor of the impact of natural gas extraction on water quality. The reduction of brines concentration overtime does not necessarily mean the groundwater quality has improved. Further statistical analysis will be conducted examining chemical constituents’ relationships to determine if a more predictive ratio reflective of natural gas extraction impact can be generated.

Sponsor: N/A

IRB/IACUC#: 1125

**1126** Poster

**Presenter:** Ndolembai S. Njesada  
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**Reduction of Malaria Mortality in the country of Chad, Sub-Sahara Africa from 2013 to 2014.**

The purpose of this study is to show the effectiveness of a malaria net distribution program with multi-faceted activities including multiple forms of communication, early diagnosis and treatment in the reduction of malaria mortality in Chad from 2013 - 2014. Malaria is a parasitic disease caused by the Plasmodium parasite transmitted through infected mosquitoes bites (anopheles). The parasites multiply rapidly in a human’s liver and then infect red blood cells. Symptoms including headache, fever, vomiting and vertigo appearing within 10 to 15 days after a mosquito bite.

Worldwide, cases of malaria are estimated at 198 million (2013). Approximately 584,000 deaths occurred mostly in African children. This equates to a child dying of malaria every minute in Africa. Despite the alarming number of cases, the mortality rate since 2000 has fallen by 47% globally with a 54% decrease in the African Region. In the Country of Chad, 27% of all morbidity and 19% of all mortality are due to malaria.

The database from the United Nations Development Program (UNDP-CHAD) and communication activities of STOP PALU CHAD from 2013 and 2014 were examined.

Confirmed cases of malaria increased by 27.28% from 2013 – 2014, primarily due to increased awareness and early detection. The mortality rate fell by 69 cases/1000 (1881 in 2013, 1729 in 2014) according to records from health facilities. Studies show in the African region many malaria cases are underreported.

A multi-faceted malaria awareness and prevention campaign was shown to be effective in reduced mortality of children in Sub-Sahara Africa. The incidence of malaria continues to be underreported due to lack of awareness, health care facilities and access to facilities.

Results show combined efforts are necessary to educate people in rural communities in reporting to health care facilities, when symptomatic, for proper diagnosis and treatment.

Sponsor: N/A

IRB/IACUC#: 1126
Introduction: Prior literature shows a positive relationship exists between motivation to exercise and weight loss. Adolescents are a prime population to study health behaviors such as physical exercise and other obesity-related factors due to the many developmental changes occurring and increasing autonomy. This shouldeering of responsibility for their health likely shifts motivation to a more prominent factor in sustaining healthy behaviors such as physical activity. The current analysis compares motivation to exercise and the impact it has on engaging in physical activity (PA). The hypothesis was teens who claimed higher motivation to exercise would subsequently evidence increased activity levels the next week compared to teens who did not exhibit high motivation to exercise.

Methods: Participants were 35 normal weight to obese teens (mean grade=10th, mean age=15.3 yrs, 77% females, 23% Hispanic). After obtaining consent and assent, teens completed questionnaires assessing sleep and health behaviors. Included was the 19-item Behavioral Regulation in Exercise Questionnaire (BREQ2) to assess their motivation to engage in PA (scale:0-4/Item; mean=27.1, SD=10). Stadiometer and digital scale measured height and weight (BMI %tile calculated). One week later teens completed additional assessments including the Past Week Modifiable Activity Questionnaire for Adolescents (MAQAPW) which provided data on # of activities engaged in; days/wk of sedentary behavior, light PA, moderate-vigorous PA, and all PA; total minutes/wk of PA; and min/day of PA. Data were from a larger prospective study assessing teen’s sleep and health. Regression analyses examined BREQ2 as a predictor of self-reported PA with sex, grade, age, and BMI %tile as covariates.

Results: Analyses showed BREQ2 predicted the frequency teens engaged in moderate-vigorous PA (29%=none, 34%=1-2 days, 31%=3-5 days, 6%=6-7 days; beta=0.476, P=0.006) and days/week they engaged in PA (mean=2.83 days; beta=0.413, P=0.048). No other PA variables were significant.

Conclusions: Motivation appears to increase how frequent teens engage in PA as well as how often they engage in moderate-vigorous PA. These two aspects of PA have been shown to protect against obesity. Further exploration into factors that both enhance and reduce motivation to engage in PA would be beneficial to reduce risk of obesity. Such findings would also assist with obesity interventions.

Sponsor N/A
IRB/IACUC# 2013-015
Public policy, private practice: Tuberculosis/latent tuberculosis infection (TB/LTBI) surveillance in the commercial healthcare sector

Objective: To estimate the prevalence and explore the pattern of TB/LTBI testing and retesting in the commercially insured US population. Domestic TB elimination is a cornerstone of US public health policy, yet progress toward elimination has slowed. One reason for this is the lack of emphasis on identifying and addressing LTBI. Systematic efforts to find and treat persons with active TB or persons with LTBI have defaulted to local and regional public health departments but, given limited resources and murky mandates, LTBI surveillance and treatment by public health is inconsistent. At the same time, TB/LTBI testing is not uncommon in the private sector. Unleveraged synergies exist between the testing conducted by private healthcare providers and the surveillance conducted by public health departments. Understanding the patterns of TB/LTBI screenings conducted in the private sector is a crucial first step toward realizing this potential.

Methods: De-identified paid medical claims for services rendered between 4/1/2010 and 3/31/2013 for a sample of 4 million people from the Optum Research Database were analyzed. People in the sample were ages 1/2010 and 3/31/2013. TB/LTBI testing via tuberculin skin testing (TST) and interferon gamma release assay (IGRA) was identified using CPT codes. The index TB/LTBI test per person was identified based on each individual’s first TST or IGRA with a service date between 6/2010 and 5/2011. Subsequent tests were identified based on service dates following the index test through 3/2013.

Results: Of the 4 million people, 67,168 (1.68%) had an index TB/LTBI test between 6/2010 and 5/2011. TSTs were more common than IGRAs; 64,788 (96.5%) of index tests were TSTs and 2,355 (3.5%) were IGRAs. Of those with an index TST, 21,645 (33.4%) had another test on a later date. Retesting methods differed depending on how quickly retesting occurred. In patients with a retest within 30 days, 6.4% received an IGRA next instead of another TST, while 2.6% of patients who had a retest in >30 days received an IGRA.

Conclusion: Much TB/LTBI testing is conducted by providers outside of the US public health system. Data collected by commercial insurers can provide insight into TB/LTBI testing in this setting. These results indicate that TSTs are far more prevalent than IGRAs, but IGRAs are being used in practice for post-TST retesting when retesting is conducted shortly after initial testing.

Sponsor N/A
IRB/IACUC#
Impact of exogenous hyaluronan on dendritic cell activation and trafficking from skin

Introduction: Hyaluronan (HA) is a polysaccharide used as dermal filler in cosmetic dermatology. A minority of patients ( Purpose: This study is to determine whether HA at different molecular weights (M.W.) can be degraded into biologically active fragments inducing migration of APCs to draining lymph nodes causing contact hypersensitivity in mice. 

Materials and Methods: Mice, divided into 3 groups of 4, were subcutaneously injected in their ears with Lifecore Biomedical HA of graded Molecular Weights (M.W.) (Group 1: 851 kDa-1.19 MDa, Group 2: 66kDa-90 kDa, Group 3:kDa). The positive control of HA tetrasaccharide (Group 4) and negative control of PBS (Group 5) were from Sigma-Aldrich. All antibodies (Ab) were from BD Pharmingen. Female BALB/c mice were injected with 200 µg HA/ear or the contralateral ear was injected with PBS (40 µL/ear). Mice were sacrificed 24 hours post-injection, auricular lymph nodes were collected, and HA and PBS draining lymph nodes were pooled separately. Ears were harvested after lymph node collection, and stored in PBS wetted gauze at -20ºC. Pooled lymph nodes were homogenized; cells were counted using a hemocytometer. Cells were incubated for 30 minutes on ice with Fc blocking Ab, stained with a phycoerythrin labeled MHC II specific Ab, or phycoerythrin labeled isotype control IgG Ab for 30 minutes on ice. DCs in the auricular lymph nodes were assessed using flow cytometry. Epidermal sheets were prepared and stained with anti-MHC II Ab. The number and morphology of Langerhans cells were evaluated microscopically.

Results: The control Ab showed insignificant binding while anti-MHC II Ab showed significant binding to a subpopulation of APCs stained for MHC II. HA with M.W. > 5000 Da did not cause MHC II positive cells to migrate out of the ears. None of the HA injections resulted in significant morphological changes or differences in Langerhans cell densities.

Conclusion: HA >5,000 Da did not cause migration of APCs to draining lymph nodes. None of the injected HA preparations cause morphological changes or emigration of Langerhans cells.

Sponsor
IRB/IACUC# 2014/15-23-A04

P53-dependent stromal senescence-induced tumor dormancy in the pre-metastatic reservoir thymus

Cancer patient survival rate has significantly improved with popularization of early diagnostics and advancement in the therapy. However, after surgical removal of primary tumor and subsequent radio-chemotherapy, some cancer patients can still suffer from recurrence of the same tumor in secondary sites of the body several years later. Metastatic tumor is the major cause of death among cancer patients. This metastatic recurrence/relapse is attributed to some minimal number of tumor cells, which are able to resist radio-chemotherapy, being in sleeping/dormant state at some organs of the body.

It is known that cancer cells can go to distant places of the body via vasculature and lymphatics, however, the largest lymph organ – thymus has just recently been suggested as a potential reservoir for tumor cell dormancy, and eventually relapse. However, the mechanisms responsible for tumor dormancy in the thymus are unknown. We believe that cancer cells can migrate to thymus and become dormant due to DNA damage caused by chemotherapy. Under the certain condition, those cancer cells are able to disseminate into other organs of the body leading to tumor relapse. It is necessary to study tumor micro-environmental elements in the thymus, so they could be targeted by the anti-tumor therapy.

Our preliminary observation shows that administration of a chemotherapeutic drug (Doxorubicin) into young wild-type mice leads to activation of p53 protein in thymus epithelial cells and induces thymus shrinkage. To link activation of p53 in thymic epithelial cells and tumor dormancy we injected human breast cancer cells in young and aged mice with subsequent Docorubicin administration. We found that tumor cells were harder to be killed in the aged involuted thymus with increased p53 in thymic epithelial cells. Our preliminary data suggest that activation of p53 in thymic epithelial cells induced by DNA-damage upon Doxorubicin promotes cell senescence of thymic epithelial cells, which leads to tumor cell dormancy/chemo-resistance.

This work is clinically relevant because our findings might be able to find new strategies to prevent tumor relapse after chemotherapy.

Sponsor  N/A
IRB/IACUC# 2014/15-45-A04
The Role of ecSOD in Phagosomal Containment of Listeria Monocytogenes

Extracellular superoxide dismutase (ecSOD) is a secreted enzyme associated with the extracellular matrix that plays a protective role during reactive oxygen species (ROS) mediated inflammatory responses. Listeria monocytogenes is an intracellular gram positive bacteria that causes listeriosis in infected individuals and animals. EcSOD has been shown to modulate the innate immune response to Listeria infection. With the use of ecSOD congenic mice (ecSOD HI, ecSOD WT, ecSOD KO), we have established that high ecSOD activity leads to decreased bacterial clearance despite an increase in neutrophil recruitment. Whereas, no ecSOD activity results in reduced neutrophil recruitment but effective bacterial clearance. Importantly, neutrophils in the livers of ecSOD KO mice show superior protective capabilities in comparison to neutrophils in ecSOD HI mice. To deduce the mechanism by which ecSOD contributes to neutrophil effector function during Listeria infection, we made use of different strains of GFP expressing Listeria monocytogenes. Neutrophils isolated from both the bone marrow and the liver of the ecSOD congenic mice were able to effectively phagocytose the bacteria. However, we observed that there was more bacterial escape from the phagosome of neutrophils isolated from the bone marrow of ecSOD KO mice in comparison to the ecSOD HI and WT mice. In contrast, there was no observable difference in the ability of neutrophils isolated from the livers of the ecSOD congenic mice to prevent Listeria escape from the phagosome. These data are contradictory to the previously reported protective nature of the ecSOD KO neutrophils and their importance for bacterial clearance from the livers of infected mice. The neutrophils used for the current in vitro studies were isolated from the tissues in the absence of infection. Neutrophils are generally not present in large numbers in tissues in the absence of infection, therefore, we inferred that the isolated neutrophils were not functionally active. In conclusion, our results suggest that our in vitro observations are not supportive of the previous in vivo data regarding the ability of ecSOD to modulate neutrophil function.

Differential Effects of Thoracic Duct Lymph on Pulmonary Macrophages

Purpose: The gut-lung axis remains a poorly defined mechanism that could impact etiology and treatment of gut and respiratory diseases. Early literature first described this gut-lung crosstalk in inflammatory bowel disease patients with chronic bronchopulmonary disease. Recent literature describes the role of intestinal lymph during acute respiratory distress syndrome (ARDS). In these studies, intestinal ischemia and reperfusion injury in animal models induces lung injury suggesting factors, such as cytokines and lipids, released from the gut during gastrointestinal shock can contribute to ARDS. The gut lymphatics provide a large pool of lymph rich in immune cells, inflammatory mediators, and lipids. Our lab has previously demonstrated lymph-enhancing techniques enhanced the flux of cytokines, chemokines and reactive oxygen and nitrogen species in thoracic and mesenteric lymph. We propose factors released from the gut travel through the lymphatics to the lung and suppress the immune response in the lung.

Methods: To test this hypothesis, alveolar macrophages from bronchoalveolar lavage fluid (BALF), lung tissue macrophages (after BALF collected) and intraperitoneal (IP) macrophages from IP lavage were isolated from healthy F344 rats. In addition, a rat alveolar macrophage cell line (NR8383) was used for in vitro studies. Macrophages were cultured for 12 hours and canine thoracic duct lymph (TDL) at 10% total volume per well and/or LPS (500ng per well) added for 24 hours. Supernatants were stored and used to measure nitric oxide (NO) and tumor necrosis factor alpha (TNFa) using Griess assay and ELISA.

Results: AM were the most sensitive to LPS activation compared to LM and IP macrophages. TDL suppressed LPS-induced NO (52% decrease) and TNFa (25% decrease) production. However, TDL did not significantly suppress LPS activation in LM and IP macrophages. In NR8383, TDL suppressed LPS-induced NO (86% decrease) and TNFa (66% decrease) production. TDL alone did not activate NR8383, AM, LM or IP macrophages and did not affect cell viability after culture.

Conclusions: Our results suggest a biological factor in lymph selectively suppresses LPS activation in alveolar macrophages. The mobilization of healthy lymph may protect the lung from chronic inflammation caused by pathogens and pulmonary disease. Future studies will focus on identifying factors in lymph that may modulate the immune response that may improve disease outcome.
Acute Lymphoblastic leukemia (ALL) is the most common type of cancer in children. It is characterized by overgrowth of the lymphocyte precursor (either B cell or T cell) that is nonfunctioning, and crowds out other immune cells. Current treatment options have a success rate of 80-90%. However, those who relapse have a survival rate of only around 25-40%. Also, side effects of current chemotherapy and radiation treatments have been shown to impact the normal growth and development of children. Research has shown that ALL of the B cell lineage is particularly resistant to killing by Natural Killer (NK) cells. NK cells are part of the innate immune system and specialize in killing tumor and virally infected cells. NK cell activation is dependent on a balance of inhibitory and activating receptors and their ligands expressed on the target cell. Our laboratory has previously cloned three immune receptors, 2B4, CS1 and LLT1, which have been shown to play a role in cancer, however their significance and role in childhood ALL have not been evaluated. In this study, we evaluated the expression of immune receptors 2B4, CS1, LLT1, NKp30 and NKp46 in pediatric ALL subjects both male and female in the age range of 3 – 18 yrs. ALL subjects and healthy subjects were enrolled at Cook Children’s Hospital and UNT Health Science Center, Fort Worth, TX with informed consent/assent according to IRB approval (UNTHSC IRB# 2008-094 & CCMC IRB# 2008-57). The blood samples were collected and peripheral blood mononuclear cells (PBMC) were isolated and analyzed by flow cytometry and real-time qPCR for expression of immune receptors. ALL subjects showed altered expression of immune receptors in the PBMC as compared to healthy subjects. There was an overall decrease in the expression of 2B4, CS1, LLT1 and NKp46 in the B lymphoblasts of ALL subjects as compared to healthy subjects. Expression and functional analysis of these receptors in a larger sample size will provide valuable insights to conduct future mechanistic studies to investigate the role of these immune receptors in ALL resistance and relapse. Funded by Cancer Research Foundation of North Texas (CRFNT).
Summary

Listeria Monocytogenes (LM) is a gram-positive, intracellular foodborne pathogen which can cause severe disease in immunocompromised individuals and is a leading cause of death from foodborne infections. LM stimulates the immune system via pathogen-associated molecular patterns (PAMPs) such as lipoproteins which interact with pattern recognition receptors (PRRs) including toll-like receptors (TLR2). These interactions induce activation of immune cells resulting in the production of cytokines such as TNFa, IL-1 and IL-6. PRRs also induce immune activity in response to damage-associated molecular patterns (DAMPs) which are released from host cells in response to cellular damage. High Mobility Group Box 1 (HMGB1) protein is a DAMP that has been shown to be actively secreted from macrophages during sterile inflammation resulting in the production of TNFa by binding to toll-like receptor 4 (TLR4). Even though HMGB1 has been shown to be an active player during sterile inflammation, nothing has been published about its function during immune responses to any pathogenic infection.

b. Purpose
The purpose of our study is to understand the effect LM infection has on transcription, translation and post translational modification of HMGB1. We are also studying the effect of HMGB1 on inflammatory cytokines such as TNFa, IL-1 and IL-6, neutrophil recruitment to infected organs, and bacterial burden during LM infection.

c. Methods
C57BL/6 mice were infected with LM and at 3 days post infection immune cells were isolated from the spleen and bone marrow. The cells were used for rt-PCR to study HMGB1 transcription, and western blotting to study the translation of HMGB1. The aforementioned cells were also incubated overnight with 10ng/mL of HMGB1, and supernatants were harvested to measure TNFa by ELISA.

d. Results
Our results indicate that LM does not have a significant effect on HMGB1 transcription and translation in the spleen and bone marrow. We also show that at 10ng/mL, HMGB1 does not enhance TNFa production in spleen and bone marrow cells.

e. Conclusion
Our results indicate that HMGB1 production is not influenced by LM infection. Furthermore, our data suggest that HMGB1 may not influence immune responses against LM in vitro. Further studies are required to elucidate the in vivo functions of HMGB1 during LM infection.

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Sponsor
R03AI109630 and UNTHSC RI6176
IRB/IACUC# 2013/14-25-A04
Extracellular superoxide dismutase (ecSOD) regulates extracellular concentrations of reactive oxygen species (ROS) to protect tissues during infection and inflammation. Using congenic mice with varying levels of ecSOD activity (ecSOD HI, WT and KO), 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. Additionally, we determined that ecSOD activity protects the extracellular matrix (ECM) from degradation and promotes egress of immature neutrophils out of the bone marrow and into the liver where they are unable to provide protection against LM. Since ecSOD can be produced by cells from the hematopoietic lineage as well as somatic cells, the potential contribution of ecSOD produced by cells from each lineage required further investigation.

In order to determine the relative contributions of ecSOD produced from either hematopoietic-derived cells or somatic cells, we generated bone marrow chimera mice using ecSOD KO mice and C57Bl/6 mice. Briefly, host mice were irradiated to eliminate hematopoietic lineage cells and reconstituted with bone marrow cells isolated from donor mice. Control groups consisted of ecSOD KO mice reconstituted with bone marrow from ecSOD KO donors (KO -> KO) or C57Bl/6 mice with bone marrow from C57Bl/6 mice (WT -> WT). Experimental groups consisted of ecSOD KO mice reconstituted with bone marrow from C57Bl/6 mice (WT -> KO) or C57Bl/6 mice with bone marrow from ecSOD KO mice (KO -> WT). All mice were then infected with LM and evaluated for neutrophil recruitment and bacterial burden.

We observed that ecSOD produced by hematopoietic cells leads to increased bacterial burden during LM infection, while ecSOD produced from somatic cells is essential for increased neutrophil recruitment. Collectively, our data suggest that ecSOD produced by both hematopoietic cells and somatic cells is involved in our observed phenomena; however, the contribution of ecSOD from each cell lineage is skewed towards either increased neutrophil recruitment or increased susceptibility to LM infection, but not both. These studies highlight the potential therapeutic value of ecSOD inhibitors to enhance immune responses during bacterial infections.
Million Veteran Program (MVP)

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. 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. 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. Our site has contributed actively in the recruitment of veteran at our institution, we continue to work towards achieving our target. All over US, more than 450,000 patients have been enrolled in MVP. The research on the 400,000 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.

Sponsor: N/A
IRB/IACUC#: VA Central IRB 10-02

Effect of Detergent Selection on Quantity of DNA Extracted and on STR Profile Developed from Bone-Derived DNA

DNA analysis is often essential to make positive associations in cases of unidentified persons, missing persons, and mass mortality incidents. In cases such as these, human skeletal remains are frequently the only source of genetic material available, but bone-derived DNA characteristically provides lower quantities of DNA and lower quality short tandem repeat (STR) profiles than that of other sample types. Conventional DNA extraction methods were developed based on the biochemical composition of soft tissues or body fluids. DNA from these unmineralized sample types is more readily extracted and contains fewer inhibitors than DNA found in bone; moreover, skeletal remains encountered in casework may be aged or subjected to environmental factors that reduce the quality of DNA obtained. These sample-specific issues support the development of specialized extraction techniques for bone in order to obtain the highest quantities of DNA and improved quality STR profiles. Prior work has demonstrated that increased DNA quantities are obtained from human skeletal remains when using Buffer ATL in conjunction with Collagenase Type II (CLSI) enzyme. It has also been determined that metals, particularly calcium, copurify with DNA when processing bone samples. These copurified metals have been shown to inhibit PCR amplification of STR markers. Building upon these findings, a protocol was designed to determine whether use of a detergent other than Buffer ATL would continue to improve upon current methods for DNA extraction from human bone.

An unembalmed human cadaver dissection was obtained through the Willed Body Program of the University of North Texas Health Science Center. DNA was purified on the EZ1® Advanced XL System (Qiagen®, Hilden, Germany) after employing the modified digestion step. The DNA isolates were quantified using the Investigator® Quantiplex HYres Kit (Qiagen®), then STR markers were amplified using the Investigator® 24Plex QS Kit (Qiagen®) and fragment analysis performed with the 3500xL Genetic Analyzer (Thermo Fisher Scientific, Inc., Carlsbad, CA). STR profiles were assessed using GeneMapper® ID-X v1.4 (Thermo Fisher Scientific). All Real-Time PCR and electropherogram data were analyzed using Microsoft® Excel (Microsoft® Corp., Redmond, WA) and RStudio® (RStudio® Inc., Boston, MA).

Though Buffer ATL yielded significantly higher quantities of DNA per milligram of bone, results indicate that using an increased strength anionic detergent, such as SDS or SLS, in conjunction with CLSI enzyme will improve the quality of STR profiles produced from human skeletal remains. Full profiles were recovered for all concentrations of SDS and SLS, while allelic drop out was observed for Buffer ATL and Triton® X-100. Mean peak heights of profiles produced using all concentrations of SDS and SLS represented a quantitative improvement over both Buffer ATL and Triton® X-100. Mean peak height ratios of profiles produced using all concentrations of SDS and SLS also represented a qualitative improvement compared to samples digested using CLSI enzyme with Buffer ATL or Triton® X-100. Unlike SDS, there are no special considerations for storage or handling of SLS detergent solutions, making it an excellent choice for use in forensic laboratories. Use of SLS consistently produces sufficient quantities of DNA and full STR profiles at all concentrations tested, and as no significant differences were observed between concentrations of SLS, the lowest tested concentration of 1% should be employed in order to conserve resources.

Sponsor: N/A
IRB/IACUC#
A Novel Multiplex Assay for an Ancestry-Informative Marker (AIM) Panel of INDELs

The current standard for forensic laboratories in criminal casework is to use Short Tandem Repeat (STR) markers to develop an evidentiary profile to compare with a reference profile. Commercially available STR amplification kits yield amplicons 100 to 500 base pairs (bp) in length. A common problem encountered by scientists is degraded DNA samples that are only 180-200 bps in length. These samples fail to amplify some loci and therefore produce an incomplete STR profile. STRs are used for identity testing because of their high discrimination power. However, there are cases where no STR match was obtained through a DNA database search and thus no investigative lead is obtained. The bioancestry of the donor of the sample could aid law enforcement in such cases. Another class of markers that could provide investigative value from degraded DNA samples is Ancestry-Informative Marker (AIM) Insertion/Deletions (INDELs). INDELs are polymorphisms that can be amplified from degraded samples due to their smaller amplicon size. AIMs have the ability provide bioancestry information. This project used a previously developed panel of AIM-INDEL markers to develop a multiplex PCR-based assay specifically for these identity-testing applications.

Sponsor n/a

IRB/IACUC#
An evaluation of the RapidHIT® ID system for field forward applications

The utilization of a new Rapid DNA (RDNA) platform to generate CODIS uploadable DNA profiles will serve to be instrumental in improving current DNA typing techniques and in reducing the backlog of forensic reference samples. The RapidHIT® ID (IntegenX; Pleasanton, CA) system is a second generation system in RDNA that has the potential to yield comparable DNA profiles to those achieved by traditional bench methods. The RapidHIT® ID platform is a self-contained, fully-automated, sample-to-profile system with a novel construction designed to reduce it’s footprint as well as the number of samples necessary to be run at a single time, making it conducive to both laboratory and field work application. The RapidHIT® ID system has the capacity to perform direct amplification, electrophoresis, and data analysis in approximately 90 minutes with nominal “hands-on” assistance required. Reliable DNA STR profiles have been generated from reference buccal swabs. The RapidHIT® ID platform was evaluated for concordance, reproducibility, and lack of contamination. Sensitivity and interpretation thresholds were established, and although the system was designed for reference buccal swabs, additional studies evaluating the effects of sample age, inhibitors, and sample collection methods were performed. This new instrumentation provided DNA STR profiles comparable to those obtained from traditional DNA genotyping methodologies, in addition to complete or partial profiles from the sensitivity studies. Based on preliminary studies, the RapidHIT® ID system is a new RDNA platform that is robust and reliable for generating STR profiles from forensic reference samples.

Massively parallel sequencing of 68 insertion/deletion markers identifies novel sequence variation for utility in human identity testing

Short tandem repeat (STR) loci are traditionally used by the forensic science community for kinship, missing persons, and human identity testing. These markers hold considerable value due to their size, ability to be multiplexed, and highly polymorphic nature. However, they are unable to provide phenotypic and biogeographic ancestry estimates and are too large for use in analysis of DNA from highly compromised substrates such as explosives or human remains. Small bi-allelic polymorphisms, such as insertions/deletions (INDELs), have been of considerable interest within the forensic science community for their utility in filling such gaps. These markers range in size from 2-6 base pairs, making them ideal for highly compromised sample types. Additionally, the ease of multiplexing large INDEL panels allows for comparable discrimination power when compared to STRs. Capillary electrophoresis is a current mainstay in the forensic DNA workflow, generating fluorescent signals to detect alleles separated by size. This method is limited by number of dyes simultaneously utilized, number of loci capable of multiplexing, sample throughput, and required amplicon size. Massively parallel sequencing (MPS) provides a solution to these limitations by targeting many loci across the genomes of multiple samples simultaneously with relatively high sequence coverage. Herein, we describe the utility of MPS, using the Nextera™ Rapid Capture Custom Enrichment Kit (Illumina, Inc., San Diego, CA), to sequence 68 INDELs in four major US population groups on the Illumina MiSeq™. We also define a novel application of the STR Allele Identification Tool: Razor (STRait Razor) to analyze INDEL sequences and capture adjacent sequence variation in the form of single nucleotide polymorphisms (SNPs). This application has enabled the discovery of unique allelic variants, which increase the discrimination power and decrease the single-locus and combined random match probabilities of four well-characterized INDELs. These findings suggest that more valuable INDELs for human identification may exist elsewhere in the genome. As such, it is recommended that these four markers be included in future INDEL multiplex panels for human identification due to their enhanced individualization potential.
Comparison of Four Differential DNA Extraction Methods for Casework Analysis of Sexual Assault Kit Swabs

Sexual assault kits comprise 40-50% of a typical Forensic Laboratory caseload. The traditional method to process these samples is time-consuming, and requires the use a dangerous chemical known as Phenol:Chloroform:isoamyl Alcohol (PCIA). The purpose of this study is to assess the relative efficacy of the PCIA method when compared to three other currently available differential extraction methods.

A single male volunteer and a single female volunteer donated semen and saliva, respectively. Aliquots of semen were serially diluted such that three decreasing concentrations of semen could be assessed alongside a consistent concentration of saliva. From these three different mixtures, swabs were made and allowed to dry in a 37 °C drying oven for two weeks, then at room temperature for an additional four weeks in order to simulate aged samples. Three days prior to DNA extraction and purification, another set of swabs were created to simulate fresh samples. The aged and unaged samples were tested in triplicate for each of the four extraction methods.

The methods to be compared include two manual and two automated methods. The manual methods include the standard differential (SD) and the Lounsbury Method, which is a modified version of the SD. The two automated methods include the AutoMate ExpressTM DNA Extraction System (ThermoFisher Scientific, Carlsbad, CA), and a method employing the use of two of Qiagen’s DNA platforms: the QIAcube and the Qiagen EZ1® Advanced XL (Qiagen®, Hilden, Germany).

Results indicate that as sperm sample concentration decreases, automated methods produce superior results both in DNA quantity obtained and in quality of STR profiles produced. Automated methods reduce hands-on time, facilitate higher through-put of samples, and reduce analyst contact with hazardous chemicals such as PCIA, making it an all around great choice for labs. All Real-Time PCR and electropherogram data were analyzed using Microsoft® Excel (Microsoft® Corp., Redmond, WA), and RStudio® (RStudio® Inc., Boston, MA).

Sponsor: N/A
IRB/IACUC#: 2015-189
Safety and Efficacy of Ledipasvir plus Sofosbuvir with or without ribavirin in hepatitis C genotype 1 patients who failed previous treatment with Simprevir plus Sofosbuvir

Combination therapy with Simeprevir (SIM), NS3/4 protease inhibitor, with Sofosbuvir (SOF), NS5b polymerase inhibitor is an FDA approved treatment option for chronic hepatitis C genotype 1 patients with an over all SVR 12 rate of 85-95%. Single tablet fixed dose combination of Ledipasvir (LDV), NS5a inhibitor, with SOF is also FDA approved for treatment of hepatitis C genotype 1 with SVR 12 rates of ≥ 95%. However, there is no data on the efficacy of retreatment with LDV+SOF in patients who failed initial treatment with SIM+SOF.

Methods: Data was collected from treatment cohorts at 2 large hepatology referral centers in Dallas-Fort Worth area. Patients included in the analysis were previously treated with SIM+SOF with or without RBV for 12 weeks but failed to achieve SVR 12 and then undergone re-treatment with LDV+SOF with or without RBV for 12-24 weeks. Patients with cirrhosis, including decompensated Child's class B or C were included.

Decompensation was defined by the presence of fluid overload, hepatic encephalopathy or variceal bleeding. Patients with HCC as the only event that defined decompensation were excluded. Patients received singlet tablet fixed-dose combination of Ledipasvir 90 mg with Sofosbuvir 400 mg PO +/- wt based ribavirin (RBV) daily for 12-24 weeks at the discretion of the treating hepatologist. Baseline and end of treatment (EOT) laboratory tests & viral load were obtained on all patients. SVR 12 defined as undetectable viral load 12 weeks after EOT was collected on all patients who had reached that time point by Nov 10, 2015. Adverse effects during treatment were obtained on all patients. Data was analyzed using 2 sided t test for continuous variables and chi-square test for categorical variables.

Results: SVR 12 was achieved for 11/13 of all patients and 10/11 for patients who were cirrhotic. 100% (29/29) had achieved EOT response. 10/29 had no side effects on treatments. Of those who had side effects, none were considered severe enough to warrant discontinuation.

Conclusions: Ledipasvir + Sofosbuvir is a viable treatment option with high SVR 12 rate in patients who have failed 12 weeks of treatment with Simprevir+Sofosbuvir. Single tablet fixed-dose combination of Ledipasvir with Sofosbuvir in patients who failed 12 weeks of treatment with Simprevir+Sofosbuvir with or without Ribavirin (RBV) daily for 12-24 weeks is well tolerated with high SVR 12 rate of ≥ 95%.

HIV-1 TAT Induces MIR-132 Expression Leading to Neurotoxicity and Aberrant Dendritic Morphology

TITLE:
HIV-1 Tat induces mir-132 expression leading to neurotoxicity and aberrant dendritic morphology

Authors: Pejman Rahimian, Johnny He
Presenter name: Pejman Rahimian

Purpose: HIV-1 Tat is involved in the pruning of neurites and loss of synapses which are the most prominent pathological hallmarks of HIV-associated neurocognitive disorders (HAND). However the underlying molecular mechanisms of this synaptodendritic loss have not been elucidated. We report for the first time the induction of a brain-enriched microRNA by HIV-1 Tat protein leading to repression of significant regulating factors in dendritic arborization and synapse formation.

Methods: Levels of mir-132 were quantitated in astrocyte cell lines (U373.MG), primary human and primary mouse astrocytes, and also in neurons (SH-SY5Y) following transfection with Tat plasmid and also in primary human astrocytes following infection with the VSVG-pseudotyped HIV-1 virus. Repression of mir-132 targets and involvement of CREB in miRNA induction were evaluated via Western blotting.

Results: We observed significant mir-132 upregulation as the result of Tat expression in both neurons and astrocytes followed by the repression of mir-132 targets in both cell types. Activation of CREB as indicated by elevated p-CREB was observed along with Tat expression while using a Tat construct defective in CREB activation abrogated mir-132 induction by Tat. We also observed significant reduction in neuronal viability along with loss of dendritic arbor following Tat expression which correlate with the repression of mir-132 targets MecP2 and p250GAP and consequently BDNF loss.

Conclusion: Our results indicate that HIV-1 Tat induces mir-132 in the brain through activation of CREB and stabilization of interaction between p-CREB and CREB-binding protein (CBP). Dysregulated mir-132 expression contributes to neurotoxicity and aberrant dendritic morphology witnessed in neurocognitive disorders associated with HIV-1 invasion of the central nervous system.

Acknowledgments (ex. funding support, etc.)

Neurobiology of Aging Training Grant-T32 AG020494
IACUC#: 2014/15-01-A04

Sponsor Neurobiology of Aging Training Grant-T32 AG020494
IRB/IACUC# 2014/15-01-A04
Purpose:
West Nile Virus (WNV) is endemic to the United States including Texas. The virus occurs in nature in a mosquito-bird-mosquito transmission cycle but mammals including humans can become incidental hosts. Mosquitoes of the genus Culex are considered the primary vector for WNV. The objective of this research is to develop an assay for detecting the presence of mammalian and/or avian DNA in the blood meal contents of blood-fed mosquitoes. Identifying the hosts and any patterns in feeding habits of the vector mosquitoes can provide more information on the natural transmission of West Nile Virus from avian reservoir hosts to Culex mosquito vectors to incidental mammalian hosts.

Methods:
Mosquitoes were collected weekly using gravid traps and CO2 light traps throughout Fort Worth. DNA was extracted from the abdomens of blood-fed mosquitoes, and the amount of blood meal was recorded. The DNA was amplified by PCR using universal vertebrate primers designed to generate 150-bp (mammals) or 120-bp (birds) 18S rDNA fragments. The PCR products were analyzed using gel electrophoresis. The PCR assay was confirmed using known mammalian and avian samples.

Results:
A total of 597 blood-fed mosquitoes were collected throughout Fort Worth in 2014. Results were recorded as avian host only, mammalian host only, or both avian and mammalian hosts. More mosquitoes with a blood meal ≤ 1/3 had no host identified compared to those with larger blood meals. Of those with the host identified, most were avian host only (76% of 292 tested with a host identified) followed by both avian and mammalian hosts (23% of 292) and only 2 of the 292 tested that had a host identified had a mammalian host only.

Conclusions:
The PCR assay using the universal vertebrate primers targeting 18S rDNA is a sensitive method that allows for the detection of both mammalian and avian host DNA in mosquito blood meals including the presence of both mammalian and avian DNA in a single vector blood meal. The assay will be used to analyze blood meal contents from mosquitoes collected in 2015 in addition to those collected in 2014 to identify any trends in feeding habits.
Regulation of Astrocyte Mitochondrial Function and Oxidative Stress by Trace Amine Associated Receptor 1 in the context of Methamphetamine Abuse and HIV-Associated Neuropathological Disorders.

As a psychostimulant, methamphetamine (METH) use leads to long-lasting, euphoric effects. Between 10-15% of human immunodeficiency virus-1 (HIV-1) patients report METH abuse, which exacerbates HIV-1 infection, accelerating the onset of HIV-associated neurocognitive disorders (HAND) and immune dysfunction. Neuroinflammation, glial activation, oxidative stress and excitotoxicity contribute to METH and HIV neuropathogenesis. However, the mechanisms through which METH and HIV affect astrocyte function are unclear. Recently, we reported trace amine associated receptor 1 (TAAR1) as a novel astrocyte receptor for METH. Previous studies suggest TAAR1 activity may be regulated by G-protein promiscuity and desensitization by b-arrestin. We hypothesize that HIV-relevant stimuli upregulate astrocyte-TAAR1 expression and that METH exposure induces alterations in TAAR1 activation and intracellular localization, thus contributing to astrocyte dysfunction. To examine TAAR1 expression was assessed by real-time PCR and fluorescent microscopy in human astrocytes in the context of HIV and METH exposure. Changes in EAAT2, which could impair astrocyte ability to clear glutamate, were examined in parallel. To assess TAAR1 regulation by interacting partners, b-arrestin phosphorylation and co-immunoprecipitation studies were performed. Further, downstream outcomes of TAAR1-mediated cAMP and calcium signaling were evaluated, focusing on mitochondrial function and oxidative stress. TAAR1 expression is increased by HIV-relevant stimuli; while EAAT2 expression is concurrently decreased. TAAR1 localizes throughout the cell body in non-activated astrocytes and becomes perinuclear, increasing in the ER during gliosis. b-arrestin is activated by IL-1β and associates with astrocyte-TAAR1. Mitochondrial dysfunction increases with METH and HAND-relevant activation, leading to reactive oxygen species. These studies delineate how dysregulation of TAAR1 may contribute to astrocyte-mediated neurodegeneration during HAND and METH abuse, while also revealing a novel therapeutic target in astroglia.

Sponsor R01DA025566, R01DA039789, 5R24HD0008836
IRB/IACUC# IRB2007-121
In Susceptible Mice Infected with M. pulmonis, Host Lung Damage is Associated with Recruitment of IL-17A+ Lymphocytes and Neutrophils into the Lung

Background:
Possessing the smallest genomes, mycoplasma induce debilitating pneumonia in humans and animals resulting in chronic airway inflammation. Exacerbating previously acquired respiratory conditions (i.e. asthma), mycoplasma have evolved to resist antibiotics. Current vaccines induce the same damage seen during actual infection. A proinflammatory cytokine contributing to chronic pathology and neutrophil-mediated host protection, IL-17A is secreted during infection with mycoplasma. Here, we investigate whether IL-17A can promote damage characteristic of mycoplasma disease. Our results will help development of vaccines that confer protection and lack side-effects.

Methods:
Murine pneumonia, induced by M. pulmonis, resembles the pulmonary pathogenesis seen in human mycoplasma diseases. Furthermore, BALB/c models have been well established for studying chronic respiratory mycoplasma infection. Briefly, M. pulmonis was administered intranasally. At select time points post infection, mice were sacrificed and aspects of pulmonary pathogenesis analyzed.

Results:
Injecting neutralizing antibodies against IL-17A into BALB/c mice reduced inflammation during infection without influencing bacterial burden. Attenuating the effects of IL-17A reduced both airway cell numbers and total lung IL-17A+ lymphocytes by Day (14). The increase in IL-17A+ cells was associated with increased airway neutrophils, appearing as early as Day (1) post-infection with M. pulmonis. The presence of neutrophils appears alongside CD4+, CD8+, and γδ T-cells that secrete IL-17A early during infection. By Day (9) post-infection, the described T-cell populations are replaced by CD4+, SCA-1+, and NK cells that contribute to IL-17A levels. Although IL-17A production by CD4+ T-cells reaches its maximum response at Day (1) post-infection, this was the only T-cell population that persisted in their production of IL-17A by Day (14).

Conclusions:
During infection with M. pulmonis, neutrophil recruitment into the lungs is associated with the presence of IL-17A+ lymphocytes. Neutrophils and IL-17A+ cells drive host damage; neutralizing IL-17A reduces airway neutrophils, total IL-17A+ lung cells and host damage. Blocking IL-17A lowers lung lesion development, thus IL-17A and neutrophils promote respiratory damage. Surprisingly, blocking IL-17A during the innate response results in more severe inflammation when compared to both controls and animals starting treatment five days' post-infection. The generation of IL-17A+ lymphocytes, and subsequent recruitment of neutrophils was associated with disease pathogenesis.

Sponsor
American Society of Microbiology (ASM)

IRB/IACUC#  2013/14-01

The in vitro Virulence Phenotype of Clostridium difficile Ribotype 027 Impacts Disease Severity in the Mouse and Hamster CDAD Models

C. difficile ribotype 027 (RT027) is the epidemic strain found primarily in North America. 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 characteristics for several RT027 and non-RT027 C. difficile clinical isolates, and how these factors may impact disease severity in the hamster and mouse C. difficile associated disease models.

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 mouse C. difficile model involved being administered for 5 days through oral gavage or drinking water. The mice were then placed on a non-antibiotic supplemented water for 48 hours IP administered 10 mg/kg of clindamycin, and orally inoculated with C. difficile spores 24h later. Survival was monitored for 10 days and fecal samples were taken each day to be processed for CFU/spore counts. The HCDAD studies involved inoculating 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 post-mortem cecal fluid samples were taken from 3 hamsters at set disease-associated time points to determine the CFU/spore counts and Toxin A/B titers. 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 mouse model, 100% of the animals infected with the non-027 isolate survived regardless of how antibiotics were administered. In contrast, 13-26% morbidity was associated with mice infected with the RT027 isolate after being given antibiotics by oral administration or through supplemented water. 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.

Sponsor
American Society of Microbiology (ASM)

IRB/IACUC#  2013/14-01, 2012/13-14-A06
Increased side-chain length confers a greater dopaminergic phenotype and increased reinforcing efficacy to cathinone analogs of MDMA

In recent years, synthetic cathinone compounds have been utilized in "Ecstasy" formulations in lieu of MDMA, some of which are congeners of MDMA. The current study aimed to assess structure-activity relations of the discriminative stimulus and reinforcing effects among three synthetic cathinone analogs of MDMA: methylone, butylone, and pentylone. Rats were trained to discriminate methamphetamine from vehicle. Dose-response studies were performed with each of the test compounds and the lowest substituting dose was then tested in the presence of a range of doses of the D1-selective antagonist SCH23390. A separate group of rats was trained to self-administer methamphetamine under a FR10 schedule of reinforcement. Rats then self-administered methamphetamine, MDMA, and the test compounds under a progressive ratio schedule of reinforcement. Each of the test compounds fully substituted for the discriminative stimulus effects of methamphetamine. SCH23390 fully and dose-dependently antagonized the methamphetamine-appropriate responding produced by these compounds with methylone being the most sensitive to the effects of SCH23390, followed by butylone, then pentylone. In the self-administration studies, breakpoints increased concurrently with side-chain length. Methylone's breakpoint was higher than saline, but the same as MDMA. The breakpoints for butylone and pentylone were both greater than saline or MDMA, but only pentylone produced responding comparable to methamphetamine. These data indicate that as side-chain length increases, the sensitivity to SCH23390 decreases and self-administration increases, suggesting that side-chain length is positively associated with dopaminergic phenotype and reinforcing efficacy. Furthermore, these synthetic cathinones may drive compulsive use of "Ecstasy" given their presence in "Ecstasy" formulations and increased reinforcing efficacy relative to MDMA.

Sponsor  T32 AG020494; N01DA-13-8908
IRB/IACUC#  2012/13-53-A05

Treatment of Hypertensive Obese Zucker Rats with Metformin Enhances Phenylephrine-Induced Bradycardia and c-Fos Expression in the NTS

With the progression of metabolic syndrome adult obese Zucker rats (OZR) develop impaired baroreflexes that coincide with a reduced ability to activate the nucleus tractus solitarius (NTS). The NTS, which receives baroreceptor afferent inputs, appears to respond less to acute rises in mean arterial pressure (MAP) as suggested by less phenylephrine (PE)-induced c-Fos expression compared to age-matched lean Zucker rats (LZR). In addition microinjection of glutamate into the NTS produces smaller reductions in splanchnic sympathetic nerve activity and MAP in adult OZR versus LZR. We have recently observed that prevention of hypertension improves baroreflexes in OZR, but they are still impaired compared to like-treated LZR. Because hyperglycemia impairs NTS function and baroreflexes in type I diabetic rats, we hypothesized that improvement of glycemia in OZR would also enhance baroreflexes and the ability to activate the NTS. OZR and LZR were treated with metformin (MET; 300 mg/kg/day in drinking water) for 3 weeks (began at 13 weeks of age) and compared to untreated age-matched rats. Blood samples were taken in conscious, unfasted rats at 9-10 am. Compared to untreated OZR, MET-treated OZR had lower blood glucose levels (179±19 vs. 120±8 mg/dl, P

Sponsor  AHA GRNT1888005, AHA 16PRE27260088
IRB/IACUC#  2013/14-11-A05
**1503**

**Poster**

**Presenter:** Trinh Nguyen

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**Authors:** Trinh Nguyen, UNT Health Science Center; Mehravan Singh PhD, UNT Health Science Center; Chang Su Phd, MD, UNT Health Science Center;

**Classification:** GSBS Student

**The role of miRNA in regulating Progesterone’s neuroprotective function in the ischemic brain**

Stroke has been reported as the fourth leading cause of death for Americans and it is a leading cause of adult disability. The risk of ischemic stroke increases significantly with aging. Gender appears to play a profound role, with the incidence being higher in women. A large body of studies has suggested that women in postmenopausal state are at greater risk of ischemic stroke and are likely to experience much more severe impacts. A considerable amount of research has supported that progesterone (P4) is a potent neuroprotectant that may exert beneficial effects in various neurodegenerative diseases and stroke. Our laboratory has reported that Brain-derived neurotrophic factor (BDNF) is a critical mediator for P4 neuroprotective actions. BDNF has well-defined roles in synaptogenesis and neuronal survival. We recently reported that P4 enhances BDNF release from glia, but not from neurons, by acting via a novel membrane-associated progesterone receptor, Pgrmc1. Here, we identified a member of the Let-7 microRNA (miRNA) family as a potential negative regulator of Pgrmc1. Our data demonstrated an inverse association between the expression levels of Let-7 and the transcripts of Pgrmc1 and BDNF in post-ischemic mouse cortex. Literature supports the antagonist (synthetic inhibitor) of Let-7 miRNA significantly reduced infarct volume and improved neurological deficits in a rodent ischemic stroke model. When combined, these lines of evidence have strongly supported our hypothesis that in the stroked brain, Let-7 negatively regulates Pgrmc1 gene expression, which disrupts P4-induced BDNF release from glia and ultimately leads to the attenuation of P4’s positive effect on synaptogenesis.

1. Cell culture: Mouse primary cortical neurons and primary cortical astrocytes were derived from postnatal day 1 male pups. Primary astrocytes were maintained in DMEM with sodium pyruvate/10% FBS + 1% penicillin/streptomycin. Primary neurons were maintained in Neurobasal A media with 10% FBS + 1% penicillin/streptomycin.

2. Treatment of primary astrocytes: Primary astrocytes were transfected with either Let-7 mimics or inhibitors. qPCR was used to confirm the overexpression and knock down of Let-7, as well as expression of their potential targets. Western blotting was used to determine the protein levels of the miRNA potential targets.

3. Treatment of neuronal cultures with conditioned media (CM) from glia: Primary astrocytes were transfected with miRNA mimics/inhibitors. Then cultures were treated with vehicle control (0.1% DMSO) or 10 nM P4 for 18 hrs. The CM was concentrated by Protein Concentrators with 9 Kda molecular-weight cutoff (Pierce) to remove P4. Concentrated CM was then applied to neuronal cultures.

4. Animal treatment: Female C57BL/6J mice were bilaterally ovariectomized at 4.5 months old to eliminate endogenous ovarian production of P4. One week afterward, P4 pellets or cholesterol pellets were implanted in these animal subcutaneously. 2 days after pellets implantation, ischemic stroke was induced in these mice using the middle cerebral arteries occlusion method. 24hrs after stroke induction, the antagonist of let-7or scrambled control were delivered to the penumbra via intracerebral ventricular (ICV) injection.

**Sponsor**

American Heart Association (13SDG17050059), NIH (AG027956) and NIH T32 (AG020494)

**IRB/IACUC#** 2012/13-42-A04

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**1504**

**Poster**

**Presenter:** Vicki A. Nejtek, Ph.D.

**Department:** Institute for Healthy Aging

**Authors:** Vicki Nejtek Phd, UNT Health Science Center; Deepika Talari M.P.H, UNT Health Science Center; Sid O’Bryant Ph.D., UNT Health Science Center;

**Classification:** Faculty (Not for Competition)

**Examining Active Theater and Clinical Outcomes as Indicators of mild TBI in Post-Deployed Veterans vs. Civilians at No-Risk for mild TBI: A Longitudinal Evaluation**

**Purpose:** Of the ~300,000 veterans who experience mild TBI, 40% have ‘residual’ neuropsychological symptoms lasting 3-months or longer – a timeframe considerably longer than the gold standard for diagnosing mild TBI in the post-deployed condition. Failure to recognize residual symptoms as a consequence of mild TBI in veterans is common as these symptoms are often misattributed to posttraumatic stress disorder (PTSD). Determining risks for mild TBI retrospectively is understudied. Here, we examined active theater and clinical indices as retrospective risk indicators for mild TBI in post-deployed veterans compared to civilians. Hypotheses: Veterans at-risk for mild TBI will have poorer depression, anxiety, and quality of life outcomes than civilians with no risk. Risks for mild TBI in veterans will be influenced by military experiences and clinical indices. Methods: Longitudinal data from 182 veterans and 74 civilian clients (n=256) receiving cognitive behavioral therapy (CBT) at Recovery Resource Council from 2013-2015 were analyzed. Descriptive statistics, frequency distributions, ANOVA and regression modeling, were used to test the hypotheses using a 95% confidence level and an alpha level of 0.05 to determine statistical significance.

**Results:** Depression, anxiety, and quality of life scores measured before, after 6- and 12- sessions of CBT were significantly worse in veterans compared to civilians. Active theater and clinical indices predicted risks for mild TBI. 74 civilians and 52 veterans had no-risk for mild TBI (n=126) and 130 veterans were at-risk for mild TBI. Veterans at-risk for mild TBI had significantly higher depression and anxiety scores and lower quality of life scores than the no-risk group measured before, after 6- and 12-sessions of CBT. Risks for mild TBI predicted PTSD severity, depression, anxiety, and quality of life scores at all three time points.

**Conclusion:** Active theater and clinical indices identified veterans at-risk for mild TBI. Even with 12-sessions of CBT, veterans at-risk for mild TBI had poorer depression, anxiety, and quality of life scores than those with no-risk. These outcomes indicate that mild TBI presents with long-lasting psychological symptoms beyond a 3-months timeframe that do not fully resolve with CBT. Veterans returning from active theater should receive a thorough neuropsychological evaluation to differentiate mild TBI from PTSD in order to receive proper treatment.

**Sponsor**

Recovery Resource Council

**IRB/IACUC#** 2014-058 N/A
Novel Risk Factors for TIA and Stroke in Young Adults

Purpose: From 1993 to 2005 the incidence of stroke in older adults (ages 55-84) substantially decreased while in younger adults (ages 20-44) the incidence more than doubled. Traditional risk factors for stroke have been well documented in older adults such as hypertension, diabetes and obesity. Fewer studies explore transient ischemic attack (TIA)/stroke risks in young adults. Thus, it is clinically relevant to examine novel risk factors that may be unique to young adults. To better understand the increasing incidence for stroke in this population, we examined physical, psychological, and cognitive indices as novel risk factors for TIA and stroke in young adults. Hypothesis: Those identified as moderate/high risk for TIA/Stroke will have higher truncal body fat percent and waist-to-hip ratio (WHR) and will perform poorer on cognitive and stress tests compared to no/low risk. <br />

Methods: Men and women ages 18-45 of all race/ethnic backgrounds were eligible to participate in this prospective, cross-sectional, pilot study. Demographic data, WHR, body fat percent, personal and family history of chronic illness, TIA/stroke, etc. were collected. Assessments included the Perceived Stress Scale, Coping Self-efficacy Scale, and the Rey-Osterrieth Complex Test. Descriptive statistics, frequency distributions, independent sample t-tests, ANOVA, and regression modeling, were used as appropriate. All analyses were conducted using a 95% confidence level and an alpha level of 0.05 to determine statistical significance.

Results: A total of 50 subjects participated in this study (n=50). Each subject was grouped as no/low risk (NL) or moderate/high risk (MH) based on their personal + family medical history + total body fat percent. The MH group had significantly higher BMI (p = 0.03), higher body fat percent (p = 0.001), and higher truncal body fat distribution (p=0.001). MH subjects had more difficulty with cognitive-based coping skills, higher perceived stress, and performed worse on the Rey-Osterrieth test than the NL group.

Conclusion: These preliminary data suggest that those who have a moderate-to-high TIA/stroke risk profile have higher stress levels, less memory recall, and reduced cognitive-based coping skills. The results inform researchers about the need to further explore these novel risks factors in a larger controlled study. Future studies are needed to identify young adults who are at risk of TIA/stroke to reduce the incidence rate in this population.

Sponsor N/A
IRB/IACUC# 2015-003

Enhanced Excitability of Vasopressin Neurons in the Supraoptic Nucleus Following 48 hr. Water Deprivation

Arginine vasopressin (AVP) is a neurohypophyseal hormone released from the Posterior pituitary by magnocellular neurosecretory cells (MNCs) located within the supraoptic (SON) and paraventricular (PVN) nuclei of the hypothalamus. AVP is involved in the regulation of body fluid homeostasis and influences blood pressure, plasma osmolality, and blood volume. The regulation of AVP release is critical to maintaining body fluid homeostasis and is dependent on the activity of MNCs. The balance of excitatory and inhibitory inputs are important elements of activity, however the mechanisms leading to changes in AVP release are not fully understood. Water deprivation (WD), a physiological challenge, was used to examine changes in excitatory neurotransmission in MNCs using patch-clamp electrophysiology.

Male Sprague-Dawley rats weighing 250 – 350 g received bilateral SON infusions of an adeno-associated virus (AAV) construct containing mouse AVP gene promoter and EGFP reporter. Two weeks following AAV infusions, rats were water deprived for 24 hr. or 48 hrs. Controls were allowed ad libitum access to water. Following water deprivation, coronal brain slices (300 µm) containing the SON were cut using standard procedures. Whole-cell patch clamp recordings were obtained from slices superfused with aCSF containing tetrodotoxin (TTX; 0.5 µM) and bicuculline methobromide (Bic; 10 µM). Baseline mEPSCs were recorded then NMDAR mediated components were pharmacologically isolated with 5 minutes drug application of AMPA antagonist 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX; 10uM). Parameters measured for mEPSCs were amplitude (pA), rise time (ms), decay time (ms), charge transfer, and mEPSC frequency.

In EGFP labeled SON neurons (i.e. confirmed vasopressinergic neurons), water deprivation increased the frequency of mEPSCs in both the 24 hr. group (p < 0.05) and the 48 hr. group (p < 0.05) when compared to controls. The water deprivation dependent enhancement in mEPSC frequency was independent of changes in mEPSC amplitude, rise time, decay time, or charge transfer.

Although no changes in amplitude, rise time, decay time, or charge transfer were detected, there was an increase in the frequency of mEPSCs following both 24 hr. and 48 hr. WD. It remains unclear how water deprivation leads to enhanced mEPSC frequency in MNC of the SON. Future studies will investigate the mechanisms that underlie this water deprivation dependent plasticity.

Sponsor Nat Heart, Lung & Blood Institute 1 R01 HL119458-01A1
IRB/IACUC# 2014/15-29
Oxidative stress and androgen replacement as a model for neurodegeneration in the SN56 cell line

Background: Sleep apnea has been linked to oxidative stress (OxS) in the form of reactive oxygen species. The presence of oxidative stress has been shown to determine either the protective or toxic property of androgens in the N27 dopaminergic cell line, which has been used as a model of Parkinson’s disease. Androgen treatment prior to OxS protects N27 cells from injury, whereas androgen treatment after OxS increases the toxicity of OxS. We sought to determine whether similar oxidative stress dependent androgen effects also occurred in the SN56 cholinergic cell line, which has been used to model Alzheimer’s disease using intermittent hypoxia as an oxidative stress.

Hypothesis: We hypothesize that testosterone given prior to oxidative stress is neuroprotective and testosterone given after oxidative stress is neurotoxic.

Materials and Methods: The pre-treatment group was exposed to 100 nM of testosterone followed by 17-40 cycles of intermittent hypoxia in a chamber with fluctuating levels of oxygen. One cycle of IH involved reducing the chamber from 20% to 1.5% oxygen for 30 seconds followed by re-oxygenation for 4 minutes. The post-treatment group was first exposed to 17 cycles of IH and then treated testosterone. The control group used SN56 cells that were not exposed to androgen or IH. Cells were lysed at 6 & 24-hour intervals. Western blots were performed for two markers of apoptosis, Poly ADP ribose polymerase (PARP) and alpha spectrin, and were normalized for beta actin levels. Additional experiments used a cell viability assay to determine cell survival 24 hours after the same treatments and 30 or 40 cycles of IH.

Results: Cleavage of PARP and alpha-spectrin was significantly increased in the post-treatment group that was lysed at 6 hours, but not in the pretreatment groups. Conversely, both pre and post treatment with testosterone appeared to reduce cell death induced by IH.

Conclusions: The results of the cells lysed at 6 hours confirm the original hypothesis that androgens given prior to oxidative stress are neuroprotective while androgens given after oxidative stress are neurotoxic in SN56 cells. However, at longer time points, testosterone appeared to only be protective to SN56 cells. These data suggest that IH, such as occurs with sleep apnea, may interact with androgens in both detrimental and beneficial ways in cholinergic cells, as they do in dopaminergic cells.

Sponsor: N/A

IRB/IACUC#: 1508

Repetitive Mild Traumatic Brain Injury in a Mouse Model

Repetitive mild traumatic brain injury has become a hot topic of academic and clinical research due to the neurological dysfunction in many retired pro athletes who have suffered such injuries. In this study, we evaluated a mouse model that simulates such injuries and analyzed cognitive and motor function post injury. The results were then correlated with histological findings.

A weight drop model was used to induce repetitive mild head injuries in isoflurane anesthetized C57/BL6 male mice. Mice (n=7) were placed on a breakable foil platform over a sponge landing pad. A 43 gram steel weight was dropped through a guide tube from 28 inches onto the dorsal surface midline of the closed skull between the ears and eyes. Following the impact, the foil platform breaks allowing the mouse to experience rotational acceleration and land on the sponge pad. A single injury was performed daily M-F and again the following M-T (a total of 7 hits over 9 days). A group of sham injury mice (n=5) were anesthetized but did not receive TBI.

Following injury, mice underwent behavioral testing for motor function, anxiety and cognitive to assess the effects of the repeated injury. Consistent with other studies of TBI in mice, animals with injury showed hyperactivity. Results showed that the mice with TBI showed significant p

The injury pattern in mice was designed to simulate the injury experience by repetitive concussion in athletes of all sports. The successful development of this model will allow future examination of pharmacological approaches to reduce mild repetitive head injury.

Sponsor: N/A

IRB/IACUC#: 2014/15-42-A04
### Non-Feminizing Estrogens Do Not Exhibit Antidepressant-Like Activity

**Short description:**
In this exploratory lead compound evaluation, we aimed at addressing the utility of two non-feminizing estrogens, specifically 2-adamantyl-17β-estradiol (Ada-E2) and 2-adamantylestrone (Ada-E1), in a well-established animal model of depression-like behavior precipitated by estrogen deprivation.

**Purpose:** To evaluate non-feminizing estrogens in fulfilling their overall premise for the treatment of climacteric symptoms.

**Methods:** Mice were divided into six animals per treatment group. Test agents were dissolved either in corn oil vehicle or in 30% v/v aqueous 2-hydroxypropyl-β-cyclodextrin. The well-known antidepressant amitriptyline, as a reference standard, was used at 15 mg/kg dose, while the estrogen receptor (ER) antagonist fulvestrant was used at 4 mg/kg dose. The control groups received vehicle only. Test compounds in corn oil vehicle were administered subcutaneously (s.c.), while those in HPβCD were given intravenously (i.v.). Each group of animals was treated daily for five consecutive days injecting the test agents 100 µg/kg or 500 µg/kg doses on each day. Antidepressant-like activity were evaluated 30 min after the last injection using the Porsolt swim test (PST). The immobility time (in seconds, defined as the duration of floating motionless after the cessation of struggling and making only movements necessary to keep the head above the water) was recorded for 6 min simultaneously by a trained observer. Drug-likeness was evaluated via the online Osiris Property Explorer. Antioxidant potencies were determined experimentally by the ferric thiocyanate and thiobarbituric acid reactive substances methods.

**Results:** Adding the bulky Ada to the already lipophilic E2 and E1 brought about further increase in the lipophilicity (logP) by >2 log units. This increase was probably the most profound contributor to their unfavorable drug-likeness score. In agreement with our earlier quantitative structure–activity relationship study, our experimental assessment also supported that an increase in logP enhances antioxidant effect of estrogen-derived synthetic steroids and their analogs. However, while E2 and E1 did show significant reduction of immobility time in the mice PST, Ada-E2 and Ada-E1 failed to manifest activity in this paradigm (Immobility time is associated with depression-like behavior). Therefore, ERs play a pivotal role in triggering depression-like behavior in estrogen-deprived animals and non-feminizing estrogen offers no remedy for this symptom.

**Conclusions:**
Our lead evaluation has confirmed that both genomic and non-genomic mechanisms are required for broad-spectrum estrogen neuroprotection and treatment of menopausal symptoms. Therefore, non-feminizing estrogens such as Ada-E2 and Ada-E1 are not appropriate for the management of symptoms that manifest through ERs such as depression.

**Sponsor** National Institutes of Health (AG031535 to LP, AG031421 to KPT), the Robert A. Welch Foundation (endowment BK-0031 to LP), and the Intramural Grant (RI6177 to KPT)

**IRB/IACUC#** 2014/15-20-A04

### Functional performance and quality of life in transtibial amputees is influenced by the type of prosthesis

**Purpose/Hypothesis:** Lower limb amputees may receive a prosthetic limb based on their functional ability, known as a K-level, ranging from least functional, K0 to most functional K4. The purpose of this study was to evaluate effects of two types of prosthetic feet on balance, walking performance and quality of life in transtibial amputees classified as either K2 or K3.

**Number of subjects:** Seven males and three female, aged 48 to 69 years old with transtibial amputations due to peripheral neuropathy or type II diabetes have completed the study; enrollment is ongoing.

**Materials/Methods:** Study participants are transtibial amputees secondary to diabetes, trauma, or vascular disease currently amputating with either a K2 or K3 prosthesis. Quality of life was established using SF 36 and the Reintegration to Normal Living Index. Clinical tests: Timed Up and Go, Short Physical Performance Battery, Dynamic Gait Index and Activity Specific Balance Confidence Scales were administered. The V-gait CAREN system measured standing balance sway, gait speed, walking kinematics and kinetics on level ground and on a 4.8 degree ramp. The Physiological Cost Index was calculated for level and ramp walking. Participants completed all test with their current prosthesis and then switched prosthesis types in order to determine immediate effects of switching. Participants were then randomized into groups for a 2-week trial period to evaluate prosthetic foot that are either at, above or below their current functional level. Results were analyzed with pared t-tests.

**Results:** Baseline quality of life, balance, and gait measures for participants currently amputating with a K2 vs K3 were significantly lower (p < Conclusions: Preliminary results suggest that K3 prosthetic feet lead to greater quality of life and functional performance. A higher functioning prosthesis for lower functioning amputees may lead to less injuries and falls due to improved balance and coordination, and it may also improve cost effectiveness.

**Sponsor** This work was funded by an AOPA Research Award administered by the Center for Prosthetics and Orthotics Learning and Outcomes/ Evidence-based Practice and NSF grant 1208623

**IRB/IACUC#** 2013-184
Astrocyte AEG-1 regulates ER stress responses in the context of HAND

Endoplasmic reticulum (ER) stress has recently been linked to neurological disorders, including HIV-associated neurocognitive disorders (HAND). We recently showed astrocyte elevated gene (AEG)-1, a multifunctional oncogene regulating astrocyte migration, proliferation and neuroinflammation. AEG-1 upregulation in Huntington’s disease model suggests its role in ER stress responses in aging and HAND. However, its involvement in ER stress responses during HIV-1 infection is not known. In this study, we investigated HIV-1 and anti-retroviral therapy (ART) drugs mediated ER stress i.e., unfolded protein response (UPR) pathway activation, and astrocyte AEG-1 expression, intracellular localization during ER stress. RT-PCR and western blot analysis revealed that HIV-1, IL-1β and ART drugs activated UPR pathway and autophagy in astrocytes. Moreover, astrocytes exposed to ER stress compounds upregulated AEG-1 expression. Confocal analysis and mPTP assay showed AEG-1 colocalization with calnexin and mitochondrial damage with ER stress. In addition, AEG-1 overexpression upregulated ER stress markers such as BiP, PERK, and CHOP that were further enhanced by IL-1β treatment. Immunocytochemical studies also showed increased autophagy markers i.e., LC3 and P62 in AEG-1 overexpressing astrocytes. In summary, our study highlights that HIV-infection and ART drugs induce ER stress in astrocytes that is further exacerbated by AEG-1. Therefore, elucidation of AEG-1 regulated UPR pathway could assist in targeting astrocyte-induced ER stress responses in HAND.

Sponsor
IRB/IACUC# IRB2007-121

Alcohol and HIV-1 differentially regulate Toll Like Receptor (TLRs) expression and signaling in Primary Human Astrocytes

About 69% of human immunodeficiency virus-1 (HIV-1)-positive individuals exhibit some form of HIV-associated neurocognitive disorders (HAND). Several studies have reported that HIV-1 virions, viral proteins and alcohol, individually have direct or indirect effects on HAND pathophysiology. Recently, we showed that alcohol activates astrocytes and regulates inflammation via cPLA2 in HAND. Toll-like receptors (TLRs) are a family of innate immune system receptors that respond to pathogen-derived and tissue damage-related ligands. TLR signaling in immune cells, astrocytes, microglia and neurons may play roles in the pathogenesis of multiple diseases. TLRs are a “missing” link in alcohol-mediated astrocytic response in context of HAND since TLR stimulation by alcohol in glial cells induces secretion of pro-inflammatory molecules. Thus, we explored the role of TLRs in alcohol-induced inflammation and cytotoxicity in primary human astrocytes with HAND. TLRs signaling gene array was performed to screen altered profiles for all 10 TLR family members and 74 downstream signaling molecules. Ingenuity pathway analysis (IPA) was performed to identify potential signaling nodes. Data suggested that HIV-1 and/or EtOH led to differential TLRs expression in astrocytes. We confirmed all 10 TLRs by real-time PCR in four independent astrocyte donors. Alcohol alone and with HIV-1, significantly upregulated TLR1, 2, 3, 4, 5 and 9 as compared to controls and HIV-1 alone. We propose that TLRs regulation plays an important role in astrocytes inflammation upon HIV-1 and EtOH exposure.

Sponsor
IRB/IACUC# IRB 2007-121
Towards elucidating mechanisms of synaptic vesicle fusion: A computational study

Objective: Neurotransmission, a process by which neurotransmitters are released from synaptic vesicles to the synaptic cleft, is essential for the neuron communication. Each neurotransmitter can influence neurons in the brain and affect the behavior during the neurotransmission. The misfortune in the neurotransmitter release can cause several neurological complications such as depression, Parkinson’s disease, Alzheimer’s disease and autism. As a critical step in the neurotransmitter release process, synaptic vesicle fusion requires vesicle membrane and plasma membrane fusion, which in turn, is facilitated by the protein machinery including SNARE complex. However, how this protein machinery helps with synaptic vesicle fusion remains unclear because the highly dynamic feature of this machinery greatly challenges currently available experimental methods. The goal of this study is to build a computational model to simulate the synaptic vesicle fusion process.

Methods: Chemistry at Harvard Molecular Mechanics (CHARMM) and Visual molecular dynamics (VMD) were used to generate SNARE/membrane complexes. The MD simulations were performed using Nanoscale Molecular Dynamics simulator on Texas Advanced Computing Center. CHARMM27 general force field was implemented to solve the equations of motion in 3D PBC. The Particle Mesh Ewald algorithm was used to calculate long-range Coulomb interactions.

Results: We built a novel all-atom computational model including SNARE complex, vesicle membrane and plasma membrane. The bicelle model of these membranes was stabilized by DHPC present in 20 nm edge of each membrane. SNARE molecules were preferentially arranged in trigonal planar and pentagonal planar conformations between vesicle membrane and plasma membrane separated at 20 angstroms apart from one another. In each of the planar conformations, SNARE molecules are arranged in such a way that C-terminals are towards the center of membranes and N-terminals are towards the edge of membranes. The transmembrane region (TMR) helices of syntaxin-1 and synaptobrevin were stabilized deep inside the plasma and vesicle membrane, respectively.

Conclusions: We successfully built a novel computational model at atomic level to simulate synaptic vesicle fusion process. The conformational dynamics of SNARE/membrane complex were investigated at the molecular level. Our efforts provided a novel tool and revealed new insights towards a clear understanding of the mechanism of neurotransmission.

Sponsor
IRB/IACUC#
Novel Androgen Receptor Variant 45 in Brain Tissue

Purpose: A membrane associated androgen receptor has been implicated in the damaging effects of testosterone in neurodegenerative disorders, such as Parkinson’s disease. An androgen receptor variant (AR45) that has a C-terminus and a unique N-terminus has been found in peripheral tissues, such as the heart, skeletal muscle, uterus, and prostate, but has not been found in the brain. Recent findings have shown that a AR45 is present in the membrane fraction of a dopaminergic neuronal cell line (N27). Therefore, we wanted to determine if AR45 was present in cortical, hippocampal, and substantia nigral neurons that are lost during Alzheimer’s and Parkinson’s disease.

Methods: In this study we used immunohistochemistry to determine the presence of AR45 presence in rat brain tissue. Tissue sections of 40 um were prepared using a cryostat. The sections were stained with primary antibodies specific for different androgen receptor sequences. The antibodies AR C-19 and AR N-20 were used to identify the C terminus and the N terminus, respectively.

Results: Since AR-45 is lacking an N-terminus, we used N-20 antibody that binds to the N-terminus as a negative control. However, AR45 does have a c-terminus, and thus we used the C-19 antibody as a marker for AR-45. C-19 immunofluorescence was present in the hippocampus, cortex, and substantia nigra. Interestingly, N-20 positive cells were not identified in the substantia nigra, indicating that only AR45 is present in these neurons.

Conclusion: This is first study to show the presence of AR45-immunoreactive positive neurons in the brain. Now the receptor has been identified, more research is needed to determine the role of AR45 in neurodegenerative diseases.

Sponsor
IRB/IACUC#  2014/15-30-A05

Angiotensin II Linked Free Radical Effects on Muscle Sympathetic Nerve Activity During Exercise

BACKGROUND: It has been identified that central nervous system (CNS) production of free radicals (FR) scavenges nitric oxide and increases central sympathetic nerve activity outflow. The increased production of FRs in the CNS is a result of increased electron transport chain flux associated with increased brain metabolism and by activation of the renin-angiotensin system (RAS). The pathophysiological increase in Ang II linked FR production is recognized as a major mechanism involved in neurogenic hypertension. During exercise, there is a physiological increase in Ang II and muscle sympathetic nerve activity (MSNA) in direct relation to increasing exercise intensity. PURPOSE: We tested the hypothesis that the exercise induced increase in Ang II linked free radical production and MSNA activity during exercise is located within the brain. METHOD: Six healthy subjects performed three randomly ordered trials of 70° upright back-supported dynamic leg cycling after ingestion of two different lipid soluble Angiotensin converting enzyme inhibitors ((ACEi) Perindopril (PER) - highly lipid soluble; Captopril (CAP) non-lipid soluble)) and/or placebo (PL). Repeated measurements of whole venous blood, MSNA, and mean arterial pressures (MAP) were obtained at rest and during steady-state heavy intensity exercise at heart rates (HR) of 120 bpm (e120). RESULTS: Peripheral venous superoxide concentrations as measured by electron paramagnetic resonance (EPR) were not significantly altered at rest (P≥0.4) and during E120 by the ACE inhibitors (P≥0.07). Likewise, baseline MSNA (PL, 25 ± 1.5 bursts/min; CAP, 21 ± 0.7 bursts/min; PER, 25 ± 0.7 bursts/min) and MAP (PL, 86 ± 2.8 mmHg vs. CAP, 84 ± 2.6 mmHg; PER, 84 ± 0.7 mmHg) were unchanged at rest (P≥0.1; P≥0.8 respectively). However, during E120 central acting PER attenuated the increases in MSNA and MAP, increasing only 15±6% for MAP and 24±8% for MSNA, when compared to PL (26 ± 6% MAP; 57±16% MSNA; PCONCLUSIONS:From these data we conclude that centrally acting PER attenuated the central increase in the exercise induced Ang II linked free radical production resulting in an increased central/peripheral NO activity induced reduction in MSNA during heavy intensity dynamic exercise.

Sponsor N/A
IRB/IACUC#  2014-062
Purpose:
To show the utility of ketamine/xylazine in a mouse model to evaluate analeptic effect evoked by TRH upon its brain-delivery via a novel prodrug approach, as well as to confirm the antidepressant-like effect of this neuroactive peptide when delivered into the brain.

Methods:
For the assessment of analeptic effect, CD1 mice were divided into groups of n = 8. Test compounds were dissolved in saline. Mice were treated with a single dose (10 µmol/kg) of prodrug, saline vehicle, TRH, respectively, through the tail vein by i.v. injections. Ten minutes after injection of drug, mice were injected i.p. with either a mixture of ketamine (100 mg/kg) and xylazine (10 mg/kg), or sodium pentobarbital (60 mg/kg).

Sleeping time was recorded starting from the loss of righting reflex until this reflex was regained. To evaluate antidepressant-like activity using the Porsolt’s swim test, test compounds were administered i.v. through the tail vein at the dose of 3 µmol/kg, in a separate study. For 6 min, the immobility time (the duration of motionless floating after the cessation of struggling and making only movements necessary to keep the head above the water) was recorded.

Results:
TRH also reduced sleeping times after ketamine/xylazine sedation. Administration of the TRH prodrug also manifested analeptic effect characteristic to the parent peptide. Like after TRH injection, immobility time in Porsolt’s swim test indicative of the peptide’s antidepressant-like activity also shortened after the administration of its prodrug when compared to saline control. Thus, the analeptic and antidepressant-like effects observed after systemic administration of the TRH prodrug has reflected its ability to penetrate the blood-brain barrier followed by the release of the parent peptide at the site of action. Delivery of TRH to the brain by specific prodrug approach would allow for reduction of TRH’s endocrine side effects and for a prolonged duration of action.

Conclusions:
Treatment by a TRH prodrug reduced the ketamine/xylazine- and sodium pentobarbital-induced sleeping time in mice, as well as shortened the immobility time in Porsolt’s swim test. These observations have indicated a successful delivery of the neuroactive peptide into the brain via its prodrug introduced here.

Sponsor: The Welch Foundation (endowment BK-0031), UNTSC Intramural Grant (Ri6177)

IRB/IACUC# 2014/15-20-A04, 2014/15-21-A05
Inhibition of tyrosine hydroxylase in substantia nigra, but not striatum, reduces locomotor activity in an open-field.

Background: The risk of locomotor impairment increases substantially during aging. There are two primary sources of locomotor impairment; aging-related Parkinsonism and Parkinson’s disease (PD). One of the three cardinal symptoms of PD is bradykinesia, which is also observed in aging-related Parkinsonism. The neurobiological basis for the manifestation of bradykinesia in PD is associated with >70% loss of dopamine (DA) in the striatum, the terminal field compartment of the nigrostriatal pathway. Coincident with bradykinesia onset in PD, others have reported 40-50% DA loss in the substantia nigra (SN), the somatodendritic compartment of this pathway. While this degree of DA loss occurs in SN in aging, DA loss in striatum has never been reported to reach 70%. We have previously shown in young male rats that DA tissue content can be specifically reduced in either DA compartment to levels previously reported in aging studies with direct delivery of the tyrosine hydroxylase (TH) inhibitor, a-methyl-p-tyrosine (AMPT) in either striatum or SN. Hypothesis: We tested the hypothesis that DA reduction in the SN alone would be sufficient to reduce locomotor activity. Methods: To ensure that locomotor function would be devoid of aging-related confounds to locomotor performance, 6 month old Brown-Norway Fischer 344 F1 rats were used. To selectively reduce DA tissue content in either striatum or SN, rats were first anesthetized to implant double guide cannula to target striatum (+1.0 AP, 2.5 ML, 7.5 DV). Following recovery, rats were placed into an open-field for three hour sessions immediately following infusion of saline or AMPT on a different day. This was repeated 5 times to acquire locomotor activity following saline or AMPT infusion. Results: Infusion of a quantity of 1.4 nmole AMPT into the SN, but not striatum, produced a significant decrease in open-field locomotor activity out to 2 hours past infusion. Infusion of 14 nmole AMPT into striatum did not produce significant decreases in open-field locomotor activity. Conclusions: The inhibition of TH activity in the SN, but not striatum, reduces open-field locomotor activity in young rats. This inhibition has been previously reported to reduce DA in SN or striatum to levels comparable seen with aging. Therefore, TH function in the SN may be a molecular component in the ability to initiate locomotor activity.

Sponsor National Institute on Aging AG040261
IRB/IACUC# 2014/15-26-A05
A Dynamic Approach to Targeting Acid-Sensing Ion Channels: Computational simulations reveal key residues in ASICs

The current molecular dynamics (MD) research project employs virtual model building as a tool in elucidating the functions associated with key calcium binding sites of acid-sensing ion channels (ASICs). These integral membrane proteins, with neuronal proton-sensitive channels associated with pain and central nervous system diseases, represent novel therapeutic targets for these diseases. ASIC1 and ASIC3 are two subtypes of ASICs with highly conserved channel “pore” sequences, but play different roles in the development of hyperalgesia after inflammatory muscle injury. It has been proposed that the removal of calcium continues to allow the ASIC3 channel to open, but this is not the case for ASIC1. The objective of this project is to identify key residues responsible for the distinct gating mechanisms of ASIC1 and ASIC3, utilizing MD simulations.

Model building through software, CHARMM-GUI membrane builder program, utilizing the RCSB-PDB (4KNY), has allowed the manipulation and examination of ASIC1’s amino acid sequence. Six simulation trajectories were carried out (cumulative 300 ns- 50 ns per trajectory) through remote access to TACC supercomputer center using NAMD simulation software.

Previous experimental work has shown that unlike ASIC3, the ASIC1 channel cannot be opened by the removal of calcium. Despite ASICs’ highly conserved channel sequence, this characteristic difference between these two subtypes may be defined by one key residue: a glutamic acid residue found in ASIC3, position 429, versus a glycine residue in ASIC1. Introduction of G429E mutation opens the ASIC1 channel. Consistent with experimental observation, analysis via VMD visualization software revealed the G429E mutant has a wider channel opening than the WT. We further identified that this opening is facilitated by the electrostatic interaction of glutamic acid 429 and asparagine 65 of lateral chains.

We identified key residue responsible for the distinct gating mechanisms of ASIC1 and ASIC3. Located at the lipoprotein interface, this key “gating” region of the pore may prove useful in the identification of novel pharmacological targets and understanding the differences in channel gating between ASIC1 and ASIC3. Novel applications are sought for the selective targeting of ASICs channel subtypes, as well as, targeting ASICs within specific regions of the body.

Sponsor
IRB/IACUC #1521

Visuomotor Integration in Atypical Development

Visuomotor Integration in Atypical Development

Purpose Children with Developmental Coordination Disorder (DCD) commonly present with impairments in both gross and fine motor functions, which could be attributed to abnormalities in visuomotor integration. These impairments negatively affect their ability to coordinate appropriate postural responses while interacting with the environment. It is unclear whether visuomotor deficits seen in DCD individuals occur in attaining visual input, integrating visual information with other sensory inputs, or implementing a motor response. The purpose of this study was to determine how individuals with DCD, compared to those of typical development and eventually to those with ASD, integrate visual information from the environment to maintain postural stability.

Methods Twelve participants aged 8 to 11 years old, eight with DCD, two with ASD and two controls participated in this study. Enrollment is ongoing. This study utilized a 12-camera motion-capture system, a Computer Assisted Rehabilitation Environment Network (CAREN), ETG 2.0 eye tracking system, a 180° wrap-around screen, and computers for controlling and integrating all components. Participants completed one or more visuomotor tasks. In the Disc Match task, participants displace their center of pressure in medial lateral direction to maintain overlap with a disc moving on the screen from left to right at 8 different frequencies. In the Shooting Ducks task participants select, aim and shoot 24 virtual moving ducks. Percentage of overlap at each frequency and time of execution per target were analyzed with t-tests.

Results Percentage of overlap time between target stimulus and Center of Pressure (COP) representation during the Disc Match task revealed overall trend of decreased scores with increased frequency of stimulus frequency, with the highest average score for 0.2 Hz and lowest average score for 0.8 Hz. All participants completed the Shooting Ducks task within the allocated 2 minute trial, however difference in strategies used to select a target, track its movement across the visual field were identified between children with atypical development and controls, resulting in a longer time to complete task. Time hovering on a target until achieving accurate aim was inefficient for DCD and ASD participants respectively.

Conclusions Preliminary results demonstrate support for the hypothesis that impaired postural responses in children with DCD and ASD are seen mostly when visuomotor integration is required to organize and execute the appropriate motor program.

Sponsor
NSF NRI-1208623, NSF SMA-1514495
IRB/IACUC #1522
Testosterone and dihydrotestosterone (DHT) exert protection through the activation of the intracellular androgen receptor (AR). However, studies suggest DHT may also exert protective effects by way of alternate mechanisms, including through prior conversion to 3beta-diol, a metabolite that can bind and activate estrogen receptors. Using the AR-deficient C6 glioma, a model of astrocytes, we found DHT was protective against iodoacetic acid (IAA) toxicity. The protective effects of DHT, as assessed by the Calcein-AM viability assay (which is a surrogate measure of cell number), were blocked by the co-application of the non-selective estrogen receptor antagonist,ICI-182,780. Using a complementary viability assay, the MTT assay, which is a surrogate for mitochondrial respiration/activity, we reproduced DHT protection and extended our results to find that 3beta-diol was also protective against IAA-induced reduction in mitochondrial activity. Interestingly, while the effects of 3beta-diol, the presumptive mediator of the effects of DHT, were blocked by ICI 182,780, they were not blocked by the estrogen receptor isomorph-selective antagonists MPP (against ERα) and PHTPP (against ERβ). Collectively, these data support our hypothesis that DHT is protective against cytotoxicity in a cell line devoid of the classical/intracellular androgen receptor, and that the metabolite of DHT, 3beta-diol, may be an important mediator of DHT’s effects in the central nervous system. Our results also suggest that the capacity to convert DHT to 3beta-diol may be relevant to the protective influence of androgens and estrogens in the postmenopausal women, a time when estrogen and progesterone levels decline significantly, but androgen levels persist.

Sponsor AG 020494, AG 022550, AG 027956
IRB/IACUC#
**Does Arthritis Risk Differ by Veteran Status in Males 35-54?**

**Introduction:** Studies suggest that arthritis is common among veterans and activity duty service members. This study assessed whether serving in the armed forces increases the risk for arthritis in a representative sample of males ages 35 to 54.

**Methods:** This was a cross-sectional analysis using 2013 Behavioral Risk Factor Surveillance System (BRFSS) data for males ages 35 to 54 in California, Florida, North Carolina, Texas, and Virginia. Multiple logistic regression was used to assess the relationship between veteran status and arthritis while controlling for age, educational level, employment status, income level, marital status, race/ethnicity, general health, activity level, activity limitations, weight status, chronic health problems, depression, alcohol use, and tobacco use.

**Results:** About 13-22% of males reported arthritis; 11-24% reported veteran status; and 24% of veterans reported arthritis. The results of adjusted analyses indicated that veteran status and arthritis are significantly related.

**Conclusions:** Overall, veteran status and arthritis were significantly related after controlling for demographic and psychosocial variables in a representative sample of males ages 35-54. Awareness of risk factors for arthritis including veteran status in males ages 35-54 can aid in the early diagnosis and treatment of this disease.

**Sponsor** N/A

**IRB/IACUC#** 2015-105

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**Design of a lower extremity exoskeleton to improve gait in elderly patients with knee osteoarthritis by reducing knee joint loading**

**Introduction:** Knee osteoarthritis (OA) is the second most common diagnosis in the United States, affecting over 51.8 million people. It is characterized by joint pain and stiffness due to irreversible articular cartilage breakdown, resulting in often fatal falls or the inability to walk. There are 744,000 hospitalizations annually for elderly fall-related injuries, with each one averaging $17,483 in healthcare costs. Despite the abundance of low-cost, conservative treatments for knee OA, including braces and orthotics, a combination of patient non-compliance and lingering joint pain result in the need for an alternative treatment that reduces knee joint pain while facilitating movement of the joint by providing compensatory support during gait. The purpose of this study is to design a passive lower extremity exoskeleton that offloads the medial compartment of the knee joint while also delivering stability to the ankle-foot junction. This passive design is inspired by commercially available unloader braces for knee OA treatment, in combination with ankle-foot orthoses designed to mechanically realign the tibiofemoral junction.

**Methods:** The initial device prototype will allow 1 degree of freedom each in the knee and ankle joints (sagittal plane) and will be modeled primarily for a 75kg adult male with a rehabilitative walking speed of 1.5-3.5 km/h. The device will be competitively lightweight with current exoskeletons with 5 or less rigid interfaces between the body and exoskeleton to allow for maximum comfort.

**Results:** Modeling, stress and failure analysis of the prototype will be accomplished using Autodesk Inventor Design Studio. Gait parameters taken from simulation subjects wearing the device, such as walking speed, knee joint angle, and medial joint force will be measured, processed, and compared to control parameters.

**Conclusion:** We hypothesize that an exoskeleton combining medial joint offloading and lower extremity stabilizing methods will provide the necessary joint pain relief and compensatory support to facilitate walking in the elderly.

**Sponsor** N/A

**IRB/IACUC#**
### The Effect of ACL Femoral Drilling on Posterolateral Corner Reconstruction

**Purpose:** This study aimed to evaluate the risk of tunnel collision with combined Posterolateral corner (PLC) and anterior cruciate ligament (ACL) reconstruction and to identify which technique reduces the risk of tunnel collision. Methods: LCL and popliteus tunnels were drilled in sixty-four medium and large synthetic femurs and sixteen synthetic knee joints. ACL tunnels were then drilled using four different techniques: transtibial, anteromedial portal with a rigid guide pin, anteromedial portal with a flexible guide pin, and outside-in. The samples without obvious tunnel collision then underwent CT scan with 2-mm slices to determine the closest distance between the tunnels and the tangential distance (mm) between them were recorded. Results: Overall frequency of tunnel collision was 24/32 (75%) in large femur specimens and 32/32 (100%) for medium femur specimens. Obvious tunnel collision was observed in all transtibial, anteromedial with flexible instruments, and anteromedial with rigid instruments regardless of femur size or side. All of the specimens without tunnel collision occurred in the large femurs from the outside in group (n=8). The mean tunnel separation in all samples was 1.93 mm, with a range of 1.06 mm to 2.54 mm. Conclusion: Consistent with previous studies, we found a high rate of collision, especially in medium size femurs. The results of our study have provided evidence for the use of outside-in ACL reconstruction and PLC with 2 lateral femoral tunnels with the least amount of collision risk.

**Sponsor**
Intramural Research Grant from John Peter Smith Hospital

**IRB/IACUC#**

### Effectiveness of Aquatic Therapy Interventions in the Management of Children with Cerebral Palsy: A Systematic Review

**Purpose**
The purpose of this systematic review was to analyze the current scope of literature regarding the effectiveness of aquatic therapy as an intervention for children with cerebral palsy (CP) and to assess the feasibility of incorporating aquatic therapy into the physical therapy management of this specific population.

**Methods**
A literature search in 3 electronic databases - PubMed, CINAHL, and Academic Search Complete - was performed, using the following search terms: “cerebral palsy,” “children with disabilities,” “aquatics,” “aquatic therapy,” and “hydrotherapy.” Articles published between 1984 and 2014 were selected. Inclusion criteria for study selection included publication in the English language (or publication in any other language with available English translation); recruitment of participants with CP ages 0-21; and the use of aquatic therapy as the main experimental intervention. Studies were excluded if they were not written in English or had no easily accessible translation or if they recruited subjects older than age 21. The initial search resulted in 280 potential articles, which were screened for the stated inclusion and exclusion criteria as well as for duplicates. Thirteen articles satisfied the inclusion criteria. There were two case reports, one case series, one pilot study, three cohort studies, five quasi-experimental studies, and one randomized controlled trial. A total of 280 children with cerebral palsy participated in these investigations. Sample size across the research studies varied from 1 to 46 children. The ages of the participants varied from 3 to 21 years old.

**Results**
The evidence suggests that aquatic therapy interventions are effective in the short term for improving gross movement and gait parameters as well as social function and self-esteem in children with CP ages 0-21, and that aquatic therapy is feasible, safe, and fun for this population.

**Conclusions**
The overall body of evidence is inconclusive due to a lack of high-quality evidence, small sample sizes, and variability in intervention parameters (frequency, duration, intensity, etc.), severity of disease, and outcome measures. More research must be conducted with larger sample sizes, higher quality study design, and more consistent outcome measures to determine effective exercise parameters and to further support the success of aquatic therapy as a physical therapy intervention for this population.

**Sponsor**
N/A

**IRB/IACUC#**
The Effects of Hearing Loss on Postural Control in Older Adults

Purpose/Hypothesis: We investigated the relationship between hearing loss and gait in adults using advanced virtual reality technologies, as well as evaluated the effects of two types of Hearing Aid (HA) technologies on measures of balance and gait. We used a regular HA that amplifies sound from all directions and frequencies and a Frequency Modulator (FM) system designed to work in conjunction with the regular HA and to selectively amplifies only one frequency of interest and not the ambient noise.

Materials/Methods: 12 adults newly diagnosed with hearing loss and 12 age- and gender- matched healthy controls participated in the study. Participants were tested for balance, gait, and functional activities at the time of hearing loss diagnosis and enrollment in the study, as well as after two months accommodation to a hearing aid. Outcome measures included: standing COP sway, performance of dual-task involving cognitive decisions, and self-selected gait speed on flat and uneven terrain in the virtual environment. Testing conditions were: No HA, HA, Ha +FM; auditory task conditions either listening only or repeating back sentences form standard audiology tests. Clinical tests of DGI, TUG, ABC Scale and SPPB were also administered. ANOVA was conducted for each of the dependent variables with respect to: group; condition of HA and condition of auditory task.

Results: Center of pressure sway variability in M/L direction was significantly increased (p

Conclusions: Hearing loss negatively impacts postural control particularly in dual-task conditions when individuals attend to both auditory and postural tasks. Use of hearing aids – especially the FM system – significantly improves not only speech recognition but also measures of balance, gait, and the ability to successfully perform dual-tasks. Individuals with hearing loss may be at greater risk of falling than individuals without hearing loss; therefore, further studies are necessary.

Sponsor Texas Medical Research Consortium grant, RI 6042 " Good hearing, Steady feet"
IRB/IACUC# 2012-114

Resident Total Knee Arthroplasty Training: The Protective Benefits of an Osteotome during Cruciate Retaining TKA

INTRODUCTION: The central objective of this study is to evaluate the effectiveness of a simple surgical technique to prevent PCL damage during performance of a Posterior cruciate retaining (CR) total knee arthroplasty (TKA) surgery. This technique involves placement of an osteotome to prevent iatrogenic injury to the PCL by the sagittal saw blade during tibial resection. This simple technique can be useful to faculty members instructing novice residents or to senior surgeons looking to perform a low volume of CR TKA as an adjunct to their private practices.

METHODS: We randomized 60 cadaveric specimens into two groups: Group I and Group II. Group I, 30 specimens, received standard tibial resections as performed during CR-TKA using a standard Y shaped PCL retractor. Group II, 30 specimens, received standard tibial resections as performed during CR-TKA using a standard Y shaped PCL retractor with the additional placement of a ½ inch osteotome. A board certified adult reconstructive orthopaedic surgeon, aligned the extramedullary tibial resection guide and positioned the osteotome. Posterior cruciate ligaments were assessed after completion of the procedures and removal of all instrumentation by 3 separate individuals to assess PCL damage. There were two states defined: PCL intact and PCL damaged.

RESULTS: A difference in PCL damage was noted in 73% (22/30) of group I and in 23% (7/30) of group II. Group I was found to be twice more likely to have an injured PCL than Group II which used an osteotome for PCL protection.

DISCUSSION AND CONCLUSION: Placement of an osteotome anterior to the PCL during CR-TKA provides a protective benefit to the patient. We speculate that the protective benefit could be increased by ensuring osteotome penetration is deeper than resection depth. This study simulated 60 tibial resections and may be applied to novice resident training.
Comparative Study on Hospital Consumer Assessment of Healthcare Providers and Systems between two General Hospitals in Indore, India

The Null Hypothesis states that there is no significant difference between the patients’ perception of their experience of services of Hospital A and Hospital B. The Alternate Hypothesis states that there is a significant difference between the patients’ perception of their experience of services of Hospital A and Hospital B.

The research aimed to recommend measures to improve the quality of services on the basis of factors underlying the difference, if any. A questionnaire was devised to compare the two hospitals over 15 parameters on a Likert scale. Random sampling was used for primary data collection through direct contact with patients just before discharge. The parameters were classified as Single-Item measures, Composite Measures and Global-Rating Measure. Measures of Central Tendency, Variance, and t-test were used to compare the results.

100 patients from each hospital were included. The values of t-test for all the parameters showed significant difference in the mean value of perceived quality of the two hospital services (all p values <0.05). Hospital A exceeded the Hospital B in terms of overall perceived quality by 54.02% and in terms of Single-Item measures, Composite Measures and Global-Rating Measure by 70.81%, 58.06%, and 27.27% respectively.

In this study, considerable difference was found in the patients’ perception of the service quality of the two general hospitals. Focus on patient-centered services, hygiene, communication, and promptness in providing services is recommended. Few underlying factors were identified, however, further research is required to identify the extent of impact of these factors on the patients’ perception of hospital services.

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Preliminary evidence of a relationship between quantitative measures of postural stability and clinical movement tests in Developmental Coordination Disorder

Developmental Coordination Disorder is typically assessed using qualitative clinical measures. However, little is known about the relationship between these measures and quantitative measures of postural stability, such as variability in Center of Pressure (CoP), commonly referred to as sway. The present study administered two clinical measures commonly used to assess DCD (MABC and DCD-Q), and measured postural stability during static and dynamic balance tasks. The static balance task (Quiet Standing) consisted of 2 conditions lasting 30 seconds each, during which the participant stood still in a natural stance with his or her eyes open, then closed. The dynamic balance task (Visual Tracking), a novel contribution to the literature on DCD, involved the participant leaning to match his or her CoP to match a dynamic target displayed in a virtual environment on a 180° wrap-around screen. The target oscillated at 8 frequencies ranging from 0.1-0.8 Hz, and changed speed randomly without warning. Participants were 8 children with DCD aged 8-10 from a variety of ethnic backgrounds. Correlation analyses showed significant negative relationships between DCD-Q score and medial-lateral sway during both the eyes open (r = -0.79, p = .02) and eyes closed (r = -0.81, p = .02) conditions of Quiet Standing. MABC total score was negatively related to the participant’s average deviation from the target position in Visual Tracking (r = -0.76, p = .03), such that participants with higher scores on the MABC were more accurate at the dynamic movement task. We also correlated Quiet Standing and Visual Tracking performance, examining each frequency separately (averaged across 2 runs per frequency). CoP velocity was related to anterior-posterior sway in the eyes closed condition of Quiet Standing, while CoP position was related to medial-lateral sway in the eyes open condition. This pattern of results suggests that quantitative data may offer a more detailed means of assessing postural stability in children with DCD than common clinical tests. However, a larger sample is needed to detect and interpret meaningful relationships between variables, specifically between frequencies in the Visual Tracking task.

Contribution of bone cement volume with increased bone loss in the fixation of a patellar implant

Purpose: Complications related to the patellofemoral joint after total knee arthroplasty (TKA) represent up to 50% of TKA re-operations. Shear forces at the bone-cement-implant interface produce wear and occasionally result in failure of fixation of the patellar implant. During revision surgery, variable amounts of patellar bone loss are observed from implant removal. Different volumes of bone cement are thus used to fill the remaining bone cavity and to fix the patellar implant. This study aims to computationally simulate and evaluate the fixation mechanics of the patellar implant-cement-bone interface with increasing amounts of bone loss.

Materials and Methods: Patellar implant fixation to bone using bone cement in revision TKA was simulated using the finite element method. To study the fixation mechanics with increasing bone loss, the diameter of the bone cavity prepared around each of the three implant pegs (used as implant anchors into the bone) was uniformly increased by 0.5 mm. This resulted in a total of 5 bone-cement-implant models, with a bone cement thickness around the pegs ranging from 0.5 mm to 2.5 mm, loaded in shear to test fixation success.

Results: Findings from the study indicate that increasing the cement thickness (bone hole diameter) is beneficial in increasing stiffness of the construct, reducing mean implant and cement stresses, reducing interface contact pressure between bone-and-cement and between cement-and-implant, and also reducing the maximum relative motion between these structures at these interfaces. Data collected from this finite element analysis support using an increased bone hole diameter, and thus bone cement filling around the implant pegs, for patellar implant fixation in revision TKA.
Noteworthy, three of the single plate constructs, having two screws removed (models S12, S13, and S23), showed less than a 6% reduction in construct stiffness. In contrast, all of the dual-plate constructs with 2 screws removed showed high stiffness reductions (greater than 55%).

Conclusions: Results support that screw number and/or location and construct type (single vs. dual) are important factors to consider in improving fixation. Position and screw number were shown to be particularly important in the single-plate construct to show an increase in stiffness as compared to the original dual plate construct without any screws removed. For the single-plate constructs, models S1-S3 all resulted in less than 2.5% stiffness reductions as compared to the control. Noteworthy, three of the single plate constructs, having two screws removed (models S12, S13, and S23), showed less than a 6% reduction in construct stiffness. In contrast, all of the dual-plate constructs with 2 screws removed showed high stiffness reductions (greater than 55%).

Physical Therapists’ role in community collaborative efforts to improve safety and prevent falls

1. Collaborative efforts of the Fort Worth Fire Department, MEDSTAR mobile healthcare, and the Fort Worth Safe Communities Coalition have led to the development of a home safety and fall prevention service designed to reduce the incidence of falls among Fort Worth residents 65 years of age or older.
2. A 19-item home safety checklist was designed to assist in the evaluation of the primary resident’s home environment to identify potential fall risks. Physical therapists’ input regarding environmental fall risks was used for development of the checklist and the training of designated firefighters that deliver the service. The one hour free home safety evaluation identifies potential fall or safety risks. Firefighters make recommendations based on observations and provide information on available community resources specific to fall prevention. The Safe Community Coalition, specifically the Falls Prevention task force on which several physical therapists serve analyzes the de-identified data from home safety assessments performed by the FWFD.
3. In a 7 month period a total of 811 individuals were contacted. From these, only 153 expressed interest in receiving the FWFD service. A total of 137 individuals provided reasons for refusal of the home safety assessments free service. These reasons consisted of: non-interested (22%), current or previous access to home health (15%), and residential relocation (11%). A significant association between fear of falls and difficulty performing sit to stand was found (p=.016), 75% of participants that fear falls have difficulty standing from a seated position.
4. Prevention of falls and associated health care costs is a priority for many communities. Physical Therapists are well positioned to lead collaborative efforts engaging community organizations and that target fall prevention. Such programs offer potential benefits both to the community and to the emergency response infrastructure. The community receives education and evaluation regarding fall prevention aimed to improve safety and prevent falls. By prevention, demands placed on emergency resources can be potentially alleviated. Factors associated with the incidence of falls can be acknowledged and interventions can be provided to prevent subsequent impairment and decline in quality of life.
The Radiographic Prepatellar Fat Thickness Ratio Correlates with Infection Risk Following Total Knee Arthroplasty

Obesity is a known risk factor for surgical site infections (SSI) following total knee arthroplasty (TKA). Current methods use body mass index (BMI) to predict infection risk in patients. However, BMI may not be the most accurate predictor because it does not account for fat distribution and muscle mass included in the calculation. We sought to assess the impact of subcutaneous fat at the surgical site on risk of infection following a TKA. It has been shown that fat tissue thickness expands without a complementary increase in blood flow, leaving subcutaneous tissue with reduced oxygenation. This wound hypoxia impairs healing by multiple mechanisms; healing wounds have high oxygen demands and leukocytes need oxygen to create reactive oxygen species against infection. We conducted a retrospective study of 330 patients who had TKAs at John Peter Smith Hospital (JPS) from 2006-2010. Pre-operative lateral knee radiographs for each patient were reviewed and measured. Both patellar thickness and prepatellar fat thickness were obtained. Soft tissue thickness was divided by the thickness of the patella to create the prepatellar fat thickness ratio (PFTR). Additionally, diabetes status, smoking status, gender, and BMI were obtained. The infection criteria used was 2 (+) cultures, or 1 (+) culture plus one of the following: gross purulence or >10 PMNs/hpf. We expect the PFTR to be a significant predictor of SSI and more accurate than BMI in this regard. It may be beneficial to assess the PFTR in the preoperative evaluation to properly inform the patient of infection risk and allow the physician to take additional precautions to reduce the risk of infection.

Sponsor: N/A
IRB/IACUC#: 2015-163

Serving Children in Need: Results from the UNTHSC Pediatric Mobile Clinic

Objective
To evaluate the activities of the UNTHSC Pediatric Mobile Clinic (PMC) from May 2014 to January 2016. The primary goal is to describe the population served and the types of health services offered, and to present future directions.

Background
Barriers to health care include cost, lack of transportation and lack of health insurance.1,2 Texas has about 1 million uninsured children, 62% of which are Medicaid eligible. Of these, 75,824 reside in Tarrant County.3,4 Mobile clinics have been found to reach more people who experience barriers in accessing health care services.2 The UNTHSC PMC was set up to provide clinical services and health education to Fort Worth neighborhoods with the greatest need for health services, and to provide preventive, screening, treatment and referral services as needed. Targeted neighborhoods in Fort Worth include Como, Morningside, North Side and Stop Six.

Methods
Data for this project was collected as part of the daily and weekly logs of the PMC. Data from May 2014 to January 2016 was analyzed and included the number and types of medical visits, number of vaccines administered and health screenings performed. Results were analyzed by age group, gender, race/ethnicity and neighborhood visited.

Results
From May 2014 to January 2016, the PMC had 259 site visits to schools and organizations in Fort Worth neighborhoods, with Morningside and North Side being the most visited. In total, there were 2788 child visits. Participants were 52% female, 70% Hispanic and 22% Black/African American. Total number of clinics, including site visits and health fairs, were 27 in Fiscal Year (FY) 1 (June – August 2014), 151 in FY 2 (September 2014 – August 2015) and 81 in FY 3 so far (September 2015 – January 2016). Services provided included vaccinations (31%), well child exams (24%), acute/episodic care (23%), medical screenings (20%), dental screenings (1%) and vision screenings. The PMC administered 584, 1493 and 846 vaccines in the first, second and third fiscal years respectively, totaling about 3000 vaccines administered. The PMC also provides case management encounters to families, and there were 147, 747 and 223 case management encounters in the first, second and third fiscal years respectively.

Conclusions
The PMC has since its onset provided valuable health services to children and families, just like other mobile clinics across the United States. It thus provides a solution to the barriers in accessing clinical and preventive health services faced by Fort Worth communities with the greatest need, including a high proportion of minority populations.

Sponsor: N/A
IRB/IACUC#: 2016-037
INTRODUCTION

Approximately 800,000 people in the United States have a stroke each year, of which 30% to 66% of all survivors have impaired hand functions. Certain therapeutic interventions such as Continuous Passive Motion (CPM) capitalize on the brain’s inherent neuroplasticity to increase adaptation to stroke. Currently, no dedicated system exists which effectively applies post-stroke hand therapy. To address this need, a soft robotic rehabilitation system capable of monitoring and assisting hand motion for post-stroke patients has recently been developed. This abstract compares simulation and experimental data on a human finger with a corresponding robotic digit to evaluate the viability of the current design for rehabilitation purposes and to ensure patient safety and performance.

METHODS/RESULTS

Glove and Soft Robotic Digits:

This system consists of five sensorized robotic digits and a wearable fixture along with a programmable control unit that monitors and modulates the trajectory of the fingers. Finger motion is accomplished by pneumatically actuated soft robotic digits based on hybrid soft-and-rigid actuator technology. Computer simulations have shown the resulting relative angles between rigid sections at the metacarpal phalangeal (MCP), proximal interphalangeal (PIP), and distal interphalangeal (DIP) joints can reach full anatomical range of motion (ROM) at a single actuation pressure of 24.3kPa.

Kinematic study:

A kinematic study was conducted to compare one subject’s index finger with a robotic digit using a motion capture system to analyze spatial and angular position. This study determined the functional anatomical ROM requirements at each joint for both the robotic digit and index finger. The achieved ROM for MCP, PIP, and DIP joints of the robotic digit are 85˚, 96˚, and 53˚, respectively, which are in good agreement with full anatomical ROM. It should be noted that the human finger (MCP: 45˚, PIP: 75˚, and DIP: 45˚) did not quite reach full ROM during testing due to obstacles in tracking. Still, these achieved ROM are consistent with the functional ROM of human fingers.

DISCUSSION

A hand therapy glove has been designed to provide flexion and extension of the fingers as an adjunct to hand rehab. A prototype has been fabricated based on initial design parameters and is able to provide joint ROM based on the literature. Functional grasp parameters have been experimentally measured in a human finger and will be used for future design improvements.

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IRB/IACUC# 2015-154
Geriatric Utilization of Drugs on the BEERs List: Physician Prescribing and Implications for Pharmacist Provided Medication Therapy Management (MTM)

Objective: Drug prescribing patterns reveal that elderly patients were prescribed inappropriate medications at 8% of doctor visits. A panel of geriatric medicine and pharmacology experts published the BEERs list as guidance for medication dispensing for seniors. Of 677,580 patients receiving prescriptions through Medicare Part D, 31.9% received a potentially inappropriate medication. The objective of this study was to identify drugs most commonly prescribed to geriatric patients, to compare those drugs to the BEERs list and to provide adverse effects (AE) that could be minimized through MTM.

Methodology: The list of 135 drugs utilized for comparison was derived from three sources (NewWest, Propublica, Aetna) and represents the most commonly dispensed and/or sold prescriptions for Medicare Part D (CMS 2013). This list was compared to BEERs list (2015). To identify MTM examples, a literature search using PubMed, Medline, CINAHL and Google Scholar was performed from 2010-2015. Key search terms were “seniors”, “geriatrics”, “medication therapy management” and “adverse effects.” Articles were excluded if they were not in English or lack detailed adverse effects.

Results: Upon comparison, 15 of the 135 drugs were listed on the BEERs list and deemed inappropriately prescribed. Specifically, antipsychotics with AE of orthostatic hypotension, bradycardia, increased fall risk and high abuse potential should be avoided. Commonly prescribed, antipsychotics, quetiapine has a black box warning of increased mortality in elderly patients with dementia-related psychosis. The most frequently prescribed inappropriate drugs were antihypertensive valsartan, proton pump inhibitor omeprazole, and antipsychotics quetiapine and olanzapine. The majority of the 11 MTM articles retrieved were observational studies. Common AE were sedation, tardive dyskinesia, anticholinergic effects and prolonged hypoglycemia.

Conclusion: The BEERs list was developed as a safeguard against inappropriate care for the elderly. A 2010 study examined pharmacist provided MTM and found that drug problems were identified for over 85% of the geriatric population, improved health outcomes for over 50% and reduced cost overall. Future research should focus on examining the MTM impact on AE reduction and the economic impact of inappropriate prescribing.

Sponsor N/A
IRB/IACUC#
A STEP in the Right Direction: An Interdisciplinary Approach to Transitional Care

Purpose: The Affordable Care Act, calls for more focus on finding innovative delivery systems that improve care, increase efficiency, and reduce costs.

Background: Hospital readmissions, excessive falls, and poor quality of life are factors that unnecessarily increase healthcare costs. The Safe Transitions for the Elderly Patients (STEP) program is a hybrid transitional care model developed by the UNT Health Science Center (UNTHSC) as part of an 1115 Waiver to address these factors in a home care setting in Tarrant County.

Objectives: The primary goals of STEP are to reduce all-cause 30 day hospital readmissions, improve quality of life, and decrease falls among Medicaid patients over 50 years through a collaborative and interdisciplinary approach to patient care.

Methods: An interprofessional team that includes a physician/geriatrician, nurse practitioner, physician assistant, social workers, physical therapists and a dietician assess and treats the patient in the home for up to 90 days post hospital discharge based on the individual patient needs.

Conclusions: Through this model, UNT Health Science Center has the opportunity to demonstrate a unique transitional care model that will improve health care delivery post-hospitalization.

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Conclusion:

Correlations between changes in FGHR and HN (r=-0.527, p=0.017) while controlling for changes in L4L5VAT. Changes from T1 to T3 were calculated. Partial correlation controlling for L4L5VAT was utilized to determine associations of changes in GHR with changes in CR, DI, and HN.

Results:

Changes from T1 to T3 were compared using paired t-tests. Partial correlations controlling for changes in L4L5VAT were utilized to determine changes in GHR with changes in CR, DI, and HN.

Methods:

A secondary data analysis was conducted on data from a 1-year prospective study in a community bariatric surgical setting. Obese patients (OB) (n=71, Mean age=44.6 years, Mean BMI=43 kg/m2) underwent assessment before (T1) and 12-months after LBS (T3). Age and gender matched controls (NW) (n=30) were also assessed. Self-report surveys included the Eating Inventory (Cognitive Restraint; CR, Disinhibition; DI, and Hunger; HN). Active GHR was measured in a fasting state (FGHR) and post-prandially (PGHR). CT scan determined central adiposity (L4L5VAT). From T1 to T3 were calculated. Partial correlation controlling for L4L5VAT was utilized to determine associations of GHR with CR, DI, and HN at T1. Changes from T1 to T3 were compared using paired t-tests. Partial correlations controlling for changes in L4L5VAT were utilized to determine changes in GHR with changes in CR, DI, and HN.

Results:

For all subjects at T1, FGHR and HN were significantly correlated (r=-0.259, p=0.014) while controlling for L4L5VAT. PGHR and HN approached significance (r=-0.195, p=0.067). At T3 there were no differences between OB and NW in FGHR, PGHR, or RGHR. For OB at T3, there were significant correlations between changes in FGHR and HN (r=-0.527, p=0.017) and C-PGHR (r=-0.465, p=0.039) while controlling for changes in L4L5VAT.

Conclusion:

Fasting and postprandial ghrelin are related to eating behavior patterns, specifically in eating in response to hunger cues. This appears to normalize after LBS regardless of loss in central VAT. Effectiveness of LBS via hormonal regulation of appetite may be independent of weight loss.

Sponsor: NIH grants H75/CCH224064, HL04297 and HL64913
IRB/IACUC#: 2007-053

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Restricted Intake and Then Some: Relationship of Changes in Ghrelin and Eating Behavior Patterns One Year After Laparoscopic Banding Surgery

Purpose:

Laparoscopic Banding Surgery (LBS) promotes loss of excess weight, presumably through reduced energy intake imposed by band restriction. There currently exists controversy regarding the direct impact that LBS may have on appetite regulating hormones such as ghrelin (GHR), independent of weight loss. Furthermore, little is known about the relationship between changes in ghrelin with eating behavior patterns after LBS. The purpose of the present study was to examine relationships between GHR and eating behavior patterns before and after LBS. It was hypothesized that (1) abnormal GHR will be associated with maladaptive eating patterns, and (2) normalization of GHR post-LBS will be associated with improved eating behavior patterns independent of reduction in central adiposity.

Methods:

A secondary data analysis was conducted on data from a 1-year prospective study in a community bariatric surgical setting. Obese patients (OB) (n=71, Mean age=44.6 years, Mean BMI=43 kg/m2) underwent assessment before (T1) and 12-months after LBS (T3). Age and gender matched controls (NW) (n=30) were also assessed. Self-report surveys included the Eating Inventory (Cognitive Restraint; CR, Disinhibition; DI, and Hunger; HN). Active GHR was measured in a fasting state (FGHR) and post-prandially (PGHR). CT scan determined central adiposity (L4L5VAT). Changes from T1 to T3 were calculated. Partial correlation controlling for L4L5VAT was utilized to determine associations of GHR with CR, DI, and HN.

Results:

For all subjects at T1, FGHR and HN were significantly correlated (r=-0.259, p=0.014) while controlling for L4L5VAT. PGHR and HN approached significance (r=-0.195, p=0.067). At T3 there were no differences between OB and NW in FGHR, PGHR, or RGHR. For OB at T3, there were significant correlations between changes in FGHR and HN (r=-0.527, p=0.017) and C-PGHR (r=-0.465, p=0.039) while controlling for changes in L4L5VAT.

Conclusion:

Fasting and postprandial ghrelin are related to eating behavior patterns, specifically in eating in response to hunger cues. This appears to normalize after LBS regardless of loss in central VAT. Effectiveness of LBS via hormonal regulation of appetite may be independent of weight loss.

Sponsor: NIH grants H75/CCH224064, HL04297 and HL64913
IRB/IACUC#: 2007-053

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A Cadaveric Study of Anatomical Variations in Neurovascular Branching Patterns of the Head and Neck

At approximately the level of the fourth cervical vertebra (C4), the common carotid artery (CCA) bifurcates into the internal carotid artery (ICA) and the external carotid artery (ECA) to supply the brain and facial structures, respectively. The purpose of this study is to examine anatomical variations in the origin and order of the left and right sides of the ascending pharyngeal artery, lingual artery, and thyrocervical trunk, which branch off the ECA, as well as the location of the vagus nerve within the carotid sheath with respect to neighboring vessels. Possible differences between left and right sides as well as males and females for these vessels were examined. This study includes data from cadavers (n = 63) made available through the University of North Texas Health Science Center (UNTHSC) Willed Body Program. Variations were documented through responses to a data sheet with multiple-choice questions; side and sex differences were evaluated using chi-square tests in SPSS. Significant differences between left and right sides for all vessel branching patterns were detected (X2 ≥ 25.9, df = 1, p ≤ 0). In addition, differences were found between males and females in the left ascending pharyngeal artery (X2 = 9.8, df = 1, p = 0.022), right thyrocervical trunk (X2 = 14.483, df = 1, p = 0.002), and left vagus nerve (X2 = 26.773, df = 1, p = 0.007). From this study it may be concluded that significant branching variations of the ECA exist. This information opens up questions such as whether or not there are evolutionary advantages to specific anatomical variations such as if certain branching patterns provide better blood flow to specific regions, or if there are physiological advantages associated with different locations of the vagus nerve. From a surgical standpoint, further study of anatomical variations can provide better insight as to whether there are complications that can be associated with particular branching patterns, or if certain vessels are more susceptible to damage from spontaneous vascular injury (e.g., stroke, aneurysm).

Sponsor: N/A
IRB/IACUC#: Alg/1623
stress and construct stiffness respectively. Noteworthy, the stiffness started to fall drastically as the taper increased past 2 degrees in the 21.0 cm diaphyseal model.

**Results**

Fixation stiffness with increasing stem taper angle after revision total hip arthroplasty

**Hypothesis**

Stable femoral fixation during total hip arthroplasty (THA) is critical to ensure adequate implant performance. Although cylindrical implant stems designs generally have shown satisfactory long-term results, in revision cases or cases with poor bone quality, tapered hip replacement stems have been suggested as a better performing alternative. The degree of the taper has yet to be biomechanically tested in such revision cases. This study aims to compare the initial fixation stability with increasing tapered stem implant geometry using two diaphyseal bone loss models simulating revision THA.

**Methods**

Using the finite element (FE) method, a numerical technique commonly used to computationally approximate solutions for complex structural mechanics problems, two femoral diaphyseal models were used to simulate revision THA. The first femoral model simulated bone loss having a diaphyseal length of only 21.0 cm. The second femoral model was further sectioned to 21.0 cm. The taper angle of the distal stem of the prosthesis - the region of the implant in contact with the bone cortex – was varied from 0 to 2.5 degrees in 0.5 degree increments.

**Results**

As the taper was increased from 0 degrees to 2.5 degrees in the 21.5 cm diaphyseal model, there was a 79%, 30%, 7%, and 14% decrease in contact area, average bone stress, average implant stress and construct stiffness respectively. As the taper was increased from 0 degrees to 2.5 degrees in the 21.0 cm diaphyseal model there, was a 75%, 29%, 6%, and 20% decrease in contact area, average bone stress, average implant stress and construct stiffness respectively. Noteworthy, the stiffness started to fall drastically as the taper increased past 2 degrees in the 21.0 cm diaphyseal model.

**Conclusions**

The ideal implant should maximize the beneficial effects of a taper and minimize the detrimental effects. At the bone diaphyseal lengths studied, although all the tapered models showed satisfactory performance, the 0 degree no taper model showed the highest stiffness. If implant stress is a concern, from our results, it appears that the 1.5 degree taper minimizes implant stress without drastically decreasing stiffness.

**Sponsor**

IRB/IACUC# 2016-020
Effect of Private Patient Rooms on Central Line-Associated Blood Stream Infection (CLABSI)

Objective: Private hospital rooms have long been hypothesized to lower the risk of hospital-acquired infection. However, the evidence base is weak and consists mostly of expert opinion and several smaller studies that include one or two hospitals. Within the field of architecture, there is much interest in "evidence-based design" and how private rooms and other design elements influence patient satisfaction and health outcomes. To assess this gap, we assessed the impact of private rooms on the incidence of central line-associated blood stream infections (CLABSI) for 1.3 million patients treated at 344 Texas hospitals.

Design: Data sources included the Texas inpatient data, American Hospital Association data, and patient satisfaction data (HCAHPS). The dependent variable was the overall CLABSI rate at each hospital, as defined by AHRQ’s Patient Safety Indicators. Explanatory variables included the percentage of acute-care beds in private rooms, patient satisfaction scores, nurses per bed, hospital type, and various other patient and hospital characteristics. Percentage of private rooms was considered as both a structural (architectural) and as a process measure of quality. A zero-inflated Poisson regression model was used for the hospital-level analysis, and logistic regression with random effects was fitted to the patient-level data. For the patient-level analysis, the percentage of private rooms was treated as a fixed effect, i.e., an architectural feature.

Conclusions: Hospitals with mostly private rooms were found to have "positive external effect" that lowered the risk of a CLABSI for all patients, regardless of whether they were assigned to a private room. Conversely, hospitals with mostly semi-private rooms were found to have "negative external effect" that increased CLABSI risk for all patients, even those assigned to a private room. On the margin, assignment to a private room offered a modest reduction in the risk of a CLABSI.

Sponsor
IRB/IACUC# 2016-028

Relationship of Lipoprotein (A) with Other Measures of Atherogenic Cholesterol

Purpose: Lipoprotein (a) [LP(a)] represents a class of lipoproteins with structural similarity to low density lipoprotein (LDL). LP(a) consists of a cholesterol-laden LDL–like particle bound to a plasminogen-like glycoprotein [apolipoprotein(a)], making it capable of contributing to both atherosclerosis and thrombosis. Indeed LP (a) has been shown to be an independent risk factor in the development of CVD and causative of CVD-related events. Nonetheless, questions remain about screening and treatment of individual with elevated levels, especially youth (< 18 yrs of age). This is due, in part, to LP(a)’s structural variability, racial/ethnic variations, difficulty defining normal levels, lack of consensus regarding method used for measurement, limited availability of interventions, and lack of long term studies demonstrating safety and efficacy of LP(a) lowering. The aim of this project is to correlate levels of LP(a) with other measures of atherogenic cholesterol (LDL-C and non HDL-C).

Methods
This is a retrospective chart review of youth (age) referred to the Cardiovascular Health and Risk Reduction Program at Cook Children’s Medical Center between Jan 2012 and Feb 2015. Records were reviewed and de-identified data collected of those routinely tested for risk factors associated with premature CVD, including total and LDL-C, HDL-C, TG and LP(a). Non HDL-C was calculated as: Total cholesterol – HDL-C. Since fasting has little effect on levels of HDL-C, LDL-C, and non HDL-C, blood samples were collected with and without fasting. Pearson’s correlations and non-parametric Spearman’s rho (P) were calculated between Lipoprotein (a) and each individual risk factor.

Results
The two sets of correlations produced similar results. LP(a) was positively and significantly, though modestly, correlated with total cholesterol, non HDL-C and LDL-C. However, LP(a) was not significantly correlated with HDL-C or TG.

Conclusions
LP (a) is associated with increased risk for premature cardiovascular disease, such as myocardial infarction and stroke. While moderate correlations to LP (a) were observed between non HDL-C and LDL-C, LP (a) seemingly remains an independent risk factor.

Sponsor  N/A
IRB/IACUC# CCMC 2012-065 N/A
Exploring mechanisms between Religiosity and Health Behaviors in African American Women

Background: Current interventions with African American (AA) women show less weight loss overall, and lower maintenance over time compared to other populations. There is great interest in culturally adapting evidence based interventions to increase effectiveness for AA populations. Seventy percent of Black women report living a religious life is important compared to 57% White women. As a result, faith is a primary adaptation for weight loss programs among AA women. While a positive relationship between faith and health has been established, how the relationship works is still being understood. In this study, the possible mediating effects of motivation on the relationship between religion and health behavior was examined.

Methods: Baseline data from the Better Me Within (BMW) program (P20MD006882) was used for this study. Religion was measured by the spiritual health locus of control (SHLOC) survey that includes passive and active subscales. The active subscale refers to those who have a belief that God is a partner in health and are hypothesized to have more positive health behaviors, whereas those with a passive score show fatalistic beliefs (e.g., health is in God’s hands) and are expected to engage in less positive health behaviors. However, other variables may play a role in this relationship such as motivation. This study evaluated means and standard deviations, and calculated simple correlations between SHLOC, motivation for physical activity and minutes of physical activity (PA). Simple linear regression models were run to evaluate the influence of SHLOC and health behaviors (e.g. PA) on motivation.

Results: A total of 158 participants were included in this analysis (Mean Age=48.9 ± 11.68, Body Mass Index (BMI)=38.15 ± 9.71 Waist circumference (WC) =43.04 ± 5.88). The majority of participant had some education after high school (80%). Participants also showed high active SHLOC (Mean=35.47 ± 7.48, max score = 44). Motivation for PA was positively and significantly correlated with active SHLOC (0.16, p

Conclusions: Results show having a more passive (fatalistic) view of health is associated with higher levels of motivation for PA. While this seems illogical, it does offer opportunities for alternative explanations. Self efficacy (Confidence for Exercise and PANSE) may be driving the relationship between motivation for PA and SHLOC. More work is needed to understand the mediators between faith and health. If self efficacy is more influential in this relationship, then adapting interventions to focus on self efficacy rather than faith may be beneficial to lifestyle interventions for AA women.

Centrally Located Visceral Adipose Tissue and Outcomes after Laparoscopic Gastric Banding Surgery

Hypothesis: A higher proportion of central VAT relative to total VAT leads to decreased efficacy of LGBS outcomes as measured by percent excess weight loss (%EWL), inflammatory marker, and insulin resistance.

Method: Thirty-three LGBS patients (21 women, 12 men) underwent pre-surgical and 6-month (T2) post-surgical testing. Average age was 45.7 years (24-66). Average baseline Body Mass Index was 43.1 kg/m² (32.4-54.0). Fasting blood samples were taken to assess cardiac C-reactive protein (CRP), insulin, and glucose. Homeostasis Model of Assessment score (HOMA) for insulin resistance was calculated using insulin and glucose. %EWL was calculated using number of pounds lost relative to number of baseline pounds above a BMI of 25. VAT was assessed using computed tomography. Proportion of central VAT was calculated as L4/L5 divided by total VAT. Patients were split into a Low- (LP) or High Proportion (HP) group based on a median split. Repeated measures t-tests were used to compare changes in CRP and HOMA from baseline to T2. Independent t-tests were used to compare differences between groups at T2 in CRP, HOMA, and %EWL.

Results: Both LP and HP showed significant reductions from baseline to T2 in CRP (p=.026 and .000 respectively), and HOMA (both p=.001). There was no significant difference at T2 between LP and HP in %EWL or HOMA. A trend toward lower CRP at T2 for HP compared to LP was observed, although results were not significant (p=.08).

Conclusion: Results of this analysis demonstrate that the relative proportion of centrally located VAT does not appear to be a significant factor in outcomes measured 6 months post-LGBS. Patients with higher or lower proportions exhibit improvements in HOMA and %EWL, although inflammation may not resolve as effectively for patients with higher proportions. Overall, it appears that the relative location of VAT does not appear to be a substantive factor in the efficacy of LGBS.

Sponsor NIH
IRB/IACUC# 2007-053
A comprehensive retrospective chart review was performed on all patients who received a hematopoietic stem cell transplant for the treatment of transplanted sickle cell patients in order to evaluate transplant as a viable treatment for sickle cell disease. Data was analyzed to assess indications and outcomes of the transplant experiences and assessment of outcomes could potentially improve the future management of sickle cell disease patients.

Materials and Methods:
Two assessments were distributed on two different occasions between two sample populations. The assessments were distributed within two weeks prior to discharge from the CCMC NICU and on the first follow up visit in the NEST clinic. 22 parents/guardians were interviewed. A higher score on either survey indicates a better quality of life.

Results:
Prior to discharge, the parents/guardians of NICU patients averaged a 96.2% score in family cohesion, 97% in infant well being, 85.9% in maternal well-being, 89% in maternal comfort, 52% in time impact, and a 79.2% score in family cohesion. On the first follow up visit, parents/guardians averaged a 80% score in parent quality of life, 65.45% in infant progress, 75.9% in overall quality of life, 84.1% in transition to home, 93.5% in NICU experience, 84.8% in maternal confidence, 43.9% in coping and adjustment, and 73.5% in maternal comfort.

Conclusions:
Overall, families feel adequately prepared for the discharge process and the transition from the NICU to home. Results from this pilot study indicate a need for more maternal counseling and parent education pertaining to each child’s development and growth. Coping and adjustment is the parameter that scored lowest overall. A follow up study with a larger sample size is needed to further identify factors that could be improved in the discharge planning process.

Sponsor: N/A
IRB/IACUC#: CCMC 2014-007
Quantitative Liver Function Test Using Cholate

As we progress with our treatment for liver related disease there is an increased need to risk-stratify patients. In normal individuals without liver disease 80% of cholate compound is taken up and degraded by the liver. However, with liver damage development of porto-systemic shunting can occur. The increased delivery of cholate to the systemic circulation is proportional to the degree of hepatic shunting and therefore the amount of liver damage.

Patients with non-alcoholic steatohepatitis (NASH) take both oral and IV cholate and blood is drawn over the course of 90 minute in 15 minute increments. The blood is then assessed for the amount of cholate in the periphery. Using a formula an average shunt value is derived for each patient. These patients are followed for 6-8 years and shunt values are compared with age, demographics, and clinical outcomes. The change of shunt values over time are also compared with clinical outcomes.

The measure of oral dose peripheral blood cholate correlates with the amount of porto-systemic shunting in patients. The average shunt value derived can be used to risk stratify patients and possibly predict death and decompensation. Patients with NASH have a consistent increase in shunt value correlated with clinical findings.

Sponsor NIH
IRB/IACUC# BRI 011-063
Exploring the Role of Protective Factors on Depressive Symptoms among Mexican American Children.

Purpose: National Health and Nutrition Examination Survey (NHANES) 2009–2012 dataset revealed that 7.6% of Americans aged 12 and over had depression. Youth, ages 12–17, had a depression rate of 5.7%. Research shows that ethnic disparities in mild, moderate, and severe depressive symptoms exist in Hispanics, compared to Non-Hispanic whites. The objective of this project is to explore the association between protective factors at the individual, relationship, and community level with depressive symptoms among Mexican American children.

Materials and Methods: Variables were selected based on the social ecological model. A cross-sectional sample of 144 children, ages 10-14, and their legal guardian were used to examine exposure to seven protective factors: 1) acculturation 2) self-worth 3) positive physical development 4) family meals together 5) parent attendance of child events 6) neighborhood safety and 7) presence of recreation centers. The total number of protective factor exposures was categorized into four levels: 1, 2, 3, ≥ 4 exposures and run in a logistic regression model as the exposure of interest with depressive symptoms as the outcome. Depressive symptoms were evaluated using the Total Score yielded from the CDI 2: Self-Report (Short) version (CDI 2: SR[S]). Depressive symptoms were dichotomized as not having depressive symptoms (Average/Lower Level) and having depressive symptoms (High Average, Elevated, and Very Elevated Levels).

Results: Of the boys (51% of sample), 10 (7%) had depressive symptoms, compared to 20 (14%) girls. Logistic regression adjusting for gender shows a relationship between protective factor exposures and depressive symptoms. Poverty, parent income, and BMI were not significantly associated with depressive symptoms and were not included as confounders. The model shows that for each increasing level of protective factor exposure there is a 0.168 (CI: 0.058, 0.490) odds for depressive symptoms.

Conclusions: As the number of exposures to protective factors increase in a Mexican American child, the child has reduced odds of having depressive symptoms. Future studies should investigate not only the total number of protective factor exposures, but which type (e.g. individual, relationship, or community level) most impact the etiology of depressive symptoms in Mexican American children.

Michels Type II Vessel Branching Pattern Variant of the Hepatic Pedicle

In the branching of the celiac trunk, the left hepatic artery arises from the common hepatic in 89% of cases. However, in 11% of cases the vessel may instead arise from the left gastric artery, an alternate branching pattern known as Michels Type II variation of hepatic arteries. This study looks into the prevalence of this particular variation in a UNT Health Science Center cadaver subset and its correlation with the statistics stated in the most recent literature.

The cadavers in this study (n = 39)were provided through the University of North Texas Health Science Center Willed Body program. For dissection protocol, dissections of the abdominal area included removal of overlying tissues to expose the celiac trunk. Literature review was performed utilizing PubMed.

Of the 39 cadavers observed, only 31 were examined due to 8 having undergone complete liver removal. The prevalence of the left hepatic artery branching off of the left gastric artery was 12.9%. The sample frequency of the Michels Type II variation correlated well with the previous findings, where 11% of people exhibited this variation. In addition, one of the cadavers with the variant branching pattern exhibited an additional variation where the cystic artery pierced the common bile duct. This was not observed in the other cadavers.

Previous research has revealed a wide range of variations in the branching patterns of the liver vasculature. The Michels classification system was established to serve as a standard nomenclature. The variation of interest, with the left hepatic artery branching from the left gastric artery, is an example of a Michels Class II variant. Similar to prior results, a prevalence of approximately 12.9% was found within the sample of hepatic pedicles evaluated. In addition to this finding, a unique arterial branching pattern where the cystic artery pierces the common bile duct was noted. This finding was present in a single cadaver. Clinically, variants with persistently reported high prevalence such as these should be screened to help prevent serious complications during surgical procedures involving these vessels, such as left gastric artery ligation and liver removal. The persistently reported high prevalence for the Michels Type II variant exemplifies the need for such pre-operative screening.
Congenital Hypothyroidism

Introduction

Congenital hypothyroidism (CH) is common, affecting between 1:3,000 and 4,000 newborn infants. Unrecognized or inadequately treated, CH leads to mental retardation. Newborn screening has made it possible to identify affected infants at a very early age, allowing thyroid therapy to be initiated usually within two weeks of birth. As a result of early diagnosis and appropriate treatment, many children with CH have normal cognitive development.

The American Academy of Pediatrics (AAP) and the European Society for Pediatric Endocrinology (ESPE) have published guidelines to assist physicians in the appropriate diagnosis and treatment of children with CH. Although early detection, correct diagnosis and timely treatment are critical to facilitate the best outcomes, little is known about provider practices when confronted with infants with congenital hypothyroidism.

We, therefore, conducted a survey of pediatric endocrine providers to categorize beliefs and clinical practices.

Methods

An on-line survey was conducted of pediatric endocrine providers in a four state region (Texas, Oklahoma, Arkansas and Louisiana). All responses were anonymous and participation voluntary. The survey was conducted from January 15th to February 15th, 2016.

Results

The survey consisted of two clinical scenarios of infants with elevated thyroid-stimulating hormone (TSH) levels in the first two weeks of life. Other than a difference in the initial TSH, Scenario 1 (50 mU/L) vs. Scenario 2 (150 mU/L), the two scenarios were identical. Survey questions were designed to explore variation in clinical practice in several key areas, including physical examination, thyroid imaging, laboratory testing and treatment/follow-up. Analysis of variance (ANOVA) was used to examine how responses to these 14 items were impacted by the differences between practitioners based on years of experience (< 15 vs. > 15 years), the differences within practitioners’ responses, and the interaction between these two predictors. At least one of the three predictors was significant, p < 0.05, for eight of the 14 items. In general, endocrine providers with ≥ 15 years of experience ordered more tests, particularly in the Scenario 1 (TSH of 50 mU/L). The largest difference seems to have occurred for thyroid blood tests. In regard to treatment, most endocrine providers used 10-15 mcg/kg/d of thyroid hormone replacement, as per current guidelines.

Conclusions

Our survey indicates that endocrine providers who completed the survey appear to understand and adhere to CH guidelines irrespective of the level of TSH elevation. Significant differences (p < 0.05) were found, however, in the responses between providers with < 15 vs. ≥ 15 years of experience and within providers when confronted with an infant who had an initial TSH of 50 vs 150 mU/L. The reason for provider variability was not addressed by our questionnaire but should be explored.

Sponsor

IRB/IACUC# CCMC 2015-080

Impact of Multiple Healthcare System Use on Psychiatric Outcomes in the State of Texas With One John Peter Smith Psychiatric Hospitalization

Purpose: In communities with more than one mental healthcare system, psychiatric patients often present to multiple systems of care, rather than receiving all care within one system. For instance, patients discharged from one inpatient setting may present soon after for additional care within a different facility. The purpose of this study is to characterize between-system patient utilization patterns and to study the ways in which these patterns are impacted by payer source and presenting problem. <br />

Methods: Using data from the Texas Health Care Information Collection's Inpatient Research Data File (THCIC-IP), we retrospectively examined psychiatric inpatient utilization patterns occurring in Texas with at least one admission at John Peter Smith Hospital for calendar years 2012-2014. Thirty-day readmissions for the same presenting problem were regarded as an indicator of poor outcome. Utilization patterns were analyzed by patient age, gender, payer source, primary diagnosis, level of comorbid health conditions and length of stay. <br />

Results: A total of 9,582 psychiatric illness episodes were treated within 82 inpatient specialty psychiatric treatment facilities in the state of Texas where at least one episode of care involved treatment at John Peter Smith Hospital during study years. This included 3,215 patients for whom primary focus of care was psychosis; 4,965 patients treated for a mood disorder and 1,260 patients treated for substance-related issues. Seeking treatment within multiple healthcare systems appeared to be more common for patients with certain kinds of presenting problems and primary payer sources. Outcomes also varied with treatment in multiple versus single care providers over time. <br />

Conclusion: These findings suggest that strategies to better educate consumers of psychiatric inpatient care about their local healthcare system alternatives and how choices may affect treatment outcome may be of benefit.

Sponsor

IRB/IACUC# 2015-173
Induced seismicity (earthquakes) from energy extraction activity in North Texas: A community perspective

**Purpose:** To examine induced seismic events in Irving, Farmer’s Branch and Dallas, Texas between 2002 and 2015 and energy extraction activity associated with these events. Potential impacts to critical infrastructure and perception to the public is examined.

**Methods:** The U.S Geologic Survey Earthquake Hazard Program database was searched for seismic events in Irving, Farmer’s Branch and Dallas occurring 2002-2015. Well locations were retrieved from Texas Railroad Commission database. Studies related to impacts of earthquakes on infrastructure, and perception of hazard were searched in Scopus, Google Scholar, Web of Science and PubMed.

**Results:** Between 2002-2015, 83 earthquakes occurred in the Irving, Farmer’s Branch, Dallas area. 86% of earthquakes (71) occurred in Irving. In January 2015, 25 earthquakes occurred within a 2-mile radius of the Old Texas Stadium. Potential structural damage to critical infrastructure including roadways, bridges, tunnels, water and gas lines, and buildings can occur. Smaller earthquakes are not life-threatening but studies confirm a public perception of fear, anxiety, physical harm, and decreased property values related to earthquakes frequency.

**Conclusion:** Induced seismicity was consistent with energy extraction activity. The area with highest earthquake activity exists at the intersection of 2 geologic fault; the Muenster Arch and Ouachita Fault. Frequency of earthquakes within a short time interval in this area is consistent with features of induced seismicity.

**Sponsor:** N/A

**IRB/IACUC#** 1639

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Induction or insufficient sleep? A look at the association between sleep disturbances and ADHD symptoms in teens

**Introduction:** Children and teens with ADHD often report sleep disturbances; however, less literature has examined the role sleep plays in ADHD symptoms. Most of the studies to-date focus on children and adults with ADHD despite numerous reports that teens chronically experience sleep restriction as evidenced by the average teen reporting a school-night sleep duration of ~7.5 hours (at least 2 hours short of their actual need: 9-10 hours). In addition to insufficient sleep, teens are at increased risk of sleep disorders such as insomnia and delayed sleep phase. Next-day consequences of these conditions are frequently daytime sleepiness, moodiness, and inattention. Thus, it is important to assess the association of sleep disorder symptoms with reported ADHD symptoms in teens. The hypothesis was that teens who evidenced sleep disorder symptoms would exhibit more ADHD symptoms.

**Methods:** Participants were 30 normal-to-obese teens (mean grade=10th, mean age=15.4 yrs, 80% females, 17% Hispanic) who reported shortened and irregular sleep patterns, but no history of sleep disorders. Following parental and teen consent, both parents and teens completed questionnaires inquiring about sleep and health. Parents and teens completed the Sleep Disorder Inventory for Students (SDISP and SDISA, respectively). Teens also reported on daytime sleepiness (Pediatric Daytime Sleepiness Scale: PDSS) and circadian phase preference (Composite Scale of Morningness: CS). Roughly one week later, parent-reported ADHD symptoms were collected using the ADHD-IV, a standardized ADHD screener. These data were collected as part of a larger, prospective study examining sleep and health in teens. Regression analyses examined parent- and teen-reported sleep disorder symptoms as a predictor of parent-reported ADHD symptoms with sex, grade, and age as covariates. Additional analyses are being conducted that will include self-reported sleep.

**Results:** Analyses showed teen-reported daytime sleepiness predicted parent-reported ADHD symptoms (beta=0.43, P=0.030). Trend findings were found such that parent-reported ADHD symptoms were predicted by parent- and teen-reported sleep disorder symptoms (beta=0.34, P=0.087 and beta=0.35, P=0.094, respectively). Phase preference was not a significant predictor of ADHD symptoms.

**Conclusions:** These findings provide evidence that daytime sleepiness, frequently the by-product of insufficient sleep the night before, is perceived as ADHD symptoms by parents. In addition, trend findings suggest that increased reported sleep disorder symptoms in teens without a history of sleep disorders also manifest as ADHD symptoms. Additional studies examining the effect of improving sleep should be done to further elucidate the connection between sleep and ADHD symptoms.

**Sponsor:** N/A

**IRB/IACUC#** 2013-015
**Literature Review of the Association Between VCD and GERD**

**Question/hypothesis:** Whether the association between VCD and GERD is due to causal relationship or the high prevalence of GERD in the general population.

**Design/methods:** An English literature review was performed on the association between VCD and GERD.

**Results:** Four studies suggesting a correlation between GERD and VCD are repeatedly mentioned in the majority of articles reviewed. The strongest evidence was demonstrated in a study of 12 patients conducted by Loughlin et al. A second study performed by Kerry et al involved only 77 patients in a tertiary care setting without a control group. A third study by Gurevich-Uvena et al was a retrospective chart review of 256 patients with no disease free control group or testing for GERD. The fourth study by Kaufman examining 225 patients with GERD helped identify different otolaryngologic manifestations of GERD but did not specify the presence of VCD. The literature also mentioned the absence of a significant correlation between anti-reflux therapy and improvement of voice-related disorders such as hoarseness and VCD.

**Conclusion:** Given the small number of studies on the association between VCD and GERD and their limitations, the lack of significant correlation between anti-reflux therapy and improvement of voice-related disorders suggests that the association between VCD and GERD is related to the high prevalence of GERD in the general population rather than a causal relationship.

**Examining the Impact of Providing Smartphones to Patients from a Managed Care Perspective: A Systematic Review**

**Objective:** The objective of this study was to explore the literature within the last decade with respect to health plan purchase of smartphones for patients to improve health outcomes. A secondary objective was to explore smartphone use and cost.

**Methods:** A systematic review using Pubmed, Medline, Cinhil Plus, Cochrane Library, Scopus, Trip and PsychInfo databases to identify studies regarding smartphone use conducted between 2005-2015. Key search terms included “mhealth”, “telehealth”, “smartphone”, “mobile applications”, “cost savings”, and “patient health outcomes”. Abstracts were screened against inclusion criteria and selected based upon relevance and quality. The most significant eligibility criteria required was that a smartphone must have been provided to the patient. Risk of bias was assessed using the Cochrane Risk of Bias Tool. Use of Covidence facilitated the summary of selected articles. Notable characteristics were summarized in tables.

**Results** The search yielded a total of 130 articles for review. Several examples within managed care were identified and focused on three key areas: disease and medication management, personal fitness and wellness and remote patient monitoring. Studies included managing these chronic diseases: Cardiac rehabilitation, COPD, Diabetes, HIV, Hypertension, Heart failure, rheumatoid arthritis, Addiction, chronic pain, and mental health diseases. Seven of ten studies related to disease management showed improvement in clinical outcomes measured. Studies in which smartphones were provided to remotely monitor patient data had the most impact in reducing hospitalization and emergency room visits. The Smartphones programs that featured mobile coaching and medication reminders had high levels of patient satisfaction and reported increased behavior change and medication adherence. Challenges reported of providing smartphones included ease of use and signal interruption. None of the studies identified thoroughly examined the costs associated with provision of smartphone to patients. Health plans must consider type of phone, additional training, cost of security and integration into healthcare models.

**Conclusion** While smartphone use is growing, 48% of smartphone users had to cancel their cell phone service for a period due to financial hardship. The purchase of smartphones by health plans may mitigate these issues while improving health outcomes.
Safety of Osteopathic Manipulative Treatment on Labor and Delivery Outcomes

1. Objective: Osteopathic Manipulative Treatment (OMT) has been used in pregnant women since its beginning, but little quality data exists on its safety. The Pregnancy Research in Osteopathic Manipulation Optimizing Treatment Effects (PROMOTE) study was a NIH-funded, randomized controlled clinical trial with the objective of evaluating the safety and efficacy of OMT during third-trimester pregnancy.

2. Materials and Methods: In PROMOTE, 400 study subjects were randomly assigned to one of three study groups: Usual Care Only (UCO), Usual Care plus Placebo Ultrasound Treatment (PUT) or Usual Care plus OMT (OMT). The primary objective of the current analysis was to evaluate safety of OMT on labor and delivery by comparing the incidence of high-risk status of pregnant women; labor and delivery outcomes such as length of labor, perineal lacerations, operative vaginal delivery, meconium-stained amniotic fluid; and APGARs of infants born to mothers in each of the three study groups.

3. Results: Data from this study showed that the application of the OMT protocol does not result in increased risk of high-risk status, in fact, women who received OMT were less likely to develop high risk status. The OMT protocol also did not increase risk of precipitous labor, conversion to caesarian section, perineal laceration, meconium-stained amniotic fluid, or requiring the use of forceps or a vacuum device. In all maternal outcomes examined, no difference was reported among the three study groups with the exception of incidence of prolonged labor. Women receiving OMT were able to successfully labor longer and vaginally deliver with no increased incidence of complications, including perineal laceration, episiotomy, and use of forceps or vacuum device.

4. Conclusion: These results suggest that the OMT protocol as applied in PROMOTE is a safe intervention during the third trimester.

Preliminary Analysis of Effect of Body Mass Index and Health Outcomes Across the Continuum of Care Post-Traumatic Injury

1. Research Objectives: Examine the impact of body mass index (BMI) on health outcomes during acute care post-traumatic injury, inpatient rehabilitation, and 3-months post-discharge

2. Design: Prospective, longitudinal

Setting: Level I trauma center; inpatient rehabilitation facility; community follow-up.

Participants: 33 patients originally admitted to a Level I trauma center; all participants then completed inpatient rehabilitation in the same hospital system, followed by a 3-month telephonic follow-up.

Interventions: Not Applicable

Main Outcome Measure(s): Patients were divided into BMI categories based on admission data. Acute care data (e.g., demographic and injury-related) was collected from patient charts and hospital trauma registry. Rehabilitation data (e.g., Functional Independence Measures) was collected from eRehab and patient charts. Health outcomes included depression and post-traumatic stress disorder screens, pain levels, and return to work status. Kruskal-Wallis and Fisher’s tests compared outcomes across BMI categories.

3. Results: 12 participants were classified as being of normal weight, 11 overweight, and 10 obese. A significantly greater number of overweight patients had more severe injuries in the acute care setting (p=.001). Individuals who were overweight were significantly more likely to have a positive depression screen at baseline (p=.001). Differences in FIM efficiency during rehabilitation approached significance (p=.0551). While no differences were found during inpatient rehabilitation or 3-month outcomes, results did indicate that overweight and obese individual’s length of stays was two days longer than people who were normal weight.

4. Conclusions: As the number of individuals considered overweight or obese now includes over two-thirds of Americans, it is critical to examine the characteristics of this population and identify strategies to achieve best outcomes. Larger samples are required to determine the relationship between BMI and health outcomes after traumatic injury.
1. Purpose: Pituitary dysfunction is an exceedingly predominant complication of traumatic brain injury (TBI) with a prevalence of up to 30%. Symptoms of a pituitary disorder, such as fatigue, concentration difficulties, depression, and hormone deficiencies, can often appear nonspecific and consequently are overlooked. Such profound deficits may impose a negative impact on patients' recovery and ultimate quality of life. Currently no protocol exists for the screening of pituitary function or hormone replacement therapy (HRT) due to critical research gaps in the area of brain injury rehabilitation. The purpose of this project was to draft a set of evidence-based recommendations regarding pituitary screening and hormone replacement therapy in TBI patients.

2. Methods: A multidisciplinary team of research personnel and clinicians who specialize in treating TBI was established to include physiatry, neuropsychology, physical therapy (PT), occupational therapy (OT), speech language pathology (SLP), and therapeutic recreation (TR). Clinicians created a research question in PICO format (Population, Intervention, Comparison, Outcome). Next, research staff conducted a systematic review using the key terms "brain injuries, pituitary screen, pituitary testing, pituitary evaluation, hormone replacement therapy." PubMed, CINAHL, PSYCInfo, and Allied Health Evidence databases were utilized. The multidisciplinary team reconvened to assess quality of evidence for each article using a modified-Oxford scale and created draft recommendations using a modified-GRADE format.

3. Results: 20 articles were assessed and deemed to have good quality of evidence in support of pituitary screening, particularly in patients with severe TBI and within the first 12 months of injury. 6 articles were assessed for hormone replacement therapy and deemed to have fair quality of evidence surrounding HRT, particularly growth hormone.

4. Conclusion: We strongly recommend that pituitary screening should be routinely performed on all patients with TBI, especially moderate to severe TBI. While further study of HRT is warranted, the available research supports a weak conditional recommendation for growth hormone replacement.

Sponsor n/a
IRB/IACUC# 2016-030

1. Objective: The aim of this study was to create a visualization tool that illustrates the motion of specific joint angles during gait cycles. An example of how this tool would be beneficial to understanding gait will be presented by comparing a patient’s joint angle before and after application of Osteopathic manipulative medicine (OMM) and heel lift therapy to improve back pain.

Design: A V-gait CAREN system was used to create realistic virtual environments in order to test functional gait and balance in situations that resemble real life. Reflective markers were placed on the head, arms, legs and torso. A 12-camera Motion Analysis System (Motion Analysis Corp., Santa Rosa, CA) tracked reflective markers placed on the body, allowing precise calculation of kinematics, gait parameters, and joint range of motion during movements using the GRAIL (Gait Real-Time Analysis interactive lab) and GOAT (GraIL offline analysis tool). A list of 17 joint parameters were compiled and separated into left and right joints on an excel sheet. For each parameter, 50 cycles of gait were analyzed.

Sample data from a preliminary subject that has gone through gait analysis via the V-gait CAREN system (Computer Assisted Rehabilitation Environment Network, Motek Medical, The Netherlands) were inputted into the list and each cycle was graphed.

Results: Graphs for joint parameters up to 50 gaits cycles were automatically generated using the excel tool and proved to be effective for visualizing gait motion.

Conclusions: Presentation of one possible way to utilize this tool looks at data from one of our existing studies that compares gait changes of a patient before and after OMM and heel lift therapy to investigate improvements in back pain. Other potential uses for this tool that is not presented would be to visualize the motion of specific joints and compare a subject with a pathologic joint to a subject with a non-pathologic joint. In addition, left and right side joint angles could be compared within one subject. Lastly, pre-treatment and post-treatment analysis can be done for patients using this tool.

Sponsor n/a
IRB/IACUC# 2012-084
Utilization of Osteopathic Manipulative Treatment within an Academic Practice Setting

Introduction: Osteopathic manipulative treatment (OMT) has historically been the foundation of treatment used by osteopathic physicians. This study assesses the utilization of OMT across multiple specialties in an academic practice setting.

Hypothesis: OMT is underutilized in multiple clinics within an osteopathic academic institution.

Methods: Electronic medical records for all clinics at the University of North Texas Health Science Center (UNTHSC) were retrospectively reviewed. All patient records which were billed with CPT codes 98925-98929, indicating use of OMT, from September 2004 through September 2015 were included. The multiple specialty clinics within the UNTHSC system were combined into seven categories. The number of office visits in which OMT was utilized in each specialty was compared to the total number of office visits within the same specialty over the same time period.

Results: A total of 35,333 records that included billing codes for OMT during the specified time period were reviewed. These encounters were found to represent 7,148 unique patients, ranging in age from 0 to 98. Females made up 67% of patients, while 33% were male. Caucasians made up nearly 74% of the patient population, accompanied by 9% African Americans and 2% Asians.

In neuromusculoskeletal medicine, 74.93% of total office visits included billing for OMT; in family medicine, 0.52%; in sports medicine, 1.61%; in obstetrics, 0.01%; in pediatrics, 0.03%; in internal medicine 0.34%; and in surgical specialties, 0.01%.

Conclusions: This study shows that the vast majority of OMT in this academic clinic setting is provided by osteopathic neuromusculoskeletal specialists, with sports medicine and family medicine as distant runners-up. This was not unexpected, due to the unique skill set acquired by osteopathic neuromusculoskeletal specialists. However, this study does highlight the lack of OMT provided in the primary care setting, and shows even lower use among specialists and surgeons. This presents a need for ongoing education and support to encourage osteopathic physicians outside of an OMT specialty to integrate the use of musculoskeletal manipulation into their practices.

Sponsor n/a
IRB/IACUC# 2014-133

Osteopathic Manipulative Techniques Alter Gastric Myoelectrical Activity in Healthy Subjects

INTRODUCTION: Osteopathic Manipulative Techniques (OMT) have been shown to alter autonomic control of heart rate. However, it is unclear if OMT affects control of gastric myoelectrical activity (GMA).

HYPOTHESIS: We hypothesized that OMT significantly alters power spectral density (PSD) analyses of electrogastrography (EGG) recordings compared with sham OMT.

METHODS: IRB approval was obtained for this protocol. Subjects were studied before and after sham treatment and OMT (both vagal and sympathetic directed techniques) on separate days in a cross-over design. 15 minute EGG recordings were obtained before and after each intervention and after a water challenge (WC; a standard vagal stimulus of GMA). The WC involved drinking 500 mL of 16 °C water over 5 min.

Percent power in the normogastric range (PPN; 2-4 counts/min) was estimated from PSD analyses of EGG recordings. Absolute percent change of PPN (ΔPPN) from baseline to post-intervention and baseline to post-WC was computed and compared using paired t-tests and two-way repeated-measures ANOVA.

RESULTS: OMT significantly altered ΔPPN versus sham control (sham: 5.3%, OMT: 24.5%, P=0.015). WC significantly altered ΔPPN compared to sham control (post-sham ΔPPN: 5.3%, post-drink ΔPPN: 30.3%, P

CONCLUSIONS: We conclude that (a) OMT significantly alters GMA compared to sham control and (b) that OMT produces similar changes in GMA to WC.

Sponsor N/A
IRB/IACUC# 2014-063
Comparative Accuracy of Physician Palpation of Sacral Anatomical Landmarks versus Musculoskeletal Ultrasound Evaluation

Ultrasoundography is useful for visualizing musculoskeletal structures due to its safety and capacity for real-time imaging. A recent publication shows the validity of ultrasonography to establish sacral base position and sacral sulcus depth. Our study will compare the palpatory examination of sacral landmarks by osteopathic physicians to sonographic findings.

This study has received institutional review board approval (#2015-188). Our enrollment goal is 40-60 subjects and we have currently recruited and collected data with 16 subjects. Each subject had an initial ultrasound measurement of each sacral sulcus and inferior lateral angle (ILA), both in a prone and extended (sphinx) position. Then 5 examiners comprised of 3 senior osteopathic physicians and 2 osteopathic residents, palpated and evaluated each landmark for symmetry, again in prone and sphinx positions. Finally, another ultrasound evaluation was performed to see if there was a change in the sacrum following the repeated examinations.

The preliminary data collected with 16 enrolled subjects were analyzed thus far. Ultrasound measurements revealed mean left to right depth difference ranging from 0.38-0.26cm between the designated sacral bony landmarks. When the subjects were transitioned from prone to sphinx position, the mean depth difference ranged from 0.23-0.06cm (±0.46-0.68). Sonography before and after physician palpation showed a depth difference of the designated landmark range from 0.37-0.07cm (±0.6-0.42). Physician palpation data have not shown a high degree of interrator reliability with the 16 subjects studied.

Our study is ongoing, but so far we are able to validate that ultrasound can identify depth differences of the sacral sulcus and the ILA. Sonography also has demonstrated that depth of the sacral landmarks change from prone to sphinx position. It is important to note that the ultrasound measurements we collected so far show that there may be relative anterior movement of the sacrum at both the sacral sulcus and ILA when the subjects are in a sphinx position. This is important to study further as standard osteopathic texts maintain that the sphinx position causes the sacral base to move anterior while the ILAs move posterior. Comparing ultrasound measurements before and after physician palpation demonstrated that repeated palpation of bony landmarks may change sacral positioning. Further data collection will be needed to adequately understand physician palpatory experience.
Identification of Estrogen-Regulated Proteins in Zebrafish Embryos by Quantitative Proteomics

To identify estrogen-induced differential protein expression impacted by deyolking in zebrafish embryos using a label-free quantitative proteomics approach.

Along with non-treated controls, zebrafish embryos were treated short-term with 1 ppm of E2. Half of the embryos were subjected to a deyolking procedure. Embryo protein extracts were processed using a bottom-up shotgun proteomics approach. The samples were analyzed using data-dependent LC-ESI-MS/MS on an LTQ-Orbitrap Velos Pro (Thermo) connected to a nano-ACQUITY UPLC system (Waters). MS/MS spectra were searched against a composite UniProt zebrafish protein database using the Mascot and SEQUEST search algorithms within Proteome Discoverer (Thermo Scientific). Label-free quantitation was performed by an MS/MS total ion current approach using Scaffold (Proteome Software), as well as calculating spectral counts. Additionally, the differentially expressed proteins were mapped to networks and biological processes through Ingenuity Pathway Analysis (IPA, QIAGEN).

The increase in the zebrafish yolk protein vitellogenin is a well-known marker of estrogen exposure. With the observation of a significant increase in vitellogenin in the treated embryos compared to non-treated control embryos, we confirmed E2’s action for our subsequent proteomics study. Estrogen-regulated proteins were identified using both spectral counting and MS/MS-based total ion current method as label-free quantitative approaches. With p2-fold change as threshold, 74 proteins were differentially regulated by the hormone by combining data from both yolk-intact and deyolked samples. Of these significantly differentially regulated proteins, 3 were found to be unique to spectral counting, while 7 were unique to yolk-intact samples. Three proteins were represented in both yolk-intact and deyolked specimen but to differing degrees of up- and down-regulation. When the differentially regulated 74 proteins were submitted for pathway analysis, 53 proteins were mapped into 1 network that merged into an E2-regulated pathway. We saw repression of several proteins such as ATP synthase alpha- and beta-subunits and eukaryotic elongation factor 2 in E2-treated embryos. However, in other models, these proteins were established previously to be activated by estrogen. Therefore, the deyolking procedure significantly alters the state of the proteome in such a way that it potentially invalidates the results of quantitative proteomics studies.

The deyolking of zebrafish embryos to increase protein coverage alters expression data obtained by quantitative proteomics.

(Supported by the Robert A. Welch Foundation, BK-0031)

Sponsor Supported by the Robert A. Welch Foundation, BK-0031
IRB/IACUC# 2012/13-23-A01
The Relationship Between Physiological and Psychological Indicators of Stress in Emotional Eaters

Background: Obesity has become an increasing problem in the United States with obesity-related conditions growing in number over the last few decades. Growing evidence proposes that stress influences food intake and food choice which contributes to obesity in many people, particularly women. The purpose of this study was to examine how physiological and psychological indicators of stress are associated with emotional eating (EE) in obese women (OB).

Hypotheses: (1) Perceived stress, anxiety, and cortisol are associated with EE; (2) Coping mediates the relationship between perceived stress, anxiety, and cortisol with EE.

Methods: This study is a secondary analysis of data obtained from an experimental study investigating stress-related eating in OB. Thirty obese but otherwise healthy women who report that they eat in response to stress were included in the study. Average BMI was 40.21 kg/m2. Average age was 36.17. Self-report surveys included the Perceived Stress Scale (PSS), State Anxiety from the State-Trait Anxiety Inventory (state anxiety; S-ANX), and Eating and Appraisal Due to Emotions and Stress (EE and Coping; COP). Fasting serum cortisol was analyzed in-house. Pearson correlation was used to determine associations between EE with PSS, S-ANX, COP, and cortisol. Subjects were categorized as high or low in EE based on the mean value. Logistic regression was used to ascertain the ability of PSS, S-ANX, and cortisol to predict high EE.

Results: HN was significantly correlated with EE (r=-.514, p=.004) and COP (r=.614, p=.000) and approached significance with cortisol (r=.356, p=.058). Logistic regression for PSS, S-ANX, and cortisol significantly predicted high EE (X2=12.845, p=.005) and correctly classified 76.7% of the cases. Variance due to EE was significant in the model (r=.622, p=.008). Variance due to EE was significant in the model (p=.037).

Conclusion: The extent to which obese women eat in response to hunger cues appears to be significantly related to a combination of life stress, degree of transient anxiety, and cortisol levels. However, this relationship appears to be mediated by the utilization of healthy coping skills. Stress and anxiety appear to show promise as evidence based targets for emotional eating in obesity.

Sponsor: UNTHSC Faculty Seed Grant
IRB/IACUC#: 2010-006
Relationship between Hostility-Irritability and Measures of Glucose Metabolism

Purpose
Hostility as a personality trait has been implicated as having a potential role in diabetes through its relationship to glucose metabolism. Research to date has consistently found a relationship primarily for women between hostility characterized by cynicism and mistrust with fasting glucose. Whether this connection extends to other aspects of glucose metabolism, or to other subtypes of hostility has not been determined. The purpose of this study was to investigate the relationship of hostility characterized by irritability on broader measures of glucose regulation. It was hypothesized that higher levels of hostility-irritability would be associated with higher fasting glucose (FG), fasting insulin (FI) and homeostatic model assessment index (HOMA-IR).

Method
A secondary data analysis was conducted on data from a 1-year prospective study in a community bariatric surgical setting. Data used for the present analysis was from the pre-surgical assessment of 71 bariatric surgery candidates (OB) and 30 age- and gender-matched normal weight controls. Mean age was 44.6 years. Mean BMI was 43 kg/m2. Irritability was measured through self-report using the Buss Hostility Inventory. FG, FI, and postprandial glucose (PG) and insulin (PI) were analyzed at a commercial laboratory. Fasting HOMA-IR score was derived according to standard calculation. FG, FI, PG, PI, and HOMA-IR were divided into high and low categories based on a median split. Logistic regression analyses were used to evaluate the ability of Irritability and gender to predict FG, FI, PG, PI, and HOMA-IR. Pearson correlation was used to explore relationships among variable, including individual Irritability scale items.

Results
Results of logistic regression models were non-significant for all indicators of glucose regulation. There were several significant correlations among individual items of the Irritability scale with FI, PI, and HOMA-IR.

Conclusion
Irritability as a subtype of the broader personality trait of hostility was not associated with measures of glucose regulation examined in this study. However, several individual items of the scale were significantly correlated with insulin, suggesting that specific aspects of hostility may be more disruptive to glucose regulation than others and should be further explored.

Sponsor
NIH grants H75/CCH224064, HL04297 and HL64913

IRB/IACUC#
2007-053
Identification of a novel allosteric modulator of acid-sensing ion channel 3

Acid-sensing ion channels (ASICs) are sodium selective channels that belong to the ENaC/DEG family of ion channels. They are sensitive to changes in extracellular pH and are expressed in both the central and peripheral nervous system. There are multiple ASIC subtypes that are involved in different pathophysiological conditions, including neurodegeneration, and most recently, epilepsy. Crystal structure of chicken ASIC1 revealed that functional ASIC is a trimer with a large extracellular domain that can interact with variety of ligands, and the focus of research has been to identify ASIC antagonists. The ASIC3 channel subtype is primarily expressed in DRG neurons and is involved in pain sensation, but may activate GABAergic interneurons. ASIC3 is modulated by nonproton ligands like 2-guanidine-4-methylquinazoline (GMQ) and agmatine. We have identified a guanidine compound with a different molecule structure than GMQ that allosterically modulates ASIC3. Here we characterize this guanidine ligand using whole-cell patch clamp electrophysiology and ASIC3 transfected CHO-K1 cells. We found that the ligand is able to activate ASIC3 channel at physiological pH of 7.4, similar to GMQ. Furthermore, the guanidine ligand alters low pH current and delays desensitization, indicating that the ligand may be an ASIC3 positive allosteric modulator. The activation by the guanidine ligand was found to be concentration dependent. In the future, we will determine the effect of the guanidine ligand on the ASIC3 window current and identify potential binding sites within ASIC3.

Sponsor: American Heart Association 12BGIA8820001; UNT Health Science Center Doctoral Student Bridge Grant; UNTHSC IAADR Intramural Grant

IRB/IACUC#
2101  Poster  Classification:  TCOM DO Student
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**Adverse Outcomes from vaginal delivery during immersion in water versus traditional vaginal delivery**

**Hypothesis:**
There are no adverse events examining four years of hospital midwifery vaginal delivery during immersion in water versus traditional vaginal delivery.

At our institution, our Certified Nurse Midwife practice has been practicing vaginal deliveries via immersion in water since 2008. In light of the ACOG committee opinion 594, we conducted a matched-pair analysis to compare the frequency of adverse events during immersion in water vs traditional vaginal delivery.

**Materials and Methods:**
A retrospective chart review was conducted for deliveries occurring at a single urban hospital from 2010 – 2014. Deliveries were grouped into waterbirths and landbirths. Women who had a waterbirth were matched by parity and gestational age to women having a traditional vaginal delivery. Adverse outcomes assessed included lacerations, episiotomy, hemorrhage, APGAR score, shoulder dystocia, and NICU admission. Conditional logistic regression was used to estimate adjusted odds ratios (AOR) and 95% confidence intervals (95% CI).

**Results:**
Of the 149 matched pairs assessed, the median age was 28; 71% were Caucasian and 20% were Hispanic. Women were similar across delivery groups in age, race, chronic conditions, and number of previous preterm births. The odds of a laceration during waterbirth delivery were observed to be 90% lower when compared with landbirth (AOR = 0.10, 95% CI: 0.01 – 0.78). Likewise, a poor 1 minute APGAR

**Conclusion:**
This study suggests that there were fewer lacerations and higher 1-minute APGAR scores among waterbirth deliveries.

Sponsor  N/A
IRB/IACUC#  2014-096

2102  Poster  Classification:  SPH Student
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**Trauma-Informed Care for Refugee Populations**

**Background:** With the growing number of refugees resettled in the United States after fleeing war torn countries devastated by genocides, mass violence, and human rights abuses, it is increasingly likely that a healthcare provider will treat a patient who has experienced one or more traumatic events. When trauma is unaddressed, healthcare providers may unknowingly trigger re-traumatization, preventing refugees from seeking or receiving healthcare services. Refugee trauma survivors require a sensitive system of care. Western medicine is unfamiliar to many refugee groups, and some services, such as cervical cancer screening, may remind them of prior trauma. Trauma-informed care is an approach for assisting trauma survivors with evidence of benefit to vulnerable populations.

**Objectives:** Introduce the trauma-informed care framework and key principles, provide examples of traumas experienced by refugees, and demonstrate how previous trauma can influence preventive health care utilization among women enrolled in the Building Bridges program.

**Methods:** A literature review of trauma-informed care and trauma among refugees resettled in the United States was conducted. Additionally, qualitative data collected by Building Bridges Lay Health Educators as part of their education and navigation services was analyzed and grouped into themes.

**Results:**
Recurring themes of rape, torture and distrust towards healthcare providers was found in literature on refugee trauma. Similarly, Building Bridges data confirms rape and violence experienced by refugee women inhibit them from seeking preventive health services.

**Conclusions:** This calls for more attention to the mental health needs of resettled refugees. Refugees need a linguistically and culturally appropriate form of care incorporating the trauma-informed framework.

Sponsor  N/A
IRB/IACUC#  2014-084
Arteriovenous Malformations (AVM): A Rare Cause of Abnormal Uterine Bleeding

Background: Uterine arteriovenous malformations (AVM) are a very rare, but life-threatening cause of uterine bleeding. Difficulty recognizing the presentation likely leads to misdiagnosis and underreporting. CASE: A 20-year-old woman with a recent history of a spontaneous abortion presented to the ER for loss of consciousness and heavy vaginal bleeding. Doppler imaging reflected increased vascularity extending down to the endometrium. The patient underwent a unilateral uterine artery embolization. CONCLUSION: Uterine AVM should be considered in reproductive age women with a recent history of pregnancy that present with heavy vaginal bleeding. Doppler imaging is a useful screening tool. Angiography confirms the diagnosis, provides a method of definitive treatment, and should be used in patients when Doppler imaging cannot exclude the presence of an AVM.

Sponsor
IRB/IACUC#  2016-032
Does Weight Relate to Mental Health Status in Females Ages 35-54?

Purpose: The purpose of this study was to assess the relationship between mental health and weight status for women during the transitional years from young adulthood to middle age.

Methods: This cross-sectional analysis used data from the 2013 BRFSS for women ages 35-45 from the states of Mississippi, Oklahoma, Oregon, Utah, and West Virginia. Multiple linear regression analysis was used to determine whether weight status was related to mental health after controlling for psychosocial and demographic variables.

Results: Participants reported relatively high numbers of days of good mental health in the past 30 days and relatively moderate levels of BMI. Mental health was not significantly related to weight status after controlling for psychosocial and demographic variables; however mental health was inversely related to the number of chronic health problems and positively related to working for wages and higher incomes.

Conclusions: Mental health and weight status were not significantly related after controlling for demographic and psychosocial variables in the target population. These results imply weight status may not be as important as other factors for women 35-45 and, thus, healthcare providers should not disregard weight, but place more emphasis on treating comorbidities with mental health.

Crucial Barriers to Health Center Deliveries in Rural Western Kenya: Accessibility, Knowledge, or Values?

Crucial Barriers to Health Center Deliveries in Rural Western Kenya: Accessibility, Knowledge, or Values?

I. Purpose
Maternal health services play a vital role in optimizing pregnancy outcomes for high-risk women in developing countries. Despite increased services, Kenya in particular has made insufficient progress to reducing their maternal mortality and attaining Millennium Development Goal 5. In order to understand why few women utilize available services, this study identified and categorized the major determinants of health center deliveries into accessibility versus knowledge and values.

II. Methods
Extensive interviews were conducted on the Nyakach Plateau in rural western Kenya with 90 native Luo women (43 pregnant and 47 previously pregnant). Subjects were asked about accessibility barriers, pregnancy knowledge, their values concerning a health center delivery, as well as their intended versus actual delivery location.

III. Results
In this cross-sectional study, 98% of the pregnant women intended to deliver at a health center but only 45% of previously pregnant mothers actually did so. Almost 100% of the sample valued health center deliveries, but 92% reported a transportation barrier followed by financial problems (76%) and a lack of services (64%). 82% walked for an average of 3 miles to their prenatal care appointments, however 55% were unable to complete the journey over rough terrain when in labor. With the sample living almost four times closer to a traditional birth attendant than to a health center, these women faced significant structural barriers that left 38% with serious problems resulting from pregnancy (including HIV/AIDS, chronic physical consequences, and death).

IV. Conclusions
These conclusions direct significant intervention efforts toward accessibility barriers, particularly transportation aid, to increase the number of health center deliveries. Knowledge and values, although important, are irrelevant if structural barriers prevent access to health services. With these conclusions, a community-based program called Mothers On the Move (MOM) was started to provide expectant mothers with transportation to nearby health centers. To date, over 600 women have experienced positive birth outcomes at Sigoti Health Center and Nyabondo Hospital as a result of accessible maternal health services.

Although specific to the Nyakach Plateau, these findings can be generalized to similar impoverished communities in the developing world.
Breast Health - Guidelines and Misconceptions

Objective: According to the Center for Disease Control (CDC, 2016), breast cancer is the second most common cancer among women. Due to the high incidence and prevalence of breast cancer, the CDC has proposed guidelines in place for self-assessment and early detection. It is crucial for women to understand risk factors and symptoms associated with breast cancer. Despite the widespread efforts in publishing these guidelines, the level of awareness regarding breast health among women is unclear. This study aimed to assess the level of breast health knowledge among women of Tarrant County, Texas, and to evaluate the effectiveness of a lay health breast educator training initiative.

Methods: The initiative conducted “train-the-trainer” educational events, where women in the community completed a lay breast health educator training session. Pre and post surveys to assess changes in breast health awareness were administered during the training. The next component was to evaluate the knowledge of the women who received a screening at any one of the nine different breast cancer screening locations throughout Tarrant County. The lay health educators’ role was not to only share information about breast health, but also to promote attendance at the screening day.

Results: A total of 134 women participated, 43 women completed pre and post survey at training and 91 women completed survey on the screening day. Over half of the participants were between the ages of 40-59, have had at least some college, and identified as either African American/Black or as Hispanic/Latina. A vast majority were aware of lump related symptoms of breast cancer. However, participants lacked awareness on other key symptoms.

Conclusion: This study indicated a general lack of knowledge regarding breast cancer awareness, and a need to promote non-lump related symptoms along with other risk factors of breast cancer. Lay breast health educators’ knowledge of breast cancer signs increased immediately following the one-hour long training session, suggesting that the knowledge learned is beneficial to their personal efficacy and ability to recognize breast cancer symptoms.

Sponsor: Greater Mount Tabor Christian Center
IRB/IACUC#: 2015-136

Refugee Women's Breastfeeding Practices and Experiences Following Resettlement in Tarrant County

Purpose: Exclusive breastfeeding for the first 6 months of life ensures that infants obtain adequate nutrients needed to support healthy growth and development. While there is robust literature on factors influencing breastfeeding initiation and duration among sub-populations of women, there is little known about the breastfeeding practices of refugee women resettled in the United States. The limited studies and anecdotal reports suggest, however, that breastfeeding practices change following resettlement. This qualitative study aims to explore refugee women’s infant feeding experiences and practices to better inform culturally appropriate education, support, and maternity care for women resettled in Tarrant County, Texas.

Methods: Refugee women between the ages of 18 and 50, who had given birth to at least one live infant were recruited into the study. Participants completed a demographic survey and participated in a focus group discussion about their breastfeeding practices and experiences. The demographic survey addressed participant age, ethnicity, time and experience breastfeeding, etc., and descriptive statistics were compiled to assess the characteristics/demographics of the study population. Bilingual research personnel conducted focus groups in their respective language using a semi-structured interview guide exploring infant feeding practices, experiences, sources of information, etc. The group discussions were audio-recorded, translated and transcribed. Systematic procedures of qualitative data analysis included intensive reading of the text and group discussion of full transcripts, followed by coding, displaying, reducing, and interpreting information.

Results: Refugee women representing different ethnic groups participated in the demographic surveys and focus groups.

Conclusions: Results of the focus groups suggest multiple influences on infant feeding practices of refugee women following resettlement in the United States. A culturally and linguistically multi-level approach to providing education and support services to refugee women is necessary to protect their breastfeeding practices. Findings from this study have implications for health providers, resettlement agencies, public health and others involved in serving this population.

Sponsor: Healthy Start, RF0081
IRB/IACUC#: 2016-002
Gender Differences in Obstructive Sleep Apnea Treatment: A Retrospective Analysis

Introduction: Obstructive Sleep Apnea (OSA) affects four times as many men as women in the United States. However, nearly 5 million women have documented OSA, and there are likely many more due to historically high rates of OSA under-diagnosis. As a result of this documented gender difference, OSA treatment providers may not be sensitive to accommodate female patients undergoing positive airway pressure (PAP) therapy, which is the gold standard for OSA treatment and is notoriously obtrusive and uncomfortable. We hypothesized in a retrospective analysis of OSA patient records that (1) PAP treatment is less effective in women vs. men and (2) that women have lower compliance rates to PAP treatment than men.

Methods: The University of North Texas Health Science Center Institutional Review Board approved this study. We studied the records of 619 patients (43% women, 57% men). Diagnosis of OSA was established by full night polysomnography (PSG) according to American Academy of Sleep Medicine (AASM) criteria. For this study, only patients prescribed for PAP machines that provide usage data, estimated apnea-hypopnea indices (AHIs), air leakage rates, recent detailed night-to-night data, and (if automated) mean and range of treatment pressures were considered. PAP data was downloaded from each patient’s machine during their office visit (see below) and was transferred into a database. Chi-square analysis assessed for gender differences in YFU vs. OFU treatment groups.

Results: In comparing men and women and effectiveness of PAP treatment, there was a greater reduction in respiratory events in men than in women (P=0.037). Men initially had a greater number of baseline events, (P=

Conclusions: The results indicate that PAP usage is substantially less in women compared to men, both in terms of 5 of sleep time and days/week, and women receive slightly less benefit from PAP use versus men. Furthermore, We contend that because women use PAP treatment less than men, they are more likely to receive inadequate treatment for their OSA.

Sponsor N/A
IRB/IACUC# 2014-094

Management of subcapsular hepatic hematoma in a post-partum female with pre-eclampsia with severe features

Background: Subcapsular hematoma is a rare complication in patients with pre-eclampsia. The presence of this complication can be life-threatening. As this is a rare complication, this case report is designed to discuss the conservative management chosen for this case.

Case: A 36 year old who was admitted for induction of labor for pre-gestational diabetes. She progressed to vaginal delivery complicated with some elevated blood pressures. She then developed pre-eclampsia with severe features with complications including: vision changes, hypotension and severe abdominal pain. Patient was found to have large subcapsular hematoma. She was managed conservatively without need for surgical intervention.

Conclusion: Subcapsular hematoma is a rare complication in patients with pre-eclampsia. Management can include surgical, expectant or embolization. Without evidence of liver rupture, expectant management can be a reasonable approach to treatment.

Sponsor n/a
IRB/IACUC# 2016-025 n/a