LSU Health New Orleans
School of Medicine

2013 MEDICAL STUDENT RESEARCH DAY

POSTER PRESENTATION ABSTRACT BOOK

MEDICAL EDUCATION BUILDING
1ST FLOOR LOBBY
1901 PERDIDO STREET

2013 Medical Student Research Day
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2013 Medical Student Research Day

This program was started to provide research opportunities for medical students. The program directors Dr. Paula Gregory & Dr. Fern Tsien match students with mentors in laboratories or clinics at LSU Health Sciences Center, Pennington Biomedical Research Center, or Children's Hospital of New Orleans. The 8-week summer research program allows students to cultivate their interest in pursuing research careers in either basic or clinical sciences. During the program students conduct their own small research project or work on part of an on-going research project.

Drs. Gregory and Tsien would like to extend their special appreciation to all mentors and poster session judges who helped make Medical Student Research Day a success! Their assistance with this project affords each student a chance to be part of a bigger, ongoing research project. The Directors would also like to thank supporters of this program: The School of Medicine at LSU Health Sciences Center, National Heart, Lung & Blood Institute, National Institute for Diabetes and Digestive and Kidney Diseases, National Institute on Alcohol Abuse and Alcoholism and American Heart Association

“The Effect of Sleeve Gastrectomy on Food Preference”

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Abstract

Obesity rates are currently rising in the United States, and one factor that contributes to this is the overconsumption of foods high in fat and sugar. It has been shown that after bariatric surgeries, obese individuals’ preference for calorically dense foods decreases, and their taste acuity and taste profiles also change. However, the effect of sleeve gastrectomy on food preference has not been examined in humans, because it is a relatively new bariatric surgery. Rodent models undergoing sleeve gastrectomy have been shown to decrease their preference for fat, and increase their preference for low caloric density foods. This pilot study is investigating the effect of sleeve gastrectomy on food preference. Our study uses a validated food preference questionnaire (Geiselman PJ et al. Physiol Behav. 1998;63(5):919-28) to study human participant’s food preferences before, and approximately 1 month after, the gastric sleeve procedure. Currently, data has been completed and analyzed on 9 participants, with an overall goal of 25 participants. Preliminary data suggests that sleeve gastrectomy decreases patient’s preference for foods high in fat when combined with simple and complex carbohydrates. The data also suggests a trend of decreased preference for foods high in fat combined with high sugar content. The study is scheduled to be completed in late Fall of 2013.

"Sodium Dysregulation: A Predictor of Mortality in Trauma Patient Who Undergo Massive Transfusion"

J. Bains, E. Bisgaard, P. Greiffenstein MD, Department of Surgery, LSU Health Sciences Center, New Orleans, LA 70112.

BACKGROUND

The association between sodium dysregulation and mortality has not been examined in trauma victims who undergo massive transfusion. As an essential component in the function of nerves and muscle, sodium is tightly regulated by multiple factors, many of which are severely impaired following major trauma and massive resuscitation. We sought to determine the correlation between abnormal serum sodium levels and the likelihood of mortality.

METHODS AND MATERIALS

A retrospective study of the trauma registry database was conducted examining patients who underwent massive transfusion for hemorrhagic shock. We identified 172 patients in the study period (2009-2011) and used the electronic medical record to examine sodium levels on arrival and during the initial 24 hour resuscitation period. Data was analyzed using student's t-test, chi-square analysis with Fisher's exact test (GraphPad Prism Software).

RESULTS

A total of 172 trauma patient who received massive transfusion from 01-02-2009 to 12-21-2011 were studied. Patients who presented with abnormal (Na > 145 mEq/L) initial serum sodium levels had a significantly higher mortality rate than those patients who presented with normal initial serum sodium levels (RR=2.1, 95% CI 1.05-4.21, P= 0.01). Furthermore, those patients with any episode of hypernatremia above 150 mEq/L during the initial 24 hour resuscitation period had an even higher likelihood of mortality (RR=2.53, 95% CI 1.55-4.11, P<0.0001). This was also true for those patients with any episode of hypernatremia above 150 mEq/L during the initial 12 hour resuscitation period (RR=2.5, 95% CI 1.53-4.22, P<0.0001). There was, however, no significant correlation between episodes of hypernatremia and mortality during the 24 hour resuscitation period.

CONCLUSIONS

The initial sodium serum levels of trauma patients who underwent massive transfusion are significant predictor of mortality. Patients who suffered from traumatic hemorrhage and had abnormal initial sodium levels were at least twice as likely to die compared to patients who presented with normal sodium levels. Due to the multifactorial nature of sodium regulation, however, further analysis is warranted prior to determining an actual clinical correlation.

Effect of prolonged Phosphodiesterase-5 Inhibition on Energy Metabolism in African American Women with Metabolic Syndrome. A pilot study.

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African American women have the highest prevalence of obesity in the US. Obesity results from an imbalance between caloric energy intake and energy expenditure. Resting Energy Expenditure (REE) accounts for about 60-80% of 24-hour energy expenditure, and it has been shown that on average, African American women have lower REE than other groups. Studies in an animal model of obesity showed that chronic treatment with a phosphodiesterase-5 (PDE-5) inhibitor, sildenafil citrate, increases energy expenditure and reduces weight gain. To test the hypothesis that chronic treatment with a PDE-5 inhibitor increases REE and activity level in humans, 46 obese African American women were randomized to 4-week treatment with either sildenafil citrate or placebo. REE and body composition were measured at the beginning and end of the study using indirect caloriometry and a Dual Energy X-Ray Absoprtiomety (DEXA) scan, respectively. Activity level was also assessed used an ActiGraph GT3X+ activity monitor worn on the wrist. Because the study is still ongoing, all data presented is still blinded. We found a direct relationship between Fat Free Mass (FFM) and REE such that increased FFM led to increased REE (n =28). Average REE both before (1697 Kcal/Day) and after (1695 Kcal/Day) treatment was approximately the same (n=28). We also analyzed subjects for activity level using minutes spent in low intensity activity, moderate intensity activity, and vigorous intensity activity as well as Physical Activity Counts/min of device wear time. There was a tendency for an increase in low intensity activity levels on weekdays after the intervention (n=19). Further analysis in the context of assigned study drug is required for any conclusions to be drawn.

“Prehospital Intraosseous Needle Use in Trauma: A potential tool for intoxicated patients”

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Exsanguination is a leading cause of early mortality in trauma victims, therefore vascular access is critical. Although developed nearly a century ago, intra-osseous (IO) needles have only recently begun to be used in civilian emergency medical response. The increasing use of these devices by pre-hospital EMS crews prompted a survey of these cases to measure safety and incidence of use among our trauma population. We conducted a retrospective review of our institutional trauma registry in order to identify those patients who presented with IO needles placed in the field. Electronic medical records were examined for pertinent clinical data and evidence of complications. We used student’s t-test for comparison of means and chi-square test for comparison of binomial data (GraphPad Prism software).We examined the records of 27,620 patients brought in by EMS as trauma activations from 2/1/2002 to 4/24/2013. In our trauma center, the incidence of use of prehospital IO needles in all trauma activations has increased from 0% in 2003 to 4.6% thus far in 2013 (**see Figure**). We identified a total of 491 patients as having IO needles placed prior to arrival during this period. Of the 340 (69%) patients who died in this group, there were 275 (56%) who died within the first 24 hrs. This is reflected in the significantly higher severity of injury as measured by Injury Severity Score (ISS), Glasgow Coma Score (GCS), and lower Probability of Survival in the IO group (See **Table**). There were no statistical differences in gender or age between the two groups, but there was significantly more penetrating trauma and burn injury in the IO group. We found no complications as a direct result of IO needle insertion. All needles were removed within 24 hours of arrival once an alternative IV access had been established as per protocol. Patients with pre-hospital IO’s undergoing mass transfusion did not receive more blood products in the first hour than those patients without IO’s.

Despite the lack of associated complications, IO needles are being primarily used in the severely injured as an access of last resort. Further investigation is warranted to better assess the efficacy of this increasingly popular mode of access. Patients under the influence of alcohol and drugs are often combative or uncooperative in the field complicating IV needle placement. This population is an ideal target for this alternative method of intravenous access after trauma due to the needles being easy to insert, difficult to remove, and the absence of associated complications.

“Fragility Fractures: Is LSU Using This “Teachable Moment” Effectively?”

Benjamin L. Bullock, C. Boustany, J. Witty, MD, S. Starr, MD, V. Dasa, MD, Department of Orthopaedic Surgery, Louisiana State University Health Sciences Center, New Orleans, LA, 70112.

ABSTRACT

Background: Osteoporosis related hip fractures can often be prevented or minimized with appropriate preventative care. However, few patients receive appropriate screening and treatment before and after a hip fracture. The purpose of this study was to identify patients treated for hip fracture within our institution’s private practice and to assess whether those patients had adequate osteoporosis management pre-fracture and post-fracture.

Methods: Charts of all patients with osteoporosis-related hip fractures treated by the faculty over a 4 year period were retrospectively reviewed. Patient age, gender, BMI, injury date, associated fracture, subsequent fractures, dual-energy x-ray absorptiometry (DXA), and pharmacologic treatments were identified. Risk factors and comorbidities as identified by the American Orthopaedic Association, and the National Osteoporosis Foundation were also recorded.

Results: A total of 95 patients that met inclusion criteria were identified for the study. The vast majority of patients had at least one risk factor for osteoporotic hip fracture (98%). Decreased patient mobility (50%) and a history of falls (39%), were the most common risk factors. The majority of patients did not receive a DXA scan at any time point (73.7%). After risk assessment, only 18.3% and 11.2% of patients received a DXA pre and post-fracture respectively. Despite having risk factors pre-fracture, a small percentage of patients received treatments including calcium (17%), vitamin D (16%), and both calcium and vitamin D in combination (13.8%). An even smaller number received the combination of calcium, vitamin D, and pharmacologic treatment such as a bisphosphonate (2.1%). These values did not substantially increase after the hip fracture (22.7%, 22.7%, 19.3%, 6.8%). Overall, only 8.6% and 6.7% of patients who met criteria received treatment. Using spearman correlations and chi square analysis, we were unable to identify any relationship between a patient’s risk profile and pre-fracture workup or treatment.

Conclusions: Patient workup and treatment before and after hip fracture is still not adequate. Despite multiple risk factors, the number of patients receiving DXA is still very low. The hip fracture event, which some authors consider a sentinel event, did not significantly increase the number of patients who received a DXA scan or pharmacologic treatment. Even with known risk factors in addition to the hip fracture, osteoporosis management did not improve post fracture.

Level of Evidence: Level IV, Case Series

“Corneal Nerve Regeneration After Lamellar Keratectomy: effect of 34 and 44 segments of PEDF +DHA”

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Common ophthalmologic surgical procedures used to correct stromal abnormalities in the cornea, such as Photorefractive Keratectomy (PRK) and Lasik, leave patients with temporary post-operative dry eye and loss of sensitivity due to afferent nerve ablation. Pigment epithelium-derived factor (PEDF) is an endogenous protein with both anti-angiogenic and neuroprotective functions [3]. In combination with DHA, PEDF is shown to induce the formation of neuroprotectin D1 (NPD1) in rabbit corneas [4]. Moreover, the combined treatment of PEDF plus DHA had an effect similar to NPD1 in stimulating nerve regeneration and thus corneal sensitivity [5]. Further investigation into the active domains of the PEDF protein have revealed both 34 and 44 amino acid segments. In addition to competing with PEDF for binding, the 44 residue fragment has been shown to have a neuroprotective role in human motor neurons [6]. While the exact mechanism of PEDF’s binding to its receptor is unclear, this data suggests that the 44 residue domain (positions 78-121) initiates the same signaling cascade as the complete 418-amino acid protein. Our research examined the combined effects that PEDF and DHA, as well as the 34 and 44 PEDF fragments, have on corneal nerve regeneration after lamellar keratectomy. Eighteen rabbits received a single incision into their right eye under general anesthesia, and treatments consisting of PEDF plus DHA, 34 mer PEDF plus DHA, and 44 mer PEDF plus DHA were applied. Both sensitivity and tear secretion have been measured for 3 weeks. Our preliminary studies show that those rabbits treated with PEDF plus DHA have increased tear secretion and sensitivity compared to vehicle treatments. Furthermore, the 34 mer PEDF-treated rabbits have noticeably less sensitivity and tear secretion compared to both the PEDF plus DHA and 44 mer PEDF plus DHA treatments—although slightly greater than vehicle-treated rabbits. We have also found that corneal epithelial cells express the PEDF-receptor that interacts with both PEDF and the 44 mer fragment.

“Synergy of Albuterol and Caffeine on Metabolic Rate: A Potential Combination Obesity Drug”

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Abstract:

Obesity is a growing epidemic in the United States, and the high cost of approved obesity drugs in the U.S. has stimulated the need to develop a safe and cost-effective alternative for the lower socioeconomic strata of society which obesity disproportionately afflicts. Caffeine 200 mg and ephedrine 20 mg given three times a day was a prescription combination obesity drug in Denmark that was effective and well-tolerated for more than a decade. In 2004, the FDA banned the sale of ephedra-containing supplements due to research citing substantial cardiovascular risks associated with its use, and the use of Ephedrine in pharmaceutical products is now tightly controlled due to its use as a starting product for the manufacture of illegal methamphetime. Albuterol, a selective beta-2 receptor agonist used as a bronchodilator to treat asthma, was chosen as a replacement for Ephedrine to determine if its combination with caffeine was synergistic in stimulating metabolic rate. A randomized, double-blind crossover study was conducted on 8 healthy males and females between the ages of 18 and 50 years old with a BMI between 19 and 40 kg/m^2 comparing caffeine 100 mg and 200 mg, albuterol 2 mg and 4 mg and their combinations to placebos. The combination of caffeine 100 mg with albuterol 4 mg increased metabolic rate to a greater degree than the sum of the individual increases seen with caffeine 100 mg and albuterol 4 mg. Since the combination of caffeine 100 mg and albuterol 4 mg appears to be synergistic in increasing metabolic rate, it may have great potential in causing weight loss in an affordable manner for the treatment of obesity.

“Improving Prediction and Usability of a Phase-Resetting Curve Simulator”

William T Coleman, William T, R. Tikidji-Hamburyan, C. Canavier, Anatomy and Cell Biology, New Orleans, Louisana State University, Health Sciences Center, Louisiana, 70112.

Simulating phase-resetting curves can be computationally costly and time consuming. A simulation can run for a long time before an event occurs that might render the entire operation useless. To improve the phase-resetting curve simulator, code for the prediction of possibly incorrect simulations, as well as other user friendly additions were added. This helped mitigate common obstacles to running productive simulations, such as crossing the causal limit and incompatible PRC data. Finally, technical directions for using and installing the simulator were written with hopes of attracting further adoption.

An Observational Study on Intra-Articular Knee Injection Preparations of Louisiana Orthopaedic Surgeons

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Background: Intra-articular corticosteroid injections (IACI) are a common treatment used by orthopaedic surgeons for the management of arthritic knee pain. Our survey's purpose was to observe if there were particular components of an IACI that were used more frequently than others since there is currently no standardization for an IACI.

Methods: The survey was administered to 272 orthopaedic surgeons in the state of Louisiana via SurveyMonkey. Data was received and analyzed using statistical methods.

Results: There was a 22% response rate (60 of 272 surveys). The most commonly used steroid was triamcinolone (56%). The most commonly used local anesthetic was lidocaine (57%). 27% percent of the respondents used the combination of triamcinolone and lidocaine in their preparation, making it the most common combination. 93% percent of responding surgeons used a 1.5 inch needle, and fifty three percent used a 22 gauge needle.

Conclusions: Our evidence supports that triamcinolone and lidocaine are the most prevalent steroid and anesthetic components, respectively, amongst surgeons in Louisiana. The combination of the two is the most commonly used combination amongst surgeons in Louisiana.

Significance: Although an IACI is a very common procedure, there is currently no standard for the specific components of the drug cocktail and little literature on the frequency of the use of these components in said cocktails. This study is unique because there no previous studies examine physician behavior or trends on such a common procedure, and there is a need for standardization based on evidence based medicine. Such standardization has the potential to improve quality of care and reduce spending.

"Recruiting African American Males into the Aerobic Plus Resistance Training and Insulin Sensitivity (ARTIIS) Study"

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African American men are particularly difficult to recruit into clinical trials. Recruitment data was obtained from a randomized, controlled exercise training study entitled Aerobic Plus Resistance Training and Insulin Sensitivity in African American Men (ARTIIS). Study eligibility criteria included men who 1) were 35-70 years old; 2) had a body mass index (BMI) >18 and <45; 3); had a family history of diabetes; 4) were not participating in regular exercise; 5) were not diabetic; and 6) did not have significant medical conditions. Participants were recruited using church, community event, email, friend, mail out, newspaper, other, and YMCA Personnel. Recruitment strategies were classified as (a) Printed Recruitment (e.g. mail-out, newspaper, and email), (b) Event Recruitment (e.g. Church and Community events), and (c) Person-to-Person Recruitment (e.g. hearing from YMCA Personnel and friend). The outcome variables include the number of individuals 1) completing pre-enrollment phone screening and 2) enrolled in the study. The target enrollment for the study is 104 men. As of July 8th 2013, there were 66 who reported how they were recruited. There were 12 recruited by Printed Recuitment,19 by Event Recruitment, and 29 by Person-to-Person Recruitment strategies proved to be the most successful strategy, recruiting 43.9 % (29/66) of all those who reported how they were recruited. The methods that are successful thus far in the study differ in comparison to other racial/ethnic recruitment methods conducted in other interventional studies. This possibly suggests that strategies that are successful in one region may not be as successful

“Leptin: An Obesity Biomarker in Pre-Menopausal vs. Post-Menopausal Women”

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Leptin is a protein hormone that induces satiety and regulates energy expenditure. It is secreted by adipose tissue and is transported to the hypothalamus where binds to its receptors. BMI is a strong predictor of serum leptin levels in both males and females; however, serum leptin levels are consistently higher in females as compared to males, regardless of BMI. Leptin is also involved in reproductive function in females and serum leptin levels have been shown to increase with the onset of menarche. Estrogen may stimulate leptin synthesis.

The objective of this retrospective data analysis was to test the hypothesis that post-menopausal females will have lower fasting serum leptin levels than pre-menopausal females, which would manifest through an inverse relationship between leptin and age. SPSS Statistics Software was used to analyze a sample of 3197 female participants ranging in age from 20 to 89, obtained from a pre-existing dataset, The NHANES III Household Adult Questionnaire Data File. Descriptive statistics were obtained and Pearson product moment correlation coefficients were estimated to determine the relationship between fasting serum leptin levels, age, and BMI. Next, the dataset was stratified by age groups and analyzed.

The descriptive statistics of the entire sample revealed mean age=46.1 years, mean BMI=26.6 kg/m^2, and mean leptin=17.9 ng/mL. This data was consistent with findings in the literature review. As expected, there was a positive correlation between leptin and BMI (r=0.673). There was no significant correlation between leptin and age (r=0.087). The average age of menopause in American females is 51. The mean leptin level of the 40-49 year old age group (n=525) was 19.6 ng/mL, while the mean leptin level of the 50-59 year old age group (n=391) was 19.1 ng/mL. From this study, it can be concluded that there was no significant change in leptin level as a direct result of change in age in our sample of females. Further research is needed to investigate the complex relationship between estrogen and leptin.

“Regulation of the tumor suppressor gene, *Nischarin*, in human breast epithelial cancer”

S.C Eastlack, Suresh Alahari, Ph.D. Department of Biochemistry, LSU Health Sciences Center, New Orleans, LA 70112

The appropriate regulation of tumor gene expression is essential for prevention of tumor initiation, growth, and metastasis in human breast cancer. One such gene, *Nischarin*, has recently been shown to play a role in preventing malignant cell behavior in cancer. This project attempts to elucidate the mechanism whereby expression of this gene is reduced in certain breast cancer cells. Previous evidence implicates epigenetic alteration of the gene promoter as a major factor in control of expression. Preliminary results of this investigation are currently indeterminate; however, some data do suggests this that hypothesis is accurate. Further analysis and refinement of experimental protocol are necessary before a conclusion can be made.

1220

1620 total

“Lysyl oxidase inhibition in the volume overloaded heart prevents adverse collagen remodeling, apoptosis, and cardiac dysfunction”

M.C. El Hajj, T.G. Voloshenyuk, PhD, M.A. Claudino, PhD, J.M. Bradley, J.D. Gardner, PhD, LSU Health Sciences Center, Department of Physiology, New Orleans, LA 70112.

Heart failure is the most prevalent and costly disease in the U.S. Our goal was to determine if the over-activation of lysyl oxidase (LOX), a collagen cross-linking enzyme, accelerates cardiac disease and failure. LOX is elevated in human failing hearts, but it is not known if LOX plays a causative role in disease. Using the aortocaval fistula (ACF) rat surgical model of volume overload, we assessed the role of LOX activity in progression of heart failure over 14 wks. LOX activity was inhibited by BAPN (100 mg/kg/d) at 2 wks post-surgery. Echocardiography was used to evaluate cardiac function and progression of LV remodeling. LOX expression and activity, collagen content, cross-linking, and typing were determined in LV homogenates. Fixed sections of mid-LV were assessed for apoptosis by TUNEL. ACF surgery caused significant ventricular dilatation (43% increase) and dysfunction (26% decreased, %FS). LOX protein expression was increased (65%) with concomitant increases in LOX activity. These increases in LOX were associated with significantly elevated collagen concentration, cross-linking, and type I/III. LOX inhibition prevented ACF-induced changes in LV collagen, and led to maintenance of systolic function. LOX inhibition also attenuated LV dilatation and prevented apoptosis, but did not reduce LV hypertrophy. These data indicate that LOX inhibition is cardioprotective in the volume overloaded heart.

“Electroretinogram Analysis in Awake Frogs”

Sharon Fellner, Robert Rosencrans, David Vumbaco, and Hamilton Farris
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Humans often combine visual and auditory information to communicate. However, disorders such as dyslexia complicate the ability to perceptually integrate such multi-modal information. This project measured the visual sensitivity of an animal model that also communicates by integrating multi-modal signals. The experimental method of the electroretinogram (ERG) was utilized in order to obtain a physiological measure of the response of the retina, including rod photoreceptors (a wave) and the bipolar and glial cells (b wave), which are found in the inner nuclear and plexiform retinal layers. Male green tree frogs, *Hyla cinerea*, were dark adapted for 14 hours and anesthetized for the collection of ERG measurements in a dark room. Intensity steps from $1.0*10^{-5}$ Cd/m^2 ($1.46*10^{-12}$) to 5000 Cd/m^2 ($7.32*10^{-4}$) were used for four 5ms flashes, with a 30s interstimulus delay period. Results from the averaged trial runs with 7 frogs were analyzed by linear regression using VLogI plots of the relative amplitudes of both the ERG a and b waves. Threshold for b wave responses (10% of maximum) determined by the Boltzman fit was $2.9 * 10^{-10}$ W/cm^2 (0.002 Cd/m^2). This threshold aligns closely with the behavioral threshold of males in a related frog species, *Engystomops pustulosus*, $7.3 *10^{-10}$ W/cm^2 (Cummings et al. 2008; Taylor et al. 2010). Saturation (90% response) occurred at an intensity of $7.3 * 10^{-4}$ W/cm^2 (5000 Cd/m^2), likely representing the intensity at which cone photoreceptors (in addition to rods) contributed to the response measured at the retina and masking the b wave. As expected, the retinal threshold is lower than its behavioral counterpart and suggests that visual signals may be used under the lowest natural ambient light conditions (Taylor et al. 2010; Jaeger 1981). Understanding the complex integration of visual and multimodal sensory signals before central integration in associated cortices is crucial for the targeting of pathologies of these communication pathways.

“Survivorship analysis for Adolescents and Young Adults (AYA) with cancer: A single Institution review”

Amanda M. Glinky, Dr. P. Prasad, MD, MPH and Dr. R. Gardner, MD, Department of Pediatrics, Division of Hematology/Oncology, Children’s Hospital, New Orleans, LA, 70118.

The adolescent and young adult (AYA) population presents a particular challenge to oncologic care. Among the AYA population, cancer is the leading cause of disease-related death. This group, defined as individuals 15-39 years of age, has their own unique set of biological and sociological issues that make their care particularly challenging. Various medical authors have suggested that AYA patients treated by pediatric oncologist have better survival rates than those treated by adult oncologists. The goal of this study was to examine ultimate patient outcomes from AYA patients between the ages of 14.5 and 21 diagnosed and treated at Children’s Hospital (CHNOLA) by the department of hematology and oncology between the years of 2002 and 2012 and compare those outcomes to the national 2010 Survival, Epidemiological and End Results (SEER) study. Over the course of the study other pertinent treatment data such as race, gender, insurance at diagnosis, treatment received, stem cell transplant information, diagnosis to treatment time and presentation to diagnosis time were collected. This data was collected in order to examine the effect of these factors on survivorship of patients at CHNOLA in order to improve future patient survivorship.

“Building a 3D model of the rhesus macaque frontal lobe for a study of depression”

Matthew G Hiller, E Richter, MD., T Weyand, PhD., Cell Biology and Anatomy, LSUHSC-NO, New Orleans, LA 70112.

Deep Brain Stimulation (DBS) is a therapeutic surgical intervention which utilizes high frequency stimulation to effectively inactivate a population of neurons. Clinical studies have shown DBS to be an adequate therapy for treatment-resistant depression. These same studies show that the subgenual cingulate gyrus, or Brodmann’s area 25, exhibits unusually high activity levels in those with depression and is correlated with decreased activity in the dorsolateral prefrontal cortex (DLPFC), orbitofrontal cortex (OFC), and mesial prefrontal cortex (MFC). These changes in prefrontal cortex activity which characterize a positive clinical response to DBS are the result of reciprocal connections within the frontal lobe which are currently not well understood.

Previous work in our lab has characterized abnormal behavior patterns in rhesus monkeys after pharmacological inactivation of the DLPFC and anterior cingulate cortex (ACC) with muscimol, a $GABA_A$ agonist. Clinical studies have shown that these areas have decreased blood flow and glucose metabolism in depressed patients. Being implicated in the pathophysiology of human depression and having obvious influences on normal behavior in macaques, we wish to investigate the connectivity between these and other frontal lobe areas to better understand the clinical response to DBS of the SCG in depressed humans.

We will surgically implant deep brain stimulators and recording electrodes in both hemispheres in order to measure evoked potentials and obtain EEG recordings of the SCG, DLPFC, OFC, and MFC in the rhesus macaque. Normally, the electrodes would be delivered through a stereotactic frame using only coordinates from a histological atlas, but we integrated these atlas coordinates into a software program used to plan DBS procedures in humans. Within this program we manually digitized MRI data in order to generate a 3D model of the scalp, skull, and cortex in each monkey. Coordinates from the histological atlas were compared to cortical structures on our 3D model in order to determine the final coordinates to be used in surgery. For example, on one occasion the atlas coordinates produced a target outside the grey matter of our particular monkey, but this wayward electrode was noticeable on the 3D map and easily corrected. We feel our methodology reduces the uncertainty in electrode placement in primate models of human disease.

“Comparing decreased unilateral knee flexion in a patient’s symptomatic knee with their asymptomatic contralateral knee: a predictor of intra-articular pathology and trigger for referral”

James R. Hollier, Dr. V. Dasa MD., Department of Orthopedics, LSU Healthcare Network, New Orleans, LA, 70112.

As the American population continues to age, the instances of joint pain will increase. The diagnosis of knee pain is a complicated task involving multiple clinical tests that requires extensive knowledge of the clinical maneuvers and disease processes. The current initial diagnostic process incorporates little quantitative measures and often leads to biased and often unnecessary referrals that keep orthopedic surgeons from logging demanded OR time. With the increasing orthopedic patient population growth surpassing the capacity of the future orthopedic surgeons, a simple and quantitative measure of joint pain must be incorporated into the primary care physician decision matrix to produce referrals more conducive to surgical intervention.

The goal of this study is to compare knee flexion in patient’s unilaterally affected knee to their asymptomatic contralateral knee and we hypothesized that a difference of 10 degrees of flexion between the affected knee and the healthy knee will correlate to clinically significant intra-articular pathology. Current research supports the idea that gait disturbance in an affected knee is linked directly with the severity of the knee injury. Using knee flexion data and comparing it to the affected knee diagnosis, KOOS, Womac, Oxford joint scores, Kellegren Lawrence X-Ray grade, and Ahlbeck X-Ray grade should form the basis of a reliable and quantitative measure of operable knee pain.

Our initial findings have shown that patients diagnosed with operable derangement of the medial or lateral meniscus averaged a 26 degree reduction in knee flexion, with 97% of those patients having a reduction of 10 degrees or greater, when comparing the symptomatic knee to the unaffected knee. Further analysis is necessary to determine the effects age, gender, arthritis, and insurance coverage would have on an individual’s range of motion at the knee joint in concurrence with the injury.

“Describing JIA in New Orleans”

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Juvenile idiopathic arthritis (JIA) is a rare autoimmune disease that causes inflammation and damage in the joints of children of all ages. To overcome small patient cohorts in research on rare conditions, 380 U.S. researchers are collaborating via the Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry, a NIH funded observational database focused on patients with rheumatic disease and their outcomes. This is a descriptive study of JIA patients enrolled in the CARRA registry at Children’s Hospital of New Orleans. Patients diagnosed before age 16 who met JIA criteria were recruited from the Rheumatology clinic. Baseline data recorded includes: demographic information; medical and family history; JIA classification; physician assessment; medication exposures; the Childhood Health Assessment Questionnaire (CHAQ) and the Health, quality of life, disease activity, and pain assessments. All information collected was de-identified and shared with the national CARRA registry. Fourteen JIA patients are included in this cohort; 3 male, 4 African-American and 10 Caucasian. Age range is 1 to 18 with an average age of 10 years. The average disease duration is 5 years. Four subtypes of JIA comprise the cohort: oligoarticular, pauciarticular, Rheumatoid factor (RF) negative polyarticular and systemic. The most common subtype of JIA is RF negative polyarticular JIA. Nine patients have been exposed to corticosteroids. Eight patients are treated with disease modifying antirheumatic drugs (DMARDs) and biologics. Of these patients, six were polyarticular subtype, one was oligoarticular subtype and one was systemic onset subtype JIA. Six patients with either oligoarticular or systemic arthritis are managed with systemic or intra-articular steroid injections alone. For this cohort, the average CHAQ is 0.77; the average disease activity score is 3.5; and the average pain score is 5. The average current functional class for this cohort is I, and worst ever functional class is II. The most common subtype in our cohort was RF negative polyarticular JIA, which differs from the most common reported subtype of oligoarticular JIA. In this cohort, 29% were African-American which suggests that African-American patients with JIA are proportional to the demographics of our population. Other studies have demonstrated that African-Americans are underrepresented in JIA. Disease subtype was associated with type of treatments used; over half required biologics or DMARDs to treat their JIA. The average CHAQ was 0.77 which corresponds with mild to moderate disability. This contrasts with an average functional class of I, which suggests that the majority of patients are able to function well in daily life. The worst functional class ever was II on average demonstrating that JIA can significantly affected the daily lives of these patients. The average disease activity score was 3.5 and the average pain score was 5, suggesting that JIA is difficult to control. While this is a small cohort, adding this information to the national CARRA database will allow rheumatologists to have more accurate information and thus, improve treatment and outcomes in patients with JIA.

“Pilot Study of the Effect of Purple Rice on Glucose Tolerance, Insulin Resistance and Inflammation”

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Abstract

The purpose of this study was to determine if eating two cups of cooked purple rice per day would improve blood glucose control, reduce the level of fats in the blood, and reduce blood markers of inflammation, when compared with two cups of brown rice. Purple rice was made by the LSU Ag Center and contains anthocyanin and resveratrol both of which have been shown to improve insulin sensitivity. The study consisted of 1 screening visit, and 8 study visits. Five subjects with fasting glucose between 100 and 200mg/dL were asked to eat 1 cup of brown or purple rice at lunch and dinner for 4 weeks, followed by 4 weeks on the other rice. An oral glucose tolerance test, chemistry-15 panel and highly sensitive C-reactive protein (HsCRP) were performed at the end of each four-week feeding period. This is an interim analysis and 4 more subjects will be randomized before the final analysis. Results show that brown rice reduced both glucose and insulin in the five study participants compared to purple rice. Since both insulin and glucose improved, brown rice non-significantly decreased insulin resistance. However, significance is likely to be seen with the additional 4 subjects. This surprising result may be due to the heat sensitivity of anthocyanin, which could have been destroyed in the cooking process. Resveratrol is heat stable, but at lower amounts than are needed to affect insulin sensitivity alone. This would explain why the purple rice had less effect on improving insulin resistance in the study subjects. hsCRP was not significantly different between the two groups. Chemistry panels did not show a statistically significant change in the brown and purple rice conditions and the values remained in the normal range suggesting no safety issues.

“Effect of colon transection on spontaneous high-amplitude-propagating contractions in children”

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Abstract:

Background and Aim: After Hirschsprung’s disease (HD) surgery, a majority of children suffer fecal incontinence caused by increased high amplitude propagating contractions (HAPCs) through the neorectum. The aim of this study was to determine whether children with HD have more HAPCs than children with colon transections for reasons other than HD.

Method: We reviewed 500 colon manometries. Children (7.6±5.1 yrs; 275 male) with functional constipation (n=237; 7.4±5.0yrs; 126 male) and chronic abdominal pain (n=48; 9.8±5.8yrs; 25 male) served as controls compared to subjects with HD (n=56; 6.9±4.1yrs; 44 male) and colon transection for other reasons (n=24; 6.1±5.8yrs; 12 male). We excluded 139 subjects without HAPCs. We documented HAPCs during 1 h fasting and 1 h postprandial. Results are mean ± SD.

Results: During fasting, HD subjects had more HAPCs (2.2±3.4/h) vs. functional constipation (0.8±2.2/h, p=0.0004) and chronic pain (0.5±1.1/h, p=0.001), but not more than colon transection (1.9±3.2/h, p=1.0). HD showed more postprandial HAPCs (4.0±5.4/h) than functional constipation (1.5±2.5/h, p<0.0001) and chronic pain (0.9±1.6/h, p<0.0001), but not more than colon transection (2.4±3.0/h, p=0.6). There were more HAPCs fasting and post-prandial after colon transection (1.9 ± 3.2/h and 2.4±3.0/h) than functional constipation (0.8±2.2/h, p=0.3 and 1.5±2.5/h, p=1.0) and chronic pain (0.5±1.1/h, p=1.0 and 0.9±1.6, p=1.0). HD subjects were divided by chief complaint: fecal incontinence or constipation. HD subjects with incontinence (n=24) had more HAPCs fasting (p=0.01) and post-prandial (p=0.01) than HD subjects with constipation (n=32).

Conclusions: Increased HAPCs followed colon transection, regardless of cause. HD subjects with incontinence had more HAPCs than subjects with colon transection for other reasons.

“A conditional model to investigate the molecular mechanism of FUS-related ALS pathogenesis”

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Amyotrophic Lateral Sclerosis is a neurodegenerative disease of motor neurons fatal to humans. About 80-90% of these patients suffer from sporadic forms of ALS while 10 to 20% exhibit familial forms. Many genes, including SOD 1, TDP-43, FUS (fused in sarcoma), Ubiquillin 2, and C9ORF72, have been linked with both forms of ALS. Both TDP-43 and FUS are found to incorporate in the cytoplasm of model cells in culture and ALS patient tissues, but despite this observation the specific mechanism of ALS pathogenesis remains unclear. The toxicity of the mutations has prevented the creation of stable neuronal cell models constitutively expressing these proteins, blocking further study of the causes of ALS.

To circumvent this barrier, our group sought to create a conditional model for ALS in which mammalian neuronal cells would only express WT or mutant versions of FUS when treated with the antibiotic doxycycline. We utilized plasmids containing ALS-causing mutations in FUS, R521C and P525L, as well as wild type FUS and made inserted each into N2A cells to create stable cell lines. A sequence encoding the FLAG polypeptide protein tag was also added to each of the plasmids to distinguish endogenous FUS expression and ectopically expressed protein. These mutants were found to be stable; showing no trace of expression of our ectopically expressed mutant protein without doxycyline treatment. We found that 24-48 hours after doxycycline treatment the WT, R521C, and P525L transfected neuronal cells exhibited robust expression of our protein of interest. Through this model of ALS pathogenesis we hope to characterize the subcellular localization of FUS/mutated-FUS to better understand its cytotoxic effects. Our long-term goal is to create a reliable conditional model of ALS pathogenesis that can be used to test small molecule drugs to treat ALS, for genetic screens to modulate toxicity, or examining potentially therapeutic siRNA treatments.

“Wound Healing Using Nanoparticle Based miRNA Delivery Systems for Light Directed Differentiation of Human Mesenchymal Stem Cells”

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Abstract: Modulation of gene expression with microRNA (miRNA) is a promising technique for improving control of wound healing and tissue repair processes, particularly in directing osteogenic and angiogenic differentiation. Attachment of miRNA to a photo-cleavable molecule and pairing with appropriate photo-oxidizer allows for easy delivery of RNA. The miRNA complex and photo-oxidizer are bound to silver or gold nanoparticles, forming the Light Activated miRNA Drug Delivery system (LAMD). This system, created by Daniel Hayes’ Lab, has proven effective in stimulating osteogenic differentiation both *in vitro* and *in vivo* using ultraviolet light (365 nm). Due to the tissue-damaging and stigmatic nature of UV rays, we have developed an additional, red-shifted activation strategy for miRNA delivery using photo-oxidizing compounds with narrow excitation spectra in the near-infrared range (690nm). This system is termed ‘visible LAMD’ or vLAMD.

Several scaffolding materials were tested and ultimately a biodegradable polycaprolactone (PCL) scaffold was chosen, inoculated with progenitor cells, and transfected with LAMD and vLAMD. The scaffold/LAMD complex was then implanted into non-healing, critical sized (4mm) calvarial defects in the parietal bone of adult male CD-1 nude mice and photo-activated with the appropriate light source. Animals were euthanized at four and twelve weeks post-surgery to undergo histological and microCT evaluation for bone formation of the defect site. Preliminary microCT evaluation of the 4- and 12-week mice using the LAMD system demonstrate greater than 20% closure of calvarial defects, compared to only 5% healing using scaffolds only. In the future, testing will be conducted for longer intervals and testing of the vLAMD is beginning at this time. In addition, other scaffold materials will be tested and implemented based on performance.

The impact of this study is significant and we believe the results will have several benefits. Firstly, the study will help further the study of adipose-derived stem cells and bring this practice to the forefront of medical advancement. In addition, the LAMD/vLAMD system can be designed for use in the surgical setting for implantation in several types of critical and non-critical bone defects *in vivo* and perhaps lead the way for implementing this system for superficial wound healing and scar tissue reduction. Finally, further studies conducted by the Hayes Lab use a similar system to LAMD for studying angiogenesis and neurogenesis.

“The Role of Osteoblasts in Digit Regeneration in Mice”

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It has been documented that mammals are capable of mounting level specific regenerative response in certain areas like distal fingertips. Upon amputation of the distal third of the terminal phalanx, mice and humans can regrow a structure that mimics the lost digit tip, whereas amputation of the distal two thirds of the terminal phalanx will fail to regenerate. Regeneration of the digit occurs in a stepwise fashion, starting with a local inflammation response, followed by prominent osteoclasts activity which degrades the bone proximally to open the bone marrow content. These events subsequently give rise to a structure called blastema, which is comprised of dedifferentiated, stem cell like cells that are capable of redifferentiation into a structure that mimics the lost digit tip. Therefore, blastema plays the key role in regeneration and has been extensively studied among developmental biologists. The source of the cells that make up blastema is still unclear, especially in mammals. In this study, we hypothesize that osteoblasts located in the endosteum and periosteum of the phalangeal bone are one of the sources for formation of blastema in digit regeneration. By tracking endosteal osteoblasts of the marrow of the distal phalanx we observed that they contribute specifically to the proximal part of the regenerate. We also observed that surgical removal of periosteum results in significant reduction of bone volume in regenerate, more specifically in the distal segment of the regenerate. These results suggest that cells both on the periosteum and endosteum participate in the regeneration of digit tip in a spatial manner.

“Effect of γ-MSH on Skin Electrolyte Homeostasis”

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The skin interstitium responds to a high salt diet by sequestering excess Na^+, K^+ and Cl^- creating a hypertonic reservoir to store the excess salt. γ -MSH is a natriuretic melanocortin which regulates blood pressure and sodium metabolism by binding to the melanocortin 3 receptor (MC3R). The $MC3R^{-/-}$ mice are hypertensive on a high salt diet. This study tests the hypothesis that $MC3R^{-/-}$ mice are not able to respond to increased circulating levels of γ-MSH, leading to an increase in sodium accumulation in the skin.

Electrolyte contents in the skin, carcass, and total body were determined through a combination of dry ashing, atomic absorption spectroscopy, and $AgNO_3$ titration. $MC3R^{-/-}$ mice had markedly decreased electrolyte content in skin, carcass, and total body indicating that γ-MSH’s effect on electrolyte storage was not specific to the skin. The relationship between water content and electrolyte levels in skin were linear indicating that γ -MSH does not affect the concentration of electrolytes within the skin. Hypertension in these mice is not related to sodium retention.

“Effect of Oxidative Stress (OS) and Neuroprotectin D1 (NPD1) on RPE Amyloid-β (Aβ) Expression”

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Age-related macular degeneration (AMD) is the most common cause of vision loss in the elderly. One of the hallmarks of AMD is the buildup of yellow deposits called drusen between the RPE and Bruch’s membrane in the retina. Drusen is composed of a wide variety of substances, including Aβ. Aβ is derived from amyloid precursor protein (APP) through a series of enzymatic reactions involving β-secretase and γ-secretase. Aβ has several isoforms, the main ones being Aβ1-40 and Aβ1-42.

RPE cells are particularly susceptible to OS, as the retina has a high rate of oxygen consumption. Recent studies have shown that that OS plays a role in Aβ formation. OS has been shown to increase the activity of the β-secretase, β-site APP cleaving enzyme (BACE-1), in rat retinas, suggesting that OS will increase Aβ levels. On the other hand, NPD1, a lipid derived from DHA, has been shown to influence the processing of APP such that less Aβ1-42 is produced.

In this project, using Western blots and dot blots, I investigated the effect of OS and NPD1 on ARPE-19 cell expression of secreted Aβ and cellular APP. With regards to the secreted Aβ, we hypothesized that OS will increase Aβ1-42 expression and that addition of NPD1 will decrease Aβ1-42 secretion. In other words, OS will shift ARPE-19 APP cleavage to a more toxic state, and NPD1 will attenuate this effect. We also hypothesized that OS will decrease whole APP levels, and addition of NPD1 will return levels back to normal. Currently, our results show that at 2 hours, treatment with H_2O_2 and TNF-α causes an increase in Aβ1-42 levels and the addition of NPD1 decreases Aβ1-42 levels back to control levels, supporting our hypothesis.

“There's no predicting! Natural History of Irritable Bowel Syndrome in Children.”

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Irritable bowel syndrome (IBS) is the most common diagnosis applied to new patients in pediatric gastroenterology clinic, but there have been few prospective studies of IBS outcomes in children. The purpose of this study was to prospectively gather information concerning symptoms, treatment, and school absence in a cohort of children with IBS.

We enrolled 144 subjects (97 female) aged 4-17 years. All met symptom based Rome criteria for IBS on the QPGIS questionnaire. We found subtypes: constipation predominant-IBS (c-IBS) in 43, diarrhea-predominant IBS (d-IBS) in 60, alternating IBS (a-IBS) in 31, and no subtype in 10. BMI was >85% in 36%. We found dyspepsia, defined by frequent upper abdominal discomfort, in 71 IBS subjects. Pain exacerbations lasting hours to days resulted in an abdominal migraine diagnosis in 39 subjects. At the initial visit 64% had missed school within the past month because of abdominal pain. Physicians prescribed medicine in 90%, cognitive behavioral therapy in 18%, and no treatment in 9%. The most frequently prescribed medicines were laxatives in 42% and gastric acid suppressants in 27% of the sample. Other medicines included anticholinergics, antidepressants, prokinetics, appetite stimulants, peppermint oil, fiber, and probiotics.

Follow-up visits varied in number and chronology, from one to 9 visits, based on clinical status. Five subjects (3%) withdrew because their diagnosis changed: 2 Crohn’s disease, 2 celiac disease. Forty-four subjects were lost to follow –up. One year after the initial visit, we interviewed 95 subjects. Twenty-one subjects (22%) were asymptomatic, 37 (39%) were improved, 26 (27%) were unchanged, and 6 (6%) were worse. (No response from 5.). Age, sex (regardless of the onset of puberty), IBS subtype, BMI, and co-morbid functional disorders did not predict outcome.

We conclude that there was no consensus treatment for IBS. The relatively common use of acid inhibitors may reflect attempts to treat co-morbid dyspepsia, or treat IBS with a safe placebo. A majority of IBS children attending GI clinic miss school because of symptoms. The natural history of IBS is uncertain, and it is unclear whether treatment alters outcome. The absence of consensus about drug treatment casts doubt on drug efficacy.

“Treatment of anal canal squamous cell cancer in a safety net hospital: factors influencing diagnostic delay and stage at presentation.”

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Anal canal squamous cell carcinoma (ACSCC), while rare in the general population, is more common in men who have sex with men (MSM), HIV positive individuals, women with cervical neoplasia and in patients with HPV infection. The City of New Orleans has the third highest prevalence of adults with HIV in the USA. The correlation between diagnostic delay, insurance status and stage of disease in ACSCC has not been previously investigated. The aim of our study was to examine diagnostic delay and its correlation with insurance status and stage of disease in ACSCC patients treated at Louisiana State University Interim Public Hospital (LSUIH), an academic safety net hospital that provides care for the uninsured. To assess diagnostic delay in the LSUIH hospital, the medical records of patients with an ICD 9 diagnosis of invasive ACSCC were analyzed for demographic data, insurance status, diagnostic interval, stage of disease, and treatment modality. There were 27 patients (16 males and 11 females; mean age 51 years;) with invasive ACSCC of whom 13 (48%) were African American, 13 (48%) Caucasians and one (4%) Hispanic. Eleven (41%) patients were HIV positive (9 MSM) and another 4 (15%) patients had history of HPV related disease and/or cervical neoplasia. Seven (26%) patients were uninsured, 7 (26%) had Medicare, 7 (26%) had private insurance and 6 (22%) had Medicaid. There were 10 patients (37%) with localized disease (stage I-II) and 18 (63%) with advanced disease (15 stage III and 3 stage IV). Mean interval between onset of symptoms and diagnosis was 51 weeks (±59 SD). Mean patient delay was 36 weeks (±53SD) whereas mean health system delay was 15 weeks (±22SD). There was no correlation between demographics, ethnicity, HIV status, insurance status, diagnostic delay and stage of disease at presentation. Diagnostic interval was longer in HIV positive patients (mean 87 weeks ±76) compared to HIV negative patients (mean 26.5 weeks ±27SD; p=0.008). This was due to a longer health system delay in HIV positive (29 weeks ±28SD) compared to HIV negative patients (6 weeks ±11SD; p=0.005). Of the African Americans 10/13 (77%) presented with stage III-IV disease compared to 8/14 (57%) of non-African American and diagnostic interval was longer in African Americans (mean 64 weeks ± 76 SD) compared to non-African American (mean 39 weeks ± 38 SD). However, these differences were not statistically significant.

Our study identified a significant delay in diagnosis mainly due to delay in seeking medical consultation. HIV status was significantly correlated with longer health system delays. The reason for this delay needs to be further investigated. African Americans presented with later stage disease and longer intervals for diagnostic evaluation.

These findings suggest the need to raise disease awareness especially among minority ethnic groups. Moreover, system changes need to be implemented in order to decrease diagnostic delays in HIV positive patients.

“Feasibility and Reproducibility of noninvasive arterial Intima-Media Thickness analysis at different vascular sites”

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Background. An abnormal Intima-Media Thickness (IMT) is the earliest non-invasively detectable structural change in the pathogenesis of Atherosclerosis (AS). Analysis of the carotid IMT (cIMT) has become an established risk marker for cardio-vascular disease in adults. It is not well established in young patients, partially due to inconsistent results. Autopsy studies revealed that vascular changes first occur in the abdominal aorta, and even in children. An IMT protocol that includes multiple vascular sites – including the abdominal aorta – may be more robust and sensitive than conventional cIMT only protocols.

Objective. To investigate in a healthy young population the feasibility and reproducibility of a modified multi-vessel IMT protocol.

Methods. After 6hour fasting, diameter and IMT were assessed twice within 6 weeks in 10 subjects (29.5±9.6) for the carotid artery (cIMT), the brachial artery (bIMT), the femoral artery (fIMT), and the abdominal aorta (aIMT). Two experienced vascular sonographers performed all scans. Measurements were obtained in diastole and averaged from 5 consecutive cycles. Semi-automated software was used for IMT analysis. The measurements were independently analyzed by two experienced readers.

Results. IMT could be acquired and analyzed in all subjects at all sites. The mean cIMT was 0.42±0.09 mm, the mean bIMT was 0.28±0.03 mm, the mean fIMT was 0.45±0.09 mm, and the mean aIMT was 0.67±0.16 mm. cIMT indexed to vessel diameter (cIMTi) was 0.075±0.020, bIMTi was 0.080±0.015, fIMTi was 0.067±0.016, and aIMTi was 0.068±0.032. The between observer intra-class correlation (ICC) coefficients were 0.95 (95% CI, 0.88-0.98) for cIMT, 0.68 (95% CI, 0.37-0.85) for bIMT, 0.62 (95% CI, 0.27-0.82) for fIMT, and 0.76 (95% CI, 0.50-0.89) for aIMT, respectively. The between study ICC coefficients were 0.85 (95% CI, 0.55-0.96) for cIMT, 0.38 (95% CI, 0.23-0.78) for bIMT, 0.23 (95% CI, 0.38-0.70) for fIMT, and 0.56 (95% CI, 0.04-0.85) for aIMT, respectively.

Conclusion. IMT analysis is feasible at all four vascular sites. Overall reproducibility is reasonable. It is best rod the carotid artery and the abdominal aorta. It may be worthwhile including the latter in future IMT protocols.

"Use of Chest Computed Tomography as a Predictor of Diastolic Dysfunction and Pulmonary Hypertension"

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Background: An increasingly common problem amongst older and overweight individuals is heart failure with left ventricular diastolic dysfunction, an abnormal relaxation of the left ventricle often associated with a history of diabetes, essential hypertension and cardiac ischemia. Diastolic dysfunction frequently results in heart failure with preserved ejection fraction, as well as an associated complication of pulmonary hypertension. Both of these conditions remain vastly underdiagnosed. Therefore, a common method for earlier detection of these disorders would be beneficial in the management and treatment of these patients. Here we have conducted a case control, retrospective chart review of individuals who have undergone both chest computed tomography angiography (CTA) and echocardiography (Echo) within 48 hours. We hypothesize that (1) there will be a correlation between left atrial size obtained on CTA and Echo, (2) main pulmonary artery (PA) size will be larger in those with elevated PA pressures, and (3) left atrial size on CTA will be larger in those with diastolic dysfunction.

Methods: Fifty-one consecutive patients who underwent both CTA and Echo within 48 hours were selected for this study. Left atrial (LA) size was determined on CTA using the maximum anterior-posterior diameter of the midline in its middle 50%. Pulmonary artery sizes were measured using the widest diameter perpendicular to the long axis at the level of pulmonary artery bifurcation. CTA measurements for left atrial and pulmonary artery sizes were compared and correlated against sizes and pressures gleaned from echo reports. Correlations between LA size on CTA and echocardiogram were measured using linear regression with Pearson correlation coefficient; CTA-determined pulmonary artery size was compared to Echo pulmonary artery pressures using paired, two-tailed t-tests. CTA left atrial sizes were compared in patients with normal or abnormal diastolic function using paired, two-tailed t-tests.

Results: There was a strong correlation between left atrial sizes ascertained on CTA and Echo ($r=0.6921$, $r^2=0.470$, $p<0.0001$, $n=47$). The main PA size measured on CTA in patients with abnormal echo pulmonary artery pressures (> 35 mmHg) was 3.20±0.34 cm, and was significantly different when compared to patients with normal PA pressures (≤35 mmHg), 2.69±0.46 cm ($p=0.01$, $n=26$). There was no significant difference in left atrial sizes on CTA between patients with diastolic dysfunction on echo, 3.71±1.05 cm, and those with normal diastolic function, 3.67±0.69 cm ($p=0.89$, $n=34$).

Conclusions: There is a strong correlation between left atrial sizes obtained on CTA and Echo. CTA also serves as a reliable predictor of abnormal pulmonary artery pressures based on determinations of main pulmonary artery size. There was no significant difference in CTA left atrial sizes between patients with normal diastolic function and those with abnormal diastolic function. This may be due to the method of collection used for diagnosis of diastolic dysfunction. Further investigation with quantifiable measures of diastolic function in a larger patient cohort is needed to further elucidate the use of CTA as a prognosticator of diastolic dysfunction.

“Combined, pioglitazone, a PPARγ agonist, and azilsartan, an ARB, have more effect on the regression of glomerulosclerosis through both the PPARγ and AT receptor pathway.”

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Chronic kidney disease (CKD) is characterized by glomerulosclerosis. PPARγ agonists and ARBs activate two different signaling pathways, PPARγ, a transcription factor, and AT_1R/AT_2R. Previous experiments have shown that both classes of drugs slow down the progression of glomerulosclerosis. To test the hypothesis that pioglitazone, a PPARγ agonist, and azilsartan, an ARB, in combination could have a greater benefit to decrease the progression of glomerulosclerosis, we tested this combination in the 5/6 nephrectomy (Nx) model of CKD. We started treatment 8 weeks after 5/6 Nx. We assessed body weight, glucose level, blood pressure, proteinuria, and creatinine clearance at weeks 0,8, and 12 and glomerulosclerosis index, plasminogen activator inhibitor-1 (PAI-1) expression level, podocyte count (WT-1), macrophage count (ED-1), collagen accumulation, AT_1 and AT_2 receptor expression, and PPARγ activity in both biopsy (week 8) and autopsy (week 12) adult male Sprague Dawley rat tissue samples. Four treatment groups, randomized with equal starting sclerosis, were determined as follows: Vehicle – untreated rats (n=7), TAK-497 – Azilsartan, 3mg/kg in DW (n=6), Pio – Pioglitazone, 2.5mg/kg in DW (n=7), and TAK/Pio – Azilsartan and Pioglitazone (n=7). At autopsy, the combined treatment group (TAK/Pio) had the lowest blood pressure and glomerulosclerosis level which links to lower PAI-1 and AT_1 expression. Podocyte density was the highest in the combination therapy group (TAK/Pio) indicating the highest levels of renoprotection. PPARγ activity was also in the combination therapy group (TAK/Pio). Thus, PPARγ agonists and ARBs have more of an effect on the regression of glomerulosclerosis when used in combination than when used individually. Our data supports that these effects are mediated by increased PPARγ activity and decreased AT receptor pathway.

"Utilization of serum hyaluronic acid as a predictive tool for HIV-associated co-morbidities in New Orleans"

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Objective: Recent data indicate that HIV-infected patients, including those co-infected with the Hepatitis C virus (HCV), exhibit elevated circulating levels of hyaluronic acid (HA) relative to HIV-negative patients. Our laboratory group has also published data indicating a role for oncogenic herpesviruses in regulating HA secretion and HA-associated signal transduction, and HA may be associated with other illnesses seen more commonly in the setting of HIV infection. However, additional studies in more diverse populations are needed to identify correlations between circulating HA levels and co-morbidities in HIV-positive patients in order to inform future mechanistic studies. Therefore, we sought to identify correlations between plasma HA levels and co-morbidities for HIV-positive patients from the LSUHSC HIV Outpatient (HOP) Clinic.

Methods: Echelon's Enzyme-Linked Immunosorbent Assay has been validated for size-sensitive HA measurements within clinical samples. This assay, in conjunction with spectrophotometry measurements conducted in the LCRC, was used to quantify HA within plasma collected from 228 HIV-positive volunteers receiving care at the HOP Clinic. Each sample was analyzed in duplicate, and wells lacking adherent HA were used for negative controls. Paired clinical data were collected through chart review, patient interviews, and laboratory analyses, including co-morbid conditions, infection status for opportunistic viruses (KSHV, HCV, HBV), $CD4^+$ T cell count, and HIV viral load. Statistical analyses were performed with assistance from the Biostatistics Core at the LCRC.

Results: HIV/HCV co-infected patients exhibited significantly higher plasma HA levels relative to HIV-infected patients ($p = 0.0005$). Less significant trends were also noted, including higher HA levels in non-Hispanic white patients relative to non-Hispanic black patients ($p = 0.0247$), and higher HA levels in non-Hispanic white patients with self-reported cardiovascular disease (CVD) relative to white patients without CVD ($p = 0.0152$). Non-significant trends included elevated plasma HA levels for males vs. females and diabetics vs. non-diabetics. No significant associations were noted for HA levels and HIV viral load, CD4 count, KSHV or HBV infection status, use of specific antiretroviral medications, smoking, or self-reported alcohol or drug use.

Conclusion: Our cross-sectional data thus far support a strong association between plasma HA levels and HIV/HCV co-infection, and future analyses will confirm whether plasma HA levels predict severity of liver disease associated with co-infection. Our observation of significantly elevated plasma HA levels for non-Hispanic white participants with self-reported CVD also requires additional confirmation using objective criteria. In summary, our data justify additional analyses to understand the potential utility of plasma HA levels as indicators for liver and/or CVD in high-risk HIV-infected populations in New Orleans.

“Changes with age in rates and types of comorbid symptoms in Autism Spectrum Disorders”

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To date, no comprehensive evaluation has been reported on the full spectrum of comorbid symptomology in individuals with Autism Spectrum Disorders (ASD) nor the associated change with age. Research suggests that there are high rates of comorbid conditions (Streiner, & Wilson, 2000; Lainhart, 1999), but focus has predominantly been on singular psychiatric comparisons, such as with depression (Ghaziuddin, Ghaziuddin, & Greden, 2002). No other study has reported comparing the two versions of the measure. In this study, we assessed the overall prevalence of comorbid symptoms in children and adolescents with ASD compared to typically developing sibling controls. We examined trends in comorbid symptoms of participants stratified by age and gender.

2849 subjects with ASD and 2755 typically developing siblings were recruited from two larger research projects: the Simons Simplex Collection and the Autism Consortium. All ASD participants were administered the Autism Diagnostic Observation Schedule (Lord et al., 1989) and Autism Diagnostic Interview (Lord et al., 1994) to confirm their diagnosis. All participants were given the Child Behavior Checklist (Achenbach 2001) to assess behavioral symptoms. Males and females were separated, and Chi squares were used to analyze percentage differences among age cohorts: <6 years, 6-12 years, and 12-18 years.

In the ASD group, we found significant differences in symptoms among age groups and within gender cohorts suggesting developmental changes. While several measures showed a decrease in prevalence with age (e.g. withdrawn/depressed symptoms) others showed relatively stable levels (aggression), or increases of prevalence with age (anxiety/depressed symptoms) across both genders. The number of comorbidities suggests that with increasing age, males with ASD suffer from the same number of comorbid symptoms, indicating a possible stabilization of symptoms. Females with ASD show significant changes in number of diagnoses, indicating that gender could be a determining factor in future comorbid syndrome development. These changes are striking compared to those found in control siblings.

“Microbial Correlation between Women with Bacterial Vaginosis and Their Male Partners”

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Background and Significance: Bacterial Vaginosis (BV) is a common syndrome characterized by significant change in the diversity of normal vaginal bacterial flora, most notably through the loss of *Lactobacillus spp.* and increase in various BV-associated taxa. Studies have shown that monogamous sexual activity may increase the chances of BV recurrence following successful treatment, yet there is debate over whether this may be due to transmission of bacteria between partners. This study seeks to further examine the role of male partners in re-infection following treatment for BV, as well as the degree to which bacterial transmission may exist between sexual partners.

Methods: Genital swabs were obtained from monogamous couples from women diagnosed with BV (Nugent score ≥ 7) (n=63) and women with normal vaginal flora (n=31). Swabs were obtained from vaginal specimens and from male penile skin and urethra. The microbiota were assessed using high throughput sequencing analysis of 16S rDNA sequences that were PCR amplified from DNA isolated swab specimens. Microbial diversity of samples was analyzed using the Quantitative Insights Into Microbial Ecology (QIIME) package.

Results: The genital microbiota of monogamous couples was more similar than the genital microbiota of non-couples in comparisons of vaginal samples to both male penile skin ($P< 0.0001$) and urethra ($P< 0.0001$). Genital microbiota was more similar between BV-affected partners than between unaffected partners when comparing both vaginal to penile skin ($P= 0.0001$) and vaginal to urethral ($P= 0.0013$) specimens. In males with BV-affected partners, penile skin samples showed significantly higher percent abundances of BV-associated taxa including *Gardnerella spp.* ($P= 0.0012$), *Shuttleworthia spp.* ($P<0.0001$), *Megasphaera spp.* ($P< 0.0001$) and family Veillonellaceae ($P= 0.0007$) than penile skin samples from males with unaffected partners. These BV-associated taxa were also found in higher abundance in BV-affected vaginal samples when compared to unaffected vaginal samples. Additionally, penile skin of males with BV-affected partners displayed a lower percent abundance of *Lactobacillus spp.* ($P= 0.0096$) than the penile skin of males with unaffected partners, and this was also reflected in vaginal comparisons. Urethral samples from males with BV-affected partners showed significantly higher percent abundances of BV-associated taxa including *Prevotella spp.* ($P= 0.0009$), *Sneathia spp.* ($P= 0.0005$), and phylum *Bacteroidetes* ($P= 0.0037$) than urethral samples from males with unaffected partners, which also correlated with comparisons of the vaginal flora of their partners.

“Intramuscular Dexamethasone vs. 5 Days of Oral Prednisone in the Treatment of Acute Exacerbation of Asthma”

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Abstract

Background: Acute asthma exacerbation is one of the most common chief complaints prompting emergency department (ED) visits yearly. The current common practice for treatment of these acute asthma patients is to administer corticosteroids in the ED and discharge the patient with a 4-5 day course of an oral corticosteroid. It has been noted that patients discharged from the ED often return with a relapse of symptoms within the next 3 weeks. 12% - 22% of patients that return to ED are noncompliant with medication. New studies have incorporated the use of intramuscular (IM) injections of corticosteroids as a treatment option. The sum total of medication is delivered all at once in the hospital, and the pharmacokinetics of the drug allows it to remain in the patient’s system for some time after administration.

Objectives: To determine whether or not the use of IM Dexamethasone is at least as effective as the standard of care of oral Prednisone in relieving or improving the asthma patient’s symptoms and preventing return to the ED.

Methods: Prior to the start of the study, patients will be randomized to standard of care (control group) or IM dexamethasone (experimental group). Patients presenting to the ED at LSU Interim Hospital in New Orleans and clinically confirmed as having an acute asthma attack by the treating physicians and/or licensed respiratory therapists will be recruited for the study. While in the hospital, the patient will answer a questionnaire conducted by the respiratory therapist. The control group will be discharged with a prescription for 40-60 mg of oral Prednisone daily for 5 days, and the experimental group will be discharged after receiving an intramuscular injection of 12 mg. of Dexamethasone. A follow up telephone survey will be conducted 5-7 days after the initial ED visit.

Results: Patients are still being recruited to the study. 88 patients will be recruited to the study, which includes 44 in the control group and 44 in the experimental group. Of the patients recruited to the control group, x% had to return to the ED with acute asthmatic symptoms, which compares to the x% of patients in the experimental group.

Conclusion: We expect to find that the IM Dexamethasone will work at least as well as the oral Prednisone, which is the current standard of care.

“Role of DHA, PEDF, and TUDCA mediated neuroprotection in Tunicamycin induced Endoplasimic Reticulum Stress in APRE-19 cells.”

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Oxidative stress can be successfully induced in APRE-19 cells using H_2O_2 and TNF-α leading to an increased expression of pro-apoptotic genes, leading to cell death. Neuroprotectin D1 (NPD1) has been found to protect these cells from apoptosis by up regulating the anti-apoptotic genes (Bcl2 and Bcl-xl), and down regulating the expression of pro-apoptotic genes (Bax and Bad). DHA and PEDF activate NPD-1 synthesis as well as decrease pro-apoptotic genes and increase anti-apoptotic gene expression. ER stress has been associated with neuronal loss, and is linked to most neurodegenerative diseases. Endoplasmic Reticulum (ER) stress can also be induced in ARPE-19 cells leading to program cell death, by using Tunicamycin (TMC). Varying concentrations of TMC were used on serum starved ARPE-19 cells to induce apoptosis, and challenged with DHA, PEDF, and Taurourosodeoxycholic acid-sodium salt (TUDCA) for protection. Hoechst stain was performed on these treated cells and Hoechst positive cells were scored. Our results indicate that TMC at 50ug/ml induce apoptosis in ARPE-19 cells. DHA and PEDF alone were unable to protect against TMC induced apoptosis, but together was able to provide substantial inhibition of apoptosis. TUDCA, a specific ER stress inhibitor, will be able to protect from TMC induced apoptosis. A Western-Blot analysis using seven different trials of combinations of TMC (50ug), DHA (100nM), and PEDF (10nG and 50nG) was performed. The antibody PUMA (anti-p53 unregulated mediator of apoptosis) was used as a probe. PUMA is a part of the Bcl-2 family of proapoptotoic proteins (Bim, Bad, Bid, Noxa), and upon activation by p53 PUMA binds to Bcl-2, localized to the mitochronidria to induce cytochrome c release, and activates the rapid induction of programmed cell death. Our results showed that TMC at 50ug per ml upregulates PUMA activation in ARPE-19 cells and DHA plus PEDF attenuated this PUMA activation . These observations elicit an important role of DHA and PEDF in ER stress induced apoptotic cell death survival.

“Mechanisms Underlying the Sleep Promoting Effect of Cherry Juice Standardized to its Proanthocyanidin Content”

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Previous studies have shown that tryptophan, melatonin, and proanthocyanidin within cherry juice may play essential roles in promoting sleep. This study utilized cherry juice standardized to its proanthocyanidin content and tested its effectiveness as a treatment for insomnia, a common health problem in the elderly. Ten participants with insomnia completed two treatment periods (cherry juice and placebo juice), 2 weeks each, separated by a 2 week washout period. Each day the participants consumed 8 ounces of juice in the morning and again 1-2 hours before bedtime. Overnight polysomnography (PSG) was used at the end of each treatment period to evaluate sleep architecture such as the distribution of sleep stages, sleep latency and state transitions. Blood samples were also taken to measure serum concentrations of free tryptophan and kynurenine in order to investigate a possible mechanism of action. Questionnaires were given before and after each two week treatment period for comparison of each treatment’s effects. The polysomnography results indicated that cherry juice significantly increased the sleep time of participants by 67 minutes compared to placebo, and increased sleep efficiency 3.1% which was not significant. The Pittsburg Sleep Quality Index, a part of the questionnaire, showed a statistically significant increase in habitual sleep efficiency and the sleep duration increased, but not significantly. Blood analysis is pending. However, based on the current data, cherry juice exhibits promise as a potential treatment for insomnia and needs to be assessed further via a larger study.

“Healing of isolated long bone fractures of the lower extremity following alcohol & drug use.”

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Abstract
BACKGROUND:
The presence of alcohol and/or drugs is commonly discovered in patients admitted to the emergency room for traumatic injury. These alcohol and drug-correlated traumatic injuries are commonly of musculoskeletal origin and, if injuries are of great enough severity, may warrant surgical correction. In adult trauma patients, isolated long bone fractures of the lower extremity are a frequent diagnosis and as these fractures occur in a weight bearing structure of the body, successful treatment often requires orthopedic surgical correction. **We hypothesize that in patients admitted for traumatic isolated long bone fracture of the lower extremity requiring surgical correction, the presence of alcohol and/or drugs in patients at the time of admission complicates fracture healing, host defense, intensive care needs, hospital stay, and patient outcomes.**

METHODS:
The study is a retrospective chart review of age 18 to 64 year old patients admitted to the LSU Interim Louisiana Hospital for traumatic isolated long bone fracture of the lower extremity requiring surgical correction (femur, tibia, or fibula) between January 1, 2002 and the present. Patients will be categorized into four possible cohorts based upon the presence or absence of alcohol in the blood and/or illicit drugs in the urine (± blood alcohol level (BAL) ± urine toxicology screen (UTox)). Measured parameters available through the LSU Trauma Registry and electronic medical records will include fracture classification, age, BAL, UTox, radiographs, as well as any additional pertinent clinical parameters previously recorded in patient medical records. Potential confounding variables such as tobacco use or immunosuppression will be excluded from the data analysis. Data will be analyzed using publicly-available statistical software.

RESULTS:
The study observed a tendency for worse outcomes in patients admitted for traumatic injury with the presence of alcohol and drugs.

"Comparators of Protective Factors of Bone Mineral Density in a New Orleans Sarcoidosis Population"

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Background: The pathophysiology of sarcoidosis involves dysregulation of dependent factors of bone metabolism, such as vitamin D and calcium, and high dose persistent treatment with steroids may lead to low bone mineral density (LBMD). Advancing age, female gender, low body mass index (BMI), smoking and steroids are risk factors for LBMD. LBMD in sarcoidosis is presumed but has yet to be described.

Methods: A retrospective chart review of biopsy-proven patients with a diagnosis of sarcoidosis for >1 year was used to compare parameters of prevalence, age (at chart review), gender, race, smoking status and designation of LBMD based results of Dual Energy Xray Absorptiometry (DEXA) studies. All calculations are based on non-parametric analyses using Fisher's exact for categorical data and Mann Whitney tests for continuous variables.

Results: 61 patients (86.9% African-American) were identified that met criteria, 38 (62.3%) with LBMD (30 with osteopenia and 8 with osteoporosis). A significant difference was found in occurrence of LBMD in patients with BMI $\geq$ vs <30 with patients BMI $\geq$ 30 having lower levels of LBMD (as is expected in the general population), but no significant differences (table) were found in occurrence of LBMD in patients age $\geq$ vs < 65, in ever vs never smokers (age between ever smokers and never smokers was not significantly different), or in males vs females (with females being significantly older than males and female age range 34-79).

Table 1. Comparison of Factors Influencing Bone Mineral Density within a New Orleans Sarcoidosis Population

	LBMD	NBMD	Odds Ratio	p Value
% ≥65 Years Old	26% (10/38)	9% (2/23)	3.75 (95% CI 0.74 to 18.96)	0.11
% Male	13% (5/38)	26% (6/23)	0.43 (95% CI 0.11 to 1.61)	0.30
% BMI≥30	18% (7/38)	52% (12/23)	0.21 (95% CI 0.06 to 0.66)	0.01
% Smoker	32% (12/37)	55% (12/22)	0.40 (95% CI 0.14 to 1.19)	0.11

Conclusion: Factors protective against LBMD in the general population were not demonstrated in this population of sarcoidosis patients. A lower risk of LBMD was not conferred by age < 65, male gender, or non-smoking status. These trends including significantly older age of females vs males suggests an abnormal distribution of LBMD in our sarcoidosis population that is not expected in the general population. Further examination of LBMD in sarcoidosis may yield evidence to support increased vigilance in steroid use and perhaps consideration/consensus to initiate steroid sparing agents earlier in the disease course, as well as earlier screening for LBMD in patients with sarcoidosis. Future studies evaluating impact of steroid use, levels of factors in bone metabolism (e.g. calcium, vitamin D, etc) and fracture risk are much needed.

“Ethanol Increases NOX -2 and -4 Activity and Collagen Formation in Cardiac Fibroblasts”

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Alcoholic cardiomyopathy commonly results from chronic alcohol abuse and is characterized by the formation of cardiac fibrosis. Recent studies demonstrate that cellular models treated with ethanol (EtOH) have a significant increase in oxidative stress as a result of increased NADPH oxidase (NOX) 2 and 4. These NOXs produce reactive species (ROS) including superoxide and hydrogen peroxide. The increased presence of ROS stimulates cardiac fibroblasts (CF) to transform into a more aggressive collagen producing phenotype, the myofibroblast. In addition to secreting excess collagen, myofibroblasts overexpress lysyl oxidase (LOX), an enzyme involved in the post-translational modification of type I and III collagens. LOX activity crosslinks collagens rendering them insoluble and less susceptible to degradation by MMPs. We hypothesize that EtOH induces oxidative stress by stimulating NOX-2/4, leading to myofibroblast activation and collagen formation. Concentrations of 0 , 25 , and 50 mM EtOh were added to CF isolated from 12 wk old male Sprague Dawley rats (~300 g body weight) and incubated for a 24h period at 37°C. CF with 0 and 50 mM EtOH were treated in the presence or absence of 1mM 4-methylpyrazole, an alcohol dehydrogenase (ADH) inhibitor. CF were analyzed for NOX activity, collagen content, collagen crosslinking, and the presence of myofibroblasts. NADPH consumption assay indicates a significant increase ($p=0.02$) in total NOX activity in cardiac fibroblasts treated with 50mM EtOH. Lysyl oxidase activity showed an increasing trend in fibroblasts treated with both 25 and 50 mM EtOH. Protein expression of NOX 2 ($p=0.0002$) and α-SMA ($p<0.05$) were significantly increased in CF treated with 50mM EtOH. Hydroxyproline assay found a significant increase in collagen secretion by CF treated with 50mM EtOH. ADH inhibition, although not significant, decreased NOX-2 protein expression and lysyl oxidase activity. These data indicate that EtOH significantly increases NOX-2 expression, NOX activity, and collagen secretion by cardiac fibroblasts. These EtOH-induced changes are at least in part dependent on the conversion of EtOH to acetaldehyde by ADH. Future studies will further assess the effect of EtOH on LOX activity, and the role of ADH.

AZD-2281, a novel PARP inhibitor approved for human testing, prevents an allergen-induced airway inflammation in mouse model of asthma

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As the prevalence of asthma and allergic disease increases around the world, it is clear that more effective therapies and disease-modifying agents are needed. Identifying therapeutic drugs that block the release or effects of T-helper type 2 (Th2) cytokines after allergen exposure is an important goal for the treatment of allergic inflammatory diseases including asthma. We recently showed using a murine model of allergic airway inflammation, that poly (ADP-ribose) polymerase (PARP) plays an important role in the pathogenesis of asthma-related lung inflammation. In this study we examined the efficacy of AZD-2281 (Olaparib), a novel PARP inhibitor that has been approved for testing in clinical trials in humans against asthma. Our results show that a single administration of AZD-2281 thirty minutes after challenge with 3% ovalbumin (OVA) prevented airway eosinophilia in C57BL/6 mice. The analysis of the BAL fluid and serum derived from the OVA challenged wild-type mice showed a significant increase in IL-4 and IL-5 while AZD-2281 treatment provided a major protection against such an increase, which partly explain the inhibition of eosinophil recruitment in the airways. Our histopathological data confirmed the concomitant suppression of OVA-induced eosinophil recruitment and mucus production upon AZD-2281 treatment. FACS analysis of the lung cell suspension derived from these mice showed that AZD-2281 markedly increased the population of T-regulatory cells and thus may shift the balance toward anti-inflammatory response upon allergen exposure. These findings further support the potential of PARP inhibition as a novel therapeutic strategy for treatment of asthma.

“Optimal Nerve Conduction Methodology For Early Detection of Diabetic Peripheral Neuropathy”

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Early detection of diabetic peripheral neuropathy (DPN) is relevant to decreasing morbidity and mortality associated with the progression of diabetes mellitus.[1] Sensory DPN is primarily characterized as small-fiber (conveying pain and temperature) neuropathy or large-fiber (conveying vibration, touch and position) neuropathy, although both may be present.[1-3] Ultimate complications of small-fiber neuropathy or large-fiber neuropathy include amputation and a debilitating lack of coordination significantly decreasing quality of life.[1] Therefore, determining the nerve(s) affected the earliest in DPN and the optimal method of detection of abnormality in these nerves is significant to maximizing preventative measures. In DPN, the most distal nerves of the lower extremity are typically the first damaged, with the sensory nerves commonly affected before the motor nerves.[4,5] Abnormality in conduction studies of the sural sensory nerve is often used to diagnose DPN. However, the medial plantar nerve is more distal; and, therefore, has been used as a better early indicator of DPN.[6] Due to the variably and poorly reported sensitivities of the sural sensory nerve action potential (SNAP) amplitude diagnostic reliability, investigators have attempted to improve diagnostic sensitivity via the sural/radial amplitude ratio (SRAR). As a much more proximal nerve, the radial nerve is less likely to be affected compared to the distal sural nerve in early DPN. However, studies comparing sural SNAP to SRAR have had varied but slightly enhanced results in regards to proving the usefulness of SRAR measurements as a more sensitive and specific method of detection for early DPN.[4,7,8] The more distal medial plantar nerve is reliably detectable under the age of 70 and identified as having greater sensitivity than the sural nerve in detecting abnormalities of large-fiber neuropathy in patients with diabetes mellitus.[3,9,10] The evaluation of the medial plantar SNAP with the dorsal sural SNAP further enhances sensitivity.[6] The medial plantar SNAP has also been determined to be of greater value in diagnosing distal sensory polyneuropathy than SRAR in cases in which clinical signs of large-fiber neuropathy are present but routine nerve conduction studies are normal.[10]

The objective of this study is to expand on the diagnostic potential of the medial plantar SNAP by determining if the medial plantar to radial sensory amplitude ratio improves the sensitivity of nerve conduction studies in the detection of early DPN.

Patients receiving routine care by referral to the LSUHSC Physical Medicine & Rehabilitation EMG and Nerve Conduction Study Laboratory who meet consensus criteria and Toronto Clinical Neuropathy Score Criteria for DPN will have their medial plantar and radial SNAP measured in addition to their routine nerve conduction study. The medial plantar/radial amplitude ratio for each participant under the age of 70 will be calculated. The rate of detection of DPN via this ratio will be compared to the more commonly used methods of detection including sural SNAP, SRAR, and medial plantar SNAP alone.

“Nucleoside Reverse Transcriptase Inhibitor-Induced Oxidative Stress Contributes to Premature Senescence and Endothelial Dysfunction”

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Long-term use of nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) is known to induce mitochondrial damage in endothelial cells, ultimately resulting in endothelial dysfunction and atherosclerosis. Though the mechanism of NRTI-induced effects on endothelial cells is not well understood, prior work suggests that mitochondrially-compartmentalized oxidative stress and premature cellular senescence may be involved. We thus investigated the potential of adjunct utilization of the antioxidant coenzyme Q10 (CoQ10) to combat NRTI-induced endothelial toxicity, and examined the role of NRTI treatment in stress-induced premature senescence in endothelial cells. Co-treatment of human aortic endothelial cells (HAEC) with CoQ10 was found to rescue cells from NRTI-induced increases in ROS levels and decreases in ATP production and oxygen consumption. In addition, we found that NRTI increased levels of endothelin-1 (ET-1), a marker for endothelial cell dysfunction, but this effect was also reversed by CoQ10 co-treatment. Interestingly, treatment of HAEC with the NRTI zidovudine (AZT) induced selective mitochondrial autophagy, or mitophagy. AZT treatment for 6-8 h increased lysosomal activity, while 8 hour treatment was found to increase colocalization of mitochondria with lysosomes, an indicator of mitophagy. The LC3-II/LC3-I ratio, a marker of autophagosomal activity, was also increased in treated cells. Finally, NRTI treatment was found to accelerate the onset of senescence, while CoQ10 co-treatment ameliorated this effect. These findings suggest that NRTI-induced autophagic degradation of mitochondria may be involved in NRTI-induced endothelial dysfunction, and that this damage likely results from oxidant injury. Moreover, oxidative stress induced by NRTIs enhances premature senescence in endothelial cells, and CoQ10 is able to attenuate this response as well.

“A retrospective analysis of PAD in orthopedic patients with asymptomatic popliteal artery calcification”

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Peripheral artery disease (PAD) is known to exist in various arterial beds throughout the circulatory system. Its presence is strongly associated with myocardial infarction, stroke, and cardiovascular death, with approximately 10% of all cardiovascular and cerebrovascular ischemic events being attributed to the direct progression of PAD. Recent epidemiological studies have recorded the prevalence of PAD to be 14.5% among individuals aged ≥ 70 years. Atherosclerosis, which accounts for 90% of PAD, is the greatest cause of morbidity and mortality of adults in the United States.

In the orthopedic setting, it is common to encounter asymptomatic calcification of the popliteal artery by plain x-ray imaging for unassociated lower extremity complaints such as arthritis. However, it is unknown whether these findings are a reliable predictor of future sequlae of PAD. Epidemiological studies using the ankle-brachial index to diagnose PAD report the prevalence of asymptomatic PAD to be 8.0% of the population aged 54 to 74 years. This is underscored by subsequent studies which have shown that asymptomatic PAD, identified by the ankle-brachial index, increases risk of death due to coronary artery disease three to six fold compared to the normal population. PAD identified as severe by ankle-brachial index was reported to be a consistent indicator of malignant prognosis, with a 64% death rate by six years follow up. These findings suggest the significance of determining whether popliteal artery calcification on x-ray may be used as a predictor of future cardiovascular events related to atherosclerosis.

There are currently no studies examining the risk of atherosclerotic events in asymptomatic orthopedic patients identified by arterial calcification on x-ray, and treatment recommendations for this population have not been established. Our study determines the incidence of asymptomatic PAD in a total joint patient population and whether there were any vascular sequelae within 2 years of initial x-ray.

Retrospective chart review was performed on all asymptomatic orthopedic patients over the last five years who received a lower extremity x-ray demonstrating atherosclerosis of lower extremity vasculature. Subsequent vascular events such as stroke and MI were identified and categorized with respect to severity and known atherosclerotic risk factors such as age, BMI, and smoking history.

“Predator Odor Stress-Induced Hyperalgesia Is Dependent on CRF1 Receptors and the Central Amygdala”

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Psychiatric stress disorders in humans are associated with altered pain processing, hyperarousal, and increased alcohol use disorders. In rats, chronic stress has been shown to produce similar behaviors. Corticotropin-releasing factor (CRF) plays important roles in emotional regulation and modulation of stress and pain responses, in part via effects on neurotransmission in the central amygdala (CeA). We have shown that systemic injection of a CRF1 receptor antagonist attenuates predator odor-induced increases in nociceptive processing. We hypothesize that the analgesic effects of R121919, a CRF1 receptor antagonist, will be reversed by inactivating the CeA with tetrodotoxin (TTX), a sodium channel blocker.

Male Wistar rats underwent stereotaxic surgery for cannula placement into the CeA. Using a conditioned place avoidance (CPA) procedure, rats were stressed and labeled as Avoider or Non-Avoider animals. Rats were injected with the CRF1R antagonist (i.p.; 10mg/2ml/kg) or vehicle (2ml/kg) followed 30 min later by an infusion of TTX (10ng in 0.5ul/side) or vehicle (0.5uL/side) into the CeA. Drug dose combinations were administered over four days in a Latin-square design. Thermal nociception was measured 30 min after the infusion using the Hargreaves method.

Predator odor stress produced hyperalgesia only in Avoider animals. Systemic R121919 reversed hyperalgesia in Avoider rats and administration of TTX into the CeA abolished this effect. In addition, TTX into the CeA produced hyperalgesia in all animals. These data suggest CRF signaling and the CeA are critical for mediating nociceptive processing in stressed animals.

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“Detection of Congenital CMV in dried blood spots of Neonates”

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One of the common causes of congenital infections in children is cytomegalovirus (CMV), and it is the most common cause of acquired sensorineural hearing loss in children. Without early diagnosis and treatment, congenital CMV infections in neonates can lead to sensorineural hearing loss in infected children. Moreover, it is difficult to make an early diagnosis because neonates infected with congenital CMV appear normal at birth. Previously neonates were treated with IV gangcylovir. Now they can be treated at home with Oral valganciclovir with the same benefits making it easier to treat them. Therefore, this study proposes to detect congenital CMV infections in dried blood spots collected at birth, which are a universal collection method in screening for other diseases in neonates. Polymerase chain reaction (PCR) screening was utilized to detect CMV in 600 dried blood spots collected from neonates at birth. Furthermore, this study will help determine if congenital CMV screening can be completed as part of the universal neonate screening at birth.