2015 Research Conference Abstracts and Poster Competition

This issue of *The Journal of the American Osteopathic Association* (*JAOA*) features abstracts from the posters presented at the 58th Annual American Osteopathic Association (AOA) Research Conference.

This year's abstracts were organized into the following categories:

This year's AOA Research Conference took place in Orlando, Florida, on Sunday, October 18, during the AOA's 2015 Osteopathic Medical Conference & Exposition. Judges met with the student presenters to discuss and review their research. At the end of the seminar, the judges identified 3 first-place winners, who received $275 each. Six second-place winners were chosen, who received $175 each. The 9 winners are as follows:

First Prize

- Amanda Lindenberg, MS, from the Midwestern University/Chicago College of Osteopathic Medicine for abstract B29, "Does Pulonary Function Change With External or Internal Rotation of the Extremities?" (see page e62)
- Christina Rose Werman, BBmE, OMS III, from the A.T. Still University–Kirksville College of Osteopathic Medicine for abstract C60, "Relating Accuracy of Asymmetrical Assessment of Osteopathic Medical Students in Directional Diagnosis on Standardized Pelvic Models and Humans" (see page e116)
- Kevin C. Ball, BS, from the A.T. Still University–Kirksville College of Osteopathic Medicine for abstract C34, "Objective Characteristics of Osteopathic Medical Students Performing Rotational Testing of Lumbar Vertebral Segments" (see page e96)

Second Prize

- Rebecca C. Smith, OMS III, from the Edward Via College of Osteopathic Medicine for abstract C36, "Use of Osteopathic Techniques to Treat Iliotibial Band Dysfunction in CrossFit Athletes" (see page e99)
- Benjamin Karamer, OMS II, from the New York Institute of Technology College of Osteopathic Medicine for abstract B30, "Hyperglycemia Limits Autophagy Via Inhibition of Nuclear Translocation of Transcription Factor EB" (see page e63)
- Yujie Linda Li, BS, from the Lake Erie College of Osteopathic Medicine for abstract B31, "Effect of Neonatal MSG Exposure on Cerebellar Nuclei" (see page e64)
- Lauren Wackerman, BS, from the West Virginia School of Osteopathic Medicine for abstract C16, "Intra-Individual Variability in Salivary Uric Acid and Insulin Levels" (see page e80)
- Erin Ivanoff, OMS III, from the Edward Via College of Osteopathic Medicine–Carolinas Campus for abstract C23, "Assessment of Respiratory Syncytial Virus Hospitalizations Following Implementation of Updated Palivizumab Treatment Recommendations" (see page e84)
- David Kline Jr, BS, from the Ohio University College of Osteopathic Medicine for abstract HS4, "Association Between Method of Delivery and Exclusively Breastfeeding at Hospital Discharge" (see page e130)

To enhance the readability of this special feature, abstracts have been edited for basic *JAOA* style only. The content has not been modified; information provided reflects information that was submitted by the primary author, including professional degrees and affiliations. Neither the AOA Research Council nor the *JAOA* assume responsibility for the abstracts' content. The winning abstracts are noted with "♦". (doi:10.7556/jaoa.2015.152)

AOA Research Fellowship

Clinical
F1—Impact of OMM & OMT

Osteopathic Manipulative Therapy in a Distressed Medical Student Population: A Biomarker Analysis

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Research Question(s)/Hypotheses: Does osteopathic manipulative therapy impact surrogate markers of psychological distress and autonomic dysregulation?

Methods: Thirty-seven (n=37) students were randomly separated into experimental, placebo, and control groups. A period of 6 weeks of osteopathic manipulative therapy was initiated. The experimental treatment protocol consisted of 7 minutes of lymphatic and autonomic focused treatments followed by a brief rest period. The placebo group received "light touch" treatments in the corresponding anatomical regions. Objective stress was measured using pre- and postintervention samples of salivary alpha-amylase (sAA) salivary immunoglobulin A (sIgA), and salivary cortisol (SC), while subjective values of stress were measured with Perceived Stress Scale (PSS) surveys repeated at weekly intervals.

Data Analysis: Salivary samples were collected at week 0 and week 6 and subsequently sent to an independent laboratory for analysis. Once pre- and postintervention quantitative data were received from the laboratory, 2-tailed *t* tests were run to observe any differences in the treatment protocol outcomes. All data analyses were performed by a researcher with no involvement in the study design.

Results: Average change in PSS scores in the experimental group from survey 0 to survey 6 significantly differed (P=.033), while average change in placebo and control groups was not significantly different (P=.353 and P=.250, respectively). Independent laboratory analysis revealed a significant difference in average sIgA change over time between experimental and control groups (P=.007), but not between experimental and placebo groups (P=.28). The results for salivary alpha-amylase and cortisol were not statistically significant.

Conclusion: The study findings suggest that brief, structured manipulative treatments may improve the health status of medical students. Further studies should be conducted to explore the role of osteopathic manipulative therapy in aiding the physiologic immunity, with particular emphasis on salivary IgA. Additionally, limitations such as participant attrition and small sample size should be addressed when designing further evaluative studies.

Acknowledgment/Funding Source: The authors would like to acknowledge the AOA for helping to fund this research. Additionally, we would like to thank the staff at Lake Erie College of Osteopathic Medicine–Bradenton, for supervising all osteopathic treatments.

Basic Science
F2—Impact of OMM & OMT

A 3-Dimensional Infrared Kinematic Method for Detection of Inherent Slow Rhythmic Cranial Motion

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Hypothesis: We proposed a method could be developed to measure slow rhythmic inherent cranial motion (less than 30 cycles per minute [cpm]) in a noninvasive, nontraumatic, precise, and objective manner using a design that may accommodate simultaneous osteopathic manipulation in future studies.

Methods: Seven baldheaded participants were recruited using posters, in-class announcements, and

word-of-mouth within the local community. Data were collected using a commercial motion capture 3-dimensional (3D) infrared (IR) video system to capture the relative distance between corresponding symmetric IR reflective markers on the participant's scalp superficial to the squamosal suture. To ensure accurate measurement of potentially confounding thoracic respiratory frequencies, 2 methods were employed: IR reflective markers were placed on the lower thoracic cage, and a thoracic respiratory transducer (collected using a separate biometric system) was strapped to the upper thoracic cage. To measure the dominant slow frequency(s) and its biparietal excursion(s), 4 trials of data capture were performed on each participant and on a skeleton model used as a control. The first 3 trials were 3 minutes in duration and the fourth was 6 minutes. Trial 2 was separated from Trial 1 by a 25-minute rest period. Each subsequent trial was separated by 1 minute. In Trial 3, participants held their breath for 10 seconds after 1 minute had elapsed in the capture period.

Data Analysis: The fast Fourier transform (FFT) of the left thoracic IR reflective marker excursion was used to identify the 4 cpm frequency interval within 5-30 cpm with the largest area under the curve using trapezoid integration to indicate the dominant thoracic respiration. This 4 cpm respiration frequency interval and the slow rhythmic cranial motion frequency intervals of 2-6, 6-10, and 10-14 cpm were used to find the corresponding area under the curve of the FFT of the biparietal excursion and the differences in minimum and maximum excursion from the corresponding inverse FFT. A mixed linear model was used to compare the area under the curve of each 4 cpm low frequency interval to the 4 cpm respiration interval for each trial in all participants and the skeleton model control. A second mixed linear model assessed the biparietal excursion associated with each of the frequency intervals in each trial.

Results: For the 2-6 cpm range in Trials 2 and 4, the relative area under the curve for participants was 2.2 mm × cpm (95% CI, 1.9-2.5) and 2.3 mm × cpm (95% CI, 2.0-2.6), which was higher than the skeleton model control (1.2 and 1.0, respectively; both $P \leq .01$). No significant interaction was found between trial and frequency interval for the biparietal excursions ($P = .94$), but Trial 4 had a slightly greater mean excursion distance than Trials 1 and 2 by 0.06 and 0.07 mm, respectively (both $P \leq .04$). After accounting for trials, the mean biparietal excursions were 0.27 mm (95% CI, 0.17-0.38) for 2-6 cpm, 0.20 mm (95% CI, 0.09-0.31) for 6-10 cpm, 0.15 mm (95% CI, 0.04-0.26) for 10-14 cpm, and 0.15 mm (95% CI, 0.04-0.26) for the 4 cpm respiratory intervals. A significant difference was found in mean biparietal excursion between the 2-6 and 6-10 cpm ranges ($P = .02$).

Conclusion: Results suggested the 3D IR video system was noninvasive, nontraumatic, precise, and objective. No traumatic complaints were submitted by any of the participants, and motion was captured in the 2-30 cpm range at less than 0.01 mm in the skeleton model control. Slow rhythmic motion was successfully captured for each participant at a biparietal excursion distance consistent with other studies. The greatest mean biparietal excursion in the present study was associated with the 2-6 cpm range. This result was nearly twice the mean biparietal excursion associated with the 4 cpm respiratory interval. Including more participants, measured for greater lengths of time to minimize the impact of extraneous sources of movement, may lead to more accurate and contextual characterization of slow rhythmic cranial motion. Future studies should also attempt to correlate the character of captured cranial motion with osteopathic manual diagnostic findings.

Acknowledgments: We wish to thank Rafael Zegarra-Parodi, DO (England), MEd, for lending his expertise in biometric capture.

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Health Services

F3—Osteopathic Philosophy

Assessment of Ear, Nose, Throat Knowledge in Osteopathic Primary Care Residents and Medical Students

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Objectives: To assess the otolaryngologic knowledge of osteopathic family medicine, emergency medicine, and pediatric residents and of fourth-year medical students. We predicted that there is an increased need for further otolaryngology training in primary care residents and fourth-year osteopathic medical students.

Design: Cross-sectional, questionnaire-based study.

Methods: A non-validated 14-question, multiple-choice examination was created specifically for the current study and was electronically distributed to residents in family practice, emergency medicine, and pediatrics, as well as to fourth-year medical students. Otolaryngology residents completed the examination as a control. The examination also included a question to determine if respondents had ever participated in an otolaryngology rotation. Questions covered common otolaryngologic complaints, treatments, and patient management. There was only 1 correct answer for each question, and examinations were graded on overall percentage correct. Scores of non-otolaryngology residents and medical students were compared with those of otolaryngology residents.

Data Analysis: A generalized linear model using a beta distribution with logit link function was used to compare percent correct between each residency program (family medicine, emergency medicine, pediatrics and students) to the otolaryngology (ENT) program. Dunnett-Hsu was used for adjustment for multiple comparisons. $P \leq .05$ were considered statistically significant. Analyses were performed using SAS 9.4 (SAS Institute Inc).

Results: Two hundred two examinations were completed (150 non-otolaryngology residents, 31 fourth-year medical students, and 21 otolaryngology residents). Of respondents, 22.5% were PGY I, 51.4% were PGYII or greater. Only 28.3% of the non-otolaryngology residents had a formal rotation in otolaryngology. The average percentage correct on the quiz was 66.04% for family medicine residents, 69.73% for emergency medicine residents, 72.72% for pediatric residents, 65.00% for fourth-year medical students, and 78.1% for otolaryngology residents. When comparing scores, significant differences in the mean scores were found between otolaryngology residents and family medicine residents ($P < .0045$) and fourth-year medical students ($P < .0064$).

Conclusion: Our nonvalidated questionnaire revealed significant differences in basic otolaryngologic knowledge in these residents and fourth-year medical students. Further, only a small minority of the non-otolaryngology residents and students had experienced a clinical rotation in otolaryngology during their training. With the costs of health care rising, our results suggest improved training in otolaryngology may lead to improved prevention, recognition, and treatment of these common complaints and may decrease the financial burden.

Funding: Funding was obtained from an AOA Research Fellowship Grant.

Basic Science

B2—Chronic Diseases & Conditions

Reverse Hairpin Constructs of gp41 as Fusion Inhibitors of HIV Infection

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Research Question(s)/Hypotheses: Known fusion inhibitors of HIV infection are purported to interrupt the activity of the HIV gp41 envelope protein

responsible for fusing cellular and viral membranes together. However, the exact mechanism of fusion inhibitors in HIV infection remains unclear as the exact structures of pre-fusion and intermediate states of gp41 are unknown.

Background: Previously studied inhibitors of HIV fusion like Enfuvirtide are derived from the C-helical domain (C-HR) of extracellular HIV-gp41. By targeting the N-helical domain (N-HR) of the same protein, such C-peptide mimics are able to interrupt the fusion process. However, Enfuvirtide use rapidly leads to the development of resistant viral strains in the patient. Alternative fusion inhibitors with a different mechanism of action would be a welcome addition to our therapeutic arsenal. Here we studied protein inhibitors of HIV fusion with the reverse mode of action, which is to target the C-HR domain. Reverse hairpin constructs of the HIV envelope protein gp41 were created to further explore the determinants of this inhibition. Our proteins contain a small C-helical segment and long N-HR, arranged in a "reverse hairpin" structure. We hypothesize that an exposed hydrophobic pocket and groove on the N-HR domain is responsible for inhibiting fusion by binding to a gp41 intermediate. We are examining whether part of the inhibitory activity arises from fraying of the C-helical segment. By increasing the stability of the hairpin, we will reduce the fraying of the C segment, highlighting the role of the hydrophobic pocket in fusion inhibition.

Methods: Reverse hairpins were prepared by overexpression in *Escherichia coli* and purified using Ni affinity chromatography. Mutations T639I and Q652L in the C-HR domain were made to increase C-peptide domain affinity for the N-HR, to determine whether exposure of the full-length groove present in the N-terminus is required to prevent fusion, or whether only partial exposure of this groove is necessary. Circular dichroism studies were used to assess protein structure and stability. Membrane mimetic solvents were used to assess the effect of membrane on their structure and integrity. Virus–cell fusion experiments were carried out using HXB2-Env pseudotyped viral particles and U87-CD4-CXCR4 cells to determine inhibitory potency.

Data Analysis: Protein purity and molecular weight were confirmed using SDS Page gel electrophoresis and mass spectroscopy. Fusion data were analyzed using a model for 1:1 binding to establish the IC50 (concentration for 50% inhibitory effect). CD data were analyzed for helical content at different temperatures to obtain melting temperatures for protein unfolding, and in the presence and absence of membrane mimetic dodecylphosphocholine.

Results: Reverse hairpin constructs with the wild-type sequence were 10 nM inhibitors of HIV-1 Env mediated fusion. The constructs displayed high helical content and melting temperature, with a dramatic lowering of melting temperature in the presence of membrane mimetic solvent. Preliminary data suggested that mutants T639I and/or Q652L, with an increased affinity of C-HR to N-HR, had lower inhibitory activity than the wild type constructs. The mutant Q652L demonstrated slower folding kinetics and correspondingly lower potency against HIV fusion.

Conclusion: The data are consistent with N-HR trimer as the source of inhibitory activity, and with unfolding of C-HR being accelerated in a membrane environment. Reduced fusion inhibitory activity and slower unfolding kinetics of the mutants indicate that exposure of the complete hydrophobic groove on the N-HR domain is required for fusion inhibition.

Acknowledgment/Funding Source: This research was supported by NIH grant GM087998 to M.G. and by the Touro University California MSMHS and COM programs.

B3—Chronic Diseases & Conditions

Aging in the Mouse Brainstem Ventral Raphe Associated with Alterations in Astrocyte Numbers

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Background: The microglia and astrocytes of the central nervous system (CNS) survey their specific area for pathogens and cellular debris and provide factors that support the maintenance and plasticity of neuronal circuits. However, as the CNS ages, the integrity of these factors appears to diminish, allowing for changes in overall activity patterns in neuronal networks that could lead to changes in behavior (eg, depressive state), pain perception, and sleeping pattern. The present study aimed to analyze any changes in glial distribution and function localized to the ventral raphe of the brainstem so as to better understand brainstem aging. The ventral raphe nuclei are a major source of CNS serotonin and play a role in pain inhibitory pathways, sleep modulation, and mood control. Since pain sensitivity, sleep-wake cycle disturbances, and depression increase with the progression of time, aging alterations in microglia and astrocyte numbers as well as neuronal numbers and serotonin expression in the ventral raphe of the brainstem have been hypothesized to influence these changes.

Hypothesis: Our central hypothesis is that aging in the mouse brainstem ventral raphe is associated with alterations in astrocyte and microglia numbers, as well as with changes in ventral raphe neuronal numbers and serotonin expression.

Methods: Brainstems were harvested from young (n=5, age 2-10 months) and old (n=5, age 23-24 months) Balb/C female mice, snap-frozen in isopentane cooled with liquid nitrogen, and cryosectioned at 14 micron. Consecutive sections were processed using standard immunofluorescence localization methods for antibodies to astrocyte markers ALDH1L1 (NeuroMAbs) and GFAP (Encor), a microglial marker IBA1 (Wako), serotonin (Sigma), or NeuN (Encor), a neuronal nuclear marker. Images of immunostained sections were obtained using a Zeiss MRm digital camera and AxioVision software. Images were thresholded and converted into binary images and the percent area of the ventral raphe immunostained (black) for each marker was calculated.

Data Analysis: Differences between groups for each antibody were analyzed using parametric statistics (ANOVA, LSD test; $P<.05$) and Statistica12 (StatSoft).

Results: Significant differences were observed between old and young groups for ALDH1L1 ($P=.00072$) and serotonin ($P=.00966$), but not for GFAP ($P=.56738$), NeuN ($P=.65344$), or IBA1 ($P=.31221$). Immunostaining for both ALDH1L1 and serotonin was significantly decreased in the old samples.

Conclusion: The results of this study indicate that with age there is a decrease in astrocytes within the ventral raphe. No differences were found in GFAP expression. This discrepancy between markers may be due to the expression of ALDH1L1 in all astrocytes, whereas GFAP labels only a limited number of astrocytes and mainly astrocytes associated with CNS white matter. No differences between neuronal or microglia markers were detected between old and young groups suggesting that these cell types remain stable in number with age within the ventral raphe of the brainstem. Aging was associated with a decrease in serotonin expression within the ventral raphe. Such a decrease could provide a mechanism for the behavioral changes observed with aging in sleep, mood, and pain sensitivity.

Acknowledgment/Funding Source: This research was supported by funding from WVSOM.

B4—Chronic Diseases & Conditions

Identification of Biomarkers in Etoposide-Treated Cells

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Research Question(s)/Hypotheses: Metabolomics is a method to examine and identify biochemical reaction products of living cells. Because the metabolome reacts dynamically to the environment, this technique can be used to provide insight into the biochemical differences of cells under varying conditions. One of the fields where this may be most valuable is anti-cancer drug therapy, in which understanding metabolic profiles may help to determine the nature of neoplastic cells. This information could then be used to develop targeted patient therapy. Additionally, cell metabolomics, which can be used to establish a holistic understanding of cell properties and functions, may be valuable in osteopathic manipulative treatment, which focuses on correcting imbalances to restore the body's property of self-regulation, self-healing, and health maintenance. A powerful approach for cancer therapeutics is to promote apoptosis in tumor cells. One common treatment is etoposide, a topoisomerase II enzyme inhibitor that causes errors in DNA synthesis and promotes apoptosis in cancer cells. Changes in levels of certain cell metabolites indicate apoptotic processes, may be used to test efficacy of pro-apoptotic drug treatments in cell culture. Apoptotic processes are typically indicated by an increase in alanine, arginine, asparagine, and glutamine and a decrease in glycine. In this study, we focused on establishing a protocol for cell metabolome sample preparation and analysis to support future studies of cellular biochemical processes. In particular, we are investigating the effects of pro-apoptotic cancer drug (etoposide) on human kidney endothelial cells (HEK293T). We are examining this through sample preparation and extraction, metabolic profiles based on nuclear magnetic resonance (NMR) spectroscopy, and metabolite identification. We hypothesize that etoposide-treated cells will have a higher concentration of apoptotic cell metabolites than untreated cells. By examining the differences between the cell metabolome, we hope to learn more about cell biochemical pathways during cancer treatment.

Methods: HEK293T cells were grown using cell culture and divided into 2 groups. The control group was exposed to 1% dimethyl sulfoxide (DMSO), whereas the experimental group was exposed to 5 mM etoposide dissolved in 1% DMSO. HEK293T-treated cells were then harvested to prepare cell endometabolome and exometabolome samples. NMR spectroscopy was used to determine chemical shifts. NMR spectra databases were then used to identify metabolites of interest.

Data Analysis: The obtained NMR spectra were analyzed for proton chemical shifts utilizing Bruker TOPSPIN software. Data were then cross-referenced to proton NMR databases to identify key metabolites. Metabolites of interest were then analyzed to determine changes in intensity across untreated and etoposide-treated samples. We were able to identify the following metabolites: alanine, asparagine, branched chain amino acids, fatty acids, glucose, glycine, pyruvate, threonine, and tyrosine from their chemical shift and evaluated their relative concentrations compared with a constant concentration of sodium formate added to each sample during extraction.

Results: Changes in metabolomic profiles were observed between untreated and etoposide-treated HEK293T cells. Firstly, we noticed etoposide-induced downregulation of glycine in the endometabolome by 53.5%, which is consistent with metabolite change in apoptotic processes. Secondly, we observed etoposide-induced downregulation of alanine in the endometabolome by 17.6%, which is unexpected as alanine is generally upregulated in apoptotic cells. However, there may be an error

range due to our small sample size: 4 for untreated cells and 4 for etoposide-treated cells.

Conclusion: In this study, we successfully developed protocols for extraction of metabolites from cell samples and NMR spectra analysis. We also achieved reproducible results in 4 sets of samples. Most significantly, we found that etoposide-treated cells expressed changes in metabolites consistent for glycine, but inconsistent with alanine for metabolite changes in apoptotic processes. Specifically, we observed a decrease in glycine and alanine, in the etoposide-treated cell endometabolome. Cell metabolomics has many valuable applications, including examination of cellular response to drug treatment, pathogen infections, toxicity, as well as osteopathic manipulative treatment. In future experiments, we hope to continue studying cell response to cancer treatment by determining if metabolite changes are consistent across other pro-apoptotic drugs, such as 5-fluorouracil, as well as across other classes of antineoplastic drugs, such as alkylating agents.

Acknowledgment/Funding Source: This research was supported by Touro University California, College of Osteopathic Medicine program.

B5—Chronic Diseases & Conditions

Determination of Diffusion Kinetics of Ketamine in Brain Tissue: Implications for In Vitro Mechanistic Studies of Drug Actions

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Introduction: Ketamine has long been used as a general anesthetic, acting in a concentration-dependent manner primarily though blockade of N-methyl-D-aspartate receptors in the brain. Recent studies have demonstrated the efficacy of ketamine, at sub-anesthetic doses, in the treatment of major depressive disorder, and in the reduction of chronic pain. However, the mechanism behind the antidepressant and pain-relieving actions of ketamine remains unclear. Mechanistic studies in vitro have been utilized to determine and characterize the mechanism(s) underlying these effects. The aim of this study was to determine the impact of the diffusion properties of ketamine on the concentration of ketamine in brain tissue during in vitro experiments.

Hypothesis: The diffusion properties of ketamine in brain tissue have a major impact on the effective dose of ketamine achieved in the brain during in vitro studies.

Methods & Analysis: Brain slices of adult mice, age 8-12 weeks, were prepared at a thickness of 300 µm using a vibrating microtome. The slices were allowed to recover in artificial cerebrospinal fluid (aCSF) for ≥60 minutes, and then incubated for 0-120 minutes in aCSF containing 17.7 µM ketamine HCl. The amount of ketamine within the brain tissue was measured using tandem high performance liquid chromatography-mass spectrometry. The diffusion and partition coefficients were determined for ketamine diffusing intro brain tissue from cerebrospinal fluid. A computational model was also generated to represent the concentration of ketamine within a brain slice as a function of depth and time. Data were analyzed using Microsoft Excel and Origin. All animal protocols were approved by the Institutional Animal Care and Use Committee.

Results: We successfully modeled the diffusion of ketamine into brain tissue using a mono-exponential function with time constant τ=7.04 minutes. This curve was then compared with a 1-dimensional model of diffusion yielding a diffusion coefficient of approximately 0.12 $cm^2 \times s^{-1}$ for ketamine diffusing into brain tissue. The brain:aCSF partition coefficient for ketamine was determined to be 5, representing strong partitioning of ketamine into brain tissue.

Conclusion: The diffusion properties of ketamine have a significant effect on drug concentrations

within brain tissue. Ketamine is highly soluble in both water and lipids, quickly equilibrating in lipid-dense brain tissue at a concentration 5 times higher than the surrounding aqueous aCSF. In previous in vitro mechanistic studies, reported concentrations of ketamine represent an 80% underestimate of the ketamine concentrations actually achieved within brain tissue. Studies of drug actions in vitro are critical to understanding the mechanism(s) through which ketamine exerts its effects. The model presented in this study will be useful in designing and interpreting in vitro studies using ketamine. However, the spectrum of actions of ketamine is concentration dependent; caution should be exercised when interpreting results derived from previous in vitro studies in which the concentrations of ketamine used greatly exceed those that produce specific effects in vivo.

B6—Chronic Diseases & Conditions

Epstein-Barr Virus LMP2A Activates the Intracellular Signaling Molecule Syk and Selective Downstream Kinases to Enhance MIP-1α Production by B Cell Lymphomas

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Background: Epstein-Barr virus (EBV) is associated with the development of malignancies such as Hodgkin's lymphoma. Hodgkin's lymphoma is characterized by the presence of Hodgkin-Reed Sternberg (HRS) cells, which are surrounded in a tumor microenvironment that promotes tumor growth and survival. Importantly, EBV-associated HRS cells express Latent Membrane Protein 2A (LMP2A), which is a functional homolog of the B cell receptor (BCR). Similar to the BCR, LMP2A contains an Immunoreceptor Tyrosine Activation Motif (ITAM) that activates the tyrosine kinase Syk to induce intracellular signaling. One important chemokine, MIP-1α, is increased in EBV-associated diseases like Hodgkin's lymphoma. Because previous studies indicate that MIP-1α levels are increased by BCR engagement in normal B cells, we hypothesize that LMP2A acts as a BCR mimic to increase MIP-1α in Hodgkin's lymphoma to establish a microenvironment that sustains HRS growth and survival.

Hypothesis: LMP2A activates the intracellular signaling molecule Syk and selective downstream kinases to increase MIP-1α production in B cell lymphomas.

Methods: ELISA and qRT-PCR was used to analyze supernatants or RNA, respectively, from LMP2A-positive or -negative B cell lymphoma lines to determine if LMP2A enhances MIP-1α expression. In addition, a B cell line expressing LMP2A with a mutation in the ITAM motif was used to determine the requirement of Syk activation in LMP2A-dependent changes in MIP-1α expression by ELISA. Furthermore, pharmacologic inhibitors of selective downstream targets of Syk were utilized to determine if these kinases were required for the LMP2A-dependent increase in MIP-1α expression by ELISA and qRT-PCR.

Results: We found that LMP2A-expressing cells produced more MIP-1α at the protein level compared with LMP2A-negative cells. Next, we found that MIP-1α production returned to basal levels in cells expressing LMP2A with a mutation in the ITAM motif. In addition, we found that specific inhibitors to Syk and PI3K blocked the LMP2A-mediated increase in MIP-1α production at the protein level. Surprisingly, even though LMP2A increases MIP-1α protein production, these changes were not seen at the RNA level, indicating that LMP2A increases MIP-1α production via a post-transcriptional mechanism.

Conclusion: These results indicate that LMP2A activates Syk and PI3K to increase MIP-1α expression

in B cell lymphomas. These data provide possible novel therapeutic interventions to enhance our treatment of EBV-associated Hodgkin's lymphoma.

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IRB/IACUC review and approval was not required for this project.

B7—Chronic Diseases & Conditions

Novel Mechanism Involved in Testosterone Modulation of Myogenic Tone in Resistance Microvessels of the Rat Mesenteric Arterial Bed

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Research Question(s)/Hypotheses: Although supplementation with the natural hormone testosterone (TES) has increased dramatically over the past decade, the role of TES in cardiovascular function is highly controversial. Specifically, we know virtually nothing concerning the ability of physiological concentrations of TES to modulate myogenic tone (MT) in the resistance vasculature. MT, a component of autoregulation, is the reflexive constriction of a blood vessel when intraluminal pressure increases. The aim of this study was to examine the vascular effects of TES on MT in a microvascular artery and to elucidate mechanisms mediating the TES-induced response. Hypotheses addressed included the following: (1) The tertiary branch of the rat mesenteric artery possesses MT; (2) TES-induced vasodilation of MT in the tertiary branch is dependent on androgen receptor activation; (3) Local conversion of TES to dihydrotestosterone (DHT) is a component of the vasodilatory response to TES on MT in the tertiary branch; (4) Exogenous DHT produces vasodilation of MT; (5) TES-induced vasodilation of MT in a tertiary branch is not due to the conversion of TES into estrogen and activation of estrogen receptors; (6) TES decreases MT in the microvessel via a nitric oxide synthase (NOS) mechanism; and(7) TES-induced vasodilation of MT in a tertiary branch vessel is endothelium dependent.

Methods: Tertiary branches of the rat mesenteric artery were isolated from male Sprague-Dawley rats, which were aged 9-15 weeks and weighed between 308 and 459 g. These vessel segments were pressurized in an arteriograph chamber via a blind sac procedure. MT was established in isolated mesenteric resistance vessels by increasing intraluminal pressure from 5 to 105 mm Hg in 15-mm increments in 4-(2-Hydroxyethyl) piperazine-1-ethanesulfonic acid (HEPES) physiological solution with calcium [1.8 mM]. The same vessel then underwent a second round of pressurization in calcium-free HEPES solution and ethylene glycol tetraacetic acid (EGTA, 2 mM). Control vessels underwent pressurization in HEPES physiological solution with calcium (1.8 mM) mimicking in time each corresponding experimental trial. The functional presence of endothelium in the preparation was confirmed by the addition of acetylcholine (ACh) to these control vessels. In a separate pressurization experiment conducted at 75 mm Hg, the effect of a physiological concentration of TES [20 nM] on MT was determined. The effect of TES (20 nM) on MT was examined in the absence and presence of various antagonists. The effect of exogenous DHT on MT was also determined. Corresponding vehicle and time control experiments were conducted for agonist and antagonist experiments. An air bubble was passed through the preparation to functionally remove the endothelium, which was confirmed by lack of vasodilation to ACh [70 micromolar (μM)]. Immunofluorescent microscopy studies were conducted to determine the presence of the enzyme

5α-reductase type 2 in the endothelium and smooth muscle of the tertiary branch of the mesenteric artery. Images were produced using a General Electric Healthcare Delta Vision Deconvolution Microscope System. The tissue was co-stained with the nuclear specific stain, 2−(4−Amidinophenyl)−6−indolecarbamidine dihydrochloride (DAPI), which was used to identify the endothelial and smooth muscle layers. The distinction between the vascular cell layers was observed by noting that the endothelial cell nuclei were oriented in the direction of blood flow, whereas smooth muscle nuclei were arranged perpendicular to the direction of flow.

Data Analysis: Data are shown as the mean ± standard error of the mean (SEM). Paired *t* test, unpaired *t* test, and ANOVA analysis followed by Tukey's multiple comparison test were used for statistical analysis where appropriate. A *P* value of less than .05 was accepted as a significant difference for all experiments. The percent MT was calculated as 1−(active/passive diameter) × 100. Statistical analyses were performed using Prism Software 6.0.

Results: MT was established in the tertiary branch at 60, 75, 90 and 105 mm Hg. Maximum MT averaged 12.45 ± 1.30%. In vessels with MT, ACh (70 μM) produced a significant increase in the mesenteric resistance vessel diameter, verifying the presence of a functional endothelium. TES (20 nM) increased microvessel diameter and thus decreased MT, but only in the presence of a functional endothelium. Inhibition of NOS with 10 μM Nω- nitro-L-arginine methyl ester (L-NAME) reversed TES-induced modulation of MT. Pretreatment with either 10 μM flutamide (androgen receptor antagonist) or 10 μM finasteride (5α-reductase inhibitor) completely inhibited TES-induced vasodilation, whereas 10 μM ICI 182,780 (estrogen receptor antagonist) did not affect TES-induced vasodilation of MT. Exogenous DHT (20 nM) significantly increased vessel diameter and thus decreased MT. Expression of the enzyme 5α-reductase type 2 which converts TES to DHT was found in the endothelium and smooth muscle of the tertiary branch.

Conclusion: Physiological concentrations of TES cause vasodilation of MT in resistance microvessels. This vasodilation is androgen receptor-mediated, requires nitric oxide production, and is microvascular endothelium-dependent. Moreover, this androgen response appears to be mediated primarily by metabolism to DHT because of the following: (1) TES is metabolized to DHT via the enzyme 5α-reductase; (2) A 5α-reductase inhibitor eliminates the vasodilatory effect of TES on MT; (3) Exogenous DHT causes vasorelaxation of MT; and (4) Expression of the enzyme 5α-reductase type 2 was detected in the endothelium and smooth muscle of the tertiary branch. In contrast, estrogen appears to have no role in TES-induced modulation of MT. To our knowledge, this is the first report to show the total dependence of TES-induced vasodilation in a resistance microvessel on local conversion to DHT. These findings strongly suggest a novel mechanism whereby androgens can modulate blood pressure, and shed new light on how hormonal supplementation may modulate cardiovascular function.

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B8—Chronic Diseases & Conditions

Hypobromous acid and oxidation of human high-density lipoprotein

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Inflammation is centrally involved in the pathogenesis of cardiovascular disease (Libby et al. *J Am Coll Cardiol.* 2009;54:2129-2138). As part of the inflammatory process, myeloperoxidase (MPO) released from neutrophils binds to high-density lipoprotein, where it forms a complex with apolipoprotein A1 and paraoxonase-1 (PON1), a cardio-protective enzyme (Huang et al. *J Clin In-*

vest. 2013;123:3815-3828). As part of this complex, MPO and PON1 reciprocally modulate one another's activity, and recent studies have demonstrated that a high plasma MPO:PON1 ratio is associated with increased risk for cardiovascular events (Enami et al. *Acta Med Iran.* 2013;51:365-371; Yunoki et al. *Atherosclerosis*. 2013;231:308-314; Haraguchi et al. *Atherosclerosis*. 2014;234:288-244). Under physiological conditions MPO catalyzes oxidation of chloride (Cl-), bromide (Br-), and thiocyanate (SCN-) to form pro-oxidant hypochlorous, hypobromous, and hypothiocyanous acids (HOCl, HOBr, and HOSCN, respectively; Klebanoff. *J Leukoc Biol*. 2005;77:598-625). Prior studies in our laboratory and others have demonstrated that both HOCl and HOSCN promote loss of HDL's cardio-protective PON1 enzyme activity (Gugliucci. *Clin Chem Lab Med* 2008;46:1403-1409; Kunes et al. *Nutr Res* 2009;29:114-22; Kosmach and Lynch. *J Am Osteopath Assoc.* 2011;111:506). However, despite several studies documenting the potential for formation of HOBr at vascular sites of inflammation (Senthilmohan and Kettle. *Arch Biochem Biophys*. 2006;445:235-44; Chapman et al. *Biochem J*. 2009;417:773-781; Li et al. *Free Rad Biol Med*. 2012;53:1954-1959), no one has yet investigated the possibility that this pro-oxidant might also affect HDL's PON1 activity.

Hypothesis: HOBr, like HOCl and HOSCN, will cause loss of PON1 activity from plasma HDL.

Methods: Freshly prepared HOBr (Wagner et al. *Free Rad Res*. 2004;38:167-175) was added to 5-fold diluted human plasma and, after 15-minute incubation, HDL's PON1 phosphotriesterase and lactonase activities were assayed using standard spectrophotometric procedures (Mackness et al. *Circulation.* 2003;107:2775-2779; Khersonsky et al. *Biochemistry.* 2005;44:6371-6382); plasma incubated with HOCl was used as a positive control. Effects of cysteine, vitamin C, and taurine on HOBr-mediated loss of PON1 activity were also investigated. Use of deidentified human plasma was approved by Midwestern University's Institutional Review Board.

Data Analysis: Results are reported as means ± SEM for pooled data from 3 independent experiments. ANOVA, with multiple comparison post-tests, was used to determine significant differences ($P<.05$).

Results: Consistent with prior observations, addition of HOCl to plasma was associated with loss of PON1 phosphotriesterase and lactonase activities. Thus, following addition of HOCl (2000 uM) to plasma, PON1 phosphotriesterase activity was observed to be 71±3 % normal while lactonase activity was 62±0 % normal ($P<.001$ compared with untreated control plasma). At the same concentration, HOBr also caused loss of PON1 activities, with phosphotriesterase and lactonase activities declining to 53±6 and 48±8 % normal, respectively ($P<.001$ compared with untreated control plasma). Similar results were observed at other concentrations of HOCl and HOBr (100-6000 uM). Interestingly, at most of these concentrations, addition of HOBr led to significantly greater loss of PON1 activity from plasma compared with HOCl ($P<.05$). In subsequent experiments, it was observed that addition of either cysteine (1000 uM) or vitamin C (100-1000 uM) to plasma attenuated the loss of PON1 activity seen following exposure to HOBr ($P<.01$). However, the protective effect of cysteine appeared to be a non-specific amino acid effect, rather than thiol-mediated, since a similar effect was observed for methionine. As reported by others, taurine (1000 uM) prevented loss of plasma PON1 during exposure to HOCl with phosphotriesterase activity remaining at 82±6 % normal, compared with 66±3 for plasma exposed to HOCl without taurine ($P<.05$). Interestingly, however, taurine, at the same concentration (1000 uM), exacerbated loss of plasma PON1 activity during exposure to HOBr, with phosphotriesterase activity declining to 47±1 normal compared with 67±1 % normal for taurine-free plasma ($P<.001$). Similar contrasting effects of

taurine on HOCl/HOBr-mediated loss of PON1 lactonase activity were also observed.

Conclusion: Our results clearly demonstrate that HOBr, like HOCl, promotes loss of the cardioprotective PON1 enzyme activity from HDL within the biological matrix of human blood plasma. Our observation that exposure of plasma HDL to HOBr caused greater loss of PON1 activity than was seen with HOCl is consistent with the known relative reactivity of these pro-oxidants (Rayner et al. *Free Rad Biol Med.* 2014;71:240-255). Similarly, the protective effects of amino acids, such as cysteine and methione, and also vitamin C against HOBr-mediated loss of PON1 activity are in agreement with results from prior studies showing similar effects of these compounds against HOCl-mediated oxidation of lipoproteins (Carr et al. *Free Rad Biol Med.* 2001;31:62-72; Pattison and Davies. *Curr Med Chem.* 2006;13:3271-3290; Rayner et al). Among our results, however, the most interesting is the contrasting effect of taurine on HOCl- vs HOBr-mediated loss of PON1 activity. Taurine is an amino acid released from neutrophils during inflammation and it is generally regarded as having antioxidant and anti-inflammatory properties (Marcinkiewicz and Kontny. *Amino Acids.* 2014;46:7-20). However, whereas inclusion of taurine, like cysteine and methionine, prevented loss of PON1 activity from plasma HDL during exposure to HOCl, it exacerbated HOBr-mediated loss of PON1 activity. Although this pro-oxidant effect of taurine might initially seem counterintuitive, at least 1 other study has reported a similar result. In this study, taurine prevented loss of antibacterial activity from lysozyme during exposure to HOCl, but worsened loss of antibacterial activity during exposure to HOBr (Petronio and Ximenes. *Protein Pept Lett.* 2013;20:1232-1237). This effect was shown to be mediated through oxidation of tryptophan residues within the active site of lysozyme by taurine bromamine. Interestingly, studies of the active site of PON1 have demonstrated that, like lysozyme, tryptophan residues also play a critical role in the biochemical mode of action of this enzyme (Josse et al. *J Appl Toxicol.* 2001;21:S7-S11). Future studies will investigate whether a similar mechanism is responsible for the effect of taurine on inactivation of PON1 by HOBr. Overall, our results may have important implications for understanding how modification of HDL during inflammation contributes to heart disease.

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B9—Chronic Diseases & Conditions

Treatment of Drug-Resistant Breast Cancer Cells With a Novel Lipid-Based Nanocarrier Formulation Containing Genistein and Paclitaxel

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Introduction: Failure of chemotherapy due to drug resistance is responsible for numerous deaths every year. The major molecular mechanism for drug resistance in cancer cells is the upregulation of the cell surface drug efflux pump P-glycoprotein. Strategies that involve effective drug delivery to cancer cells while inhibiting the action of P-glycoprotein offer an opportunity to overcome drug resistance and effectively treat cancer. Formulations of a novel lipid-based nanocarrier containing the commonly used chemotherapeutic agent Paclitaxel along with the P-glycoprotein inhibitor Genistein were tested for their ability to effectively deliver drugs to drug resistant breast cancer cells in this study.

Hypothesis: Drug-resistance in breast cancer cells can be overcome by the use of lipid-based nanocarriers to effectively deliver a combination of Paclitaxel and Genistein.

Materials and Methods: Lipid nanocarrier were prepared using a combination of vitamin E, argan oil, solutol, water, and either Paclitaxel or Genistein in an ethanol solution. The alcohol was removed by evaporation and the resulting particles were reconstituted and characterized. Cultured breast cancer MCF-7 (Paclitaxel-sensitive) and MCF-7Res (Paclitaxel-resistant) cells lines were exposed to various doses of Paclitaxel and nanocarriers formulations consisting of Paclitaxel and/or Genistein in varying ratios. Cell viability was assessed and the IC50 was determined for each formulation.

Results: Delivery of Paclitaxel via lipid nanocarriers resulted in a significant reduction in the IC50 as compared with treatment without the nanocarriers in both MCF-7P and MCF-7 R cell lines. When these cells were exposed to nanocarriers consisting of Paclitaxel mixed with nanocarriers consisting of Genistein, they demonstrated a further reduction in IC50 or increased cell death. The calculated combination indices show a strong synergistic effect of Paclitaxel and Genistein containing nanocarriers when mixed in 2:1 ratios. Nanocarriers by themselves or with Genistein alone did not show significant toxicity toward either cell line.

Discussion: Lipid-based nanocarriers offer superior drug delivery and can be used for drug-synergism to overcome drug resistance in breast cancer cells. While the molecular mechanisms responsible for enhanced drug delivery and observed synergistic effect of Paclitaxel and Genistein need further investigation, this study offers great hope for the development of novel treatments to overcome chemoresistance in breast cancer patients.

B10—Chronic Diseases & Conditions

Sanguinarine and TRAIL Combination Therapy for Treatment of Human Papillomavirus–Infected Cervical Cancer Cells

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Introduction: Infection of normal cervical cells by the human papillomavirus (HPV) can transform these cells into radiation and chemotherapy-resistant cancerous cells. Induction of apoptosis in the transformed cells is a key strategy in successfully treating HPV-induced cervical cancer. TRAIL (tumor necrosis factor-related apoptosis-inducing ligand) has been shown to selectively induce apoptosis in cancer cells by binding to death receptors and activating extrinsic pathways for apoptosis. However, certain cervical cancers, such as the cultured cell line SiHa, are remarkably resistant to TRAIL. In this study, we have explored the use of sanguinarine, an extract from the plant *Sanguinaria canadensis*, to sensitize SiHa cells to TRAIL. Sanguinarine has been shown to induce apoptosis in cancer cells by activating multiple cell death pathways, including the upregulation of death receptors via reactive oxygen species.

Hypothesis: Because sanguinarine may lead to oxidative stress and upregulation of death receptors, we hypothesize that it can potentially sensitize SiHa cells to TRAIL and lead to apoptosis.

Methods: Cultured SiHa cells were exposed to sub-lethal doses of sanguinarine in combination with TRAIL. Cell viability changes were assessed, and induction of apoptosis was further investigated by assays for caspase activation and the production of reactive oxygen species. Flow cytometry was performed to measure upregulation of death receptors 4/5.

Results: Sanguinarine treatment led to a significant increase in oxidative stress and the upregula-

tion of death receptors in SiHa cells. When combined with TRAIL, sanguinarine led to the induction of apoptosis via activation of the caspase cascade and resulted in a significant reduction in SiHa cell viability.

Conclusion: The observed synergistic effect of sanguinarine and TRAIL on SiHa cells is promising for the treatment of cervical, and possibly other, HPV-induced cancers. Oxidative stress caused by sanguinarine seems to play a central role in this synergy. The molecular pathways that link reactive oxygen species and the upregulation of death receptors need further investigation. This knowledge will enable us to devise more effective treatments for patients with this devastating disease.

B11—Chronic Diseases & Conditions

Effect of Smad3 Deficiency on Human Endothelial Cells

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Introduction: Increased cardiac levels of transforming growth factor β (TGF-β) superfamily ligands have been detected both in patients and animal models of heart failure, and their levels are positively correlated with the severity of the condition. We have previously detected microvascular defects in animal models of heart failure. Our in vitro studies using human cardiac endothelial cells have shown that a TGF-β pathway inhibitor increases endothelial cell proliferation and vascular network formation. Cellular effects of TGF-β are known to be mediated by activation of both canonical and non-canonical pathways leading to the activation of Smad2/Smad3 transcription factors and multiple mitogen-activated protein kinase (MAPK) pathways.

Hypothesis: We hypothesize that endothelial Smad3 activity suppresses the formation of vascular networks. Therefore, Smad3 deficiency in endothelial cells will then enhance their angiogenic potential.

Methods: We created a stable human umbilical vein endothelial cell line (HUVEC) expressing Smad3 short hairpin ribonucleic acid (shRNA). Smad3 knockdown was validated using immunoblotting and quantitative polymerase chain reaction (qPCR). Quantitative PCR was also utilized to detect differences in gene expression between control and Smad3-deficient cells treated with or without TGF-β2. Endothelial cell migration was studied using the Platypus assay. Both cell lines were treated with or without TGF-β2 and were assessed for proliferation. Lastly, proliferation of these cells in co-cultures of HUVEC with human cardiac fibroblasts was quantified using Ki67 as a proliferation marker.

Results: We showed that TGF-β2 reduced proliferation in control but not in Smad3-deficient HUVEC. Similarly, we observed increased proliferation of the Smad3 knockdown cell line after 1 day in co-culture with cardiac fibroblasts. Gene expression analysis revealed that TGF-β2 increased the abundance of messenger RNAs (mRNAs) for cyclin-dependent kinase inhibitors CDKN1A and CDKN1B (p21 and p27 proteins, respectively) in control but not in Smad3 deficient endothelial cells. Additionally, migration on fibronectin was substantially enhanced in the HUVEC line with Smad3 knockdown.

Conclusions: Smad3-deficient endothelial cells were resistant to the TGF-β2–induced suppression of proliferation. These cells exhibited enhanced migration and decreased expression of cyclin-dependent kinase inhibitors. We conclude that Smad3 deficiency will likely increase the angiogenic potential of endothelial cells. This hypothesis will be further tested in vascular sprouting experiments on aortic explants from Smad3 knockout mice.

Funding: This project was supported in part by the Kansas City University Office of Research Summer Student Research Fellowship grant to Nicole Cabalo.

B12—Chronic Diseases & Conditions

Cellular and Molecular Mechanisms of Alzheimer's Disease Pathogenesis: The Role of Autoantibodies in Mediating β-Amyloid$_{42}$ Internalization and Plaque Formation

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Given the contentious nature of an underlying mechanism for the pathoetiology of Alzheimer disease (AD), it is of utmost importance to understand how the proposed hallmarks that define the disease develop and progress. The presence of extravasated plasma components such as immunoglobulin G (IgG) antibodies and amyloid peptides have been widely reported in the cerebral cortex of AD brains. Moreover, the amyloid plaques that build up in the brain regions implicated in AD consist of a conglomerate of proteins, namely β-amyloid$_{42}$ (Aβ_{42}) and cellular debris. Overwhelming evidence in current basic and translational sciences have elucidated a defective blood-brain barrier in AD brains, pointing toward this breach as a means by which peripheral blood components, like IgG and Aβ_{42}, enter the brain parenchyma and bind to neurons. We hypothesize the possible role of these plasma components in mediating endocytosis and its link to intraneuronal Aβ_{42} deposition and the generation of amyloid plaques in AD brains.

Our research efforts have focused on the pathways by which Aβ_{42}-burdened neurons undergo internalization and subsequent cell death to ultimately contribute to the formation of the pathological plaques observed throughout the implicated regions on autopsy. The objective of this project is to understand the generation of amyloid plaques, particularly Aβ_{42} in AD brains. Specifically, the aims addressed are as follows: to determine if autoantibody-induced endocytosis facilitates internalization of Aβ_{42} into neuronal cells and subsequent amyloid plaque formation; to assess the bivalency of autoantibodies as a necessary component for cross-linking of neuronal surface proteins; and to test if receptor stripping occurs, and if so, via classic endocytosis-lysosomal pathway.

Studies in our laboratory have been directed at illustrating the role between the widely reported IgG-positivity of neurons in these regions of AD pathology among the coincident amyloid plaques nearby. Current literature has shown Aβ_{42} to bind with highest affinity to the α7 subtype of the nicotinic acetylcholine receptor (α7nAChR). This surface protein acts as the cognate receptor which determines the specificity of neuronal subtype (cortical pyramidal neurons) predisposed to Aβ_{42}-neurotoxicity throughout disease development.

Immunohistochemistry was used to investigate the relative distributions of Aβ_{42}, α7nAChR, human IgG, and cathepsinD in AD and age-matched, non-demented control brains. Differentiated SH-SY5Y human neuroblastoma cells were used to test the possibility that IgG autoantibodies can elicit intraneuronal Aβ_{42} accumulation through induction of endocytosis. Internalization of surface proteins and subcellular trafficking of Aβ_{42} was visualized with confocal immunofluorescence microscopy and image analysis software. Cells were treated for up to 72 hours with antibodies against selected neuronal surface antigens or with serum, whole- or purified-IgG, from either AD or controls, in conjunction with Aβ_{42}. An array of inhibitors was used to test the requirement for endocytosis. Lastly, monovalent antibodies were used to determine the dependence of endocytosis on the cross-linking capacity of the normally bivalent IgG.

Pyramidal neurons in AD brains with Aβ_{42} immunolabeling also showed IgG immunoreactivity. A marked increase in neuronal cathepsinD immunostaining reflected expansion of the lysosomal system in these cells in the AD cortex compared with that of controls. Consecutive section immunohistochem-

istry suggested co-localization of α7nAChR and $A\beta_{42}$ to compartments within the endocytic pathway. IgG from human sera had an affinity for differentiated SH-SY5Y cells, but not their undifferentiated counterparts, alluding to the presence of autoantibodies directed toward neuronal surface antigens. Furthermore, coincident treatment with $A\beta_{42}$ enhanced the autoantibody-mediated endocytosis. Using different fluorophores, we also demonstrated a co-localization between IgG, α7nAChR, and $A\beta_{42}$ that was temporally related to the early endosomal marker, Rab11, and at later time points to the late endosomal/early lysosomal marker, LAMP-1. Lastly, results using monovalent antibodies suggest that the cross-linking capacity of neuron-binding antibodies may play a key role in inducing endocytosis of $A\beta_{42}$ in these cells.

In conclusion, using a human neuroblastoma cell line, experiments were conducted to test the endocytic mechanism by which $A\beta_{42}$ enters vulnerable neurons, forms aggregates, and effectively induces neurotoxicity. We have demonstrated autoantibody-mediated endocytosis and accumulation of neuronal surface proteins, serum IgG, and $A\beta_{42}$ within the lysosomal compartment of SH-SY5Y cells as integral players in this phenomenon. Accumulation of these serum components within neurons is thought to disrupt their homeostasis, ultimately leading to the amyloid plaque development. Preventing plasma extravasation by restoring the structural and functional integrity of the blood-brain barrier may curtail initiation and progression of AD pathology. Our research has demonstrated the utility in autoantibodies present in the serum at inducing and enhancing $A\beta_{42}$ internalization, effectively describing the role in which these enigmatic immune effector molecules work to bring about the amyloid plaques associated with AD pathology.

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B13—Chronic Diseases & Conditions

Herpes Simplex Virus (HSV) Modulation of *Staphylococcus aureus* and *Candida albicans* Adherence to HeLa cells

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Hypothesis: HSV-1 or HSV-2 entry into HeLa cells affects subsequent adherence of *Staphylococcus aureus* and *Candida albicans*.

Background: Colonization sites on the oral and genital mucosa are shared by HSV-1, HSV-2, *S aureus* and *C albicans*; however, their interactions are poorly understood. The continuous production and subsequent entry of virus into cells can occur clinically. This would result in altered expression of potential receptors for adherence, the initial step in biofilm formation, of other pathogens, such as *S aureus* and *C albicans*. The focus of this study is to determine the effect non-replicating HSV-1 and HSV-2 have on adherence of *S aureus* and *C albicans* to HeLa cells.

Methods: HeLa cells (85% confluence, 96 well plate) infected for 3 hours with HSV-1 gL86 or HSV-2 333gJ- (MOI 100) were incubated (30 minutes; 37°C; 5% CO_2; 10:1 organism: HeLa cell ratio; n=16) with *S aureus* ATCC25923 (18 hours; mannitol salts; 37°C) and/or *C albicans* (yeast or germ tube; 48 hours; Fungisel; 37°C). Germ tubes were prepared after 3 hr incubation in FBS. Post-incubation, the monolayers were washed (3x; PBS), lysed (RIPA) and lysate was plated onto Fungisel and mannitol salts media for standard viability colony count (CFU/mL).

Data Analysis: All assays were performed with an n=8 and repeated at least once. Data were analyzed by ANOVA with post-hoc analysis by Student-Newman-Keuls Multiple Comparisons Test where appropriate (GraphPad InStat).

Results: HSV-1 and HSV-2 decreased the level of HeLa-associated *S aureus* as compared with virus-free HeLa cell controls (0.59 and 0.79 of control, respectively; $P<.05$). In contrast, HSV-1 and HSV-2 enhanced cell association of *C albicans* germ tube and yeast forms (1.47 and 1.28 of control, respectively; $P<.05$). Co-incubation of *S aureus* and yeast enhanced inhibition of staphylococcal biofilm with HSV-1–infected cells (0.26 of controls; $P<.05$) and HSV-2 infected cells (0.59 of virus-free controls; $P<.05$). *C albicans* germ tubes also decreased *S aureus* binding as compared with control for both HSV-1– and HSV-2–infected HeLa cells (0.33 and 0.55 of control, respectively; $P<.05$). The yeast and germ tube biofilm pattern in the presence of *S aureus* was more variable with yeast biofilm levels on HSV-1–infected cells decreased (0.71 of control; $P<.05$), while germ tube biofilm level significantly increased (1.81 of control; $P<.05$). Both germ tube and yeast biofilm levels in the presence of *S aureus* on HSV-2–infected cells were slightly decreased to unaffected (0.86; $P<.05$ and 1.07, respectively).

Conclusion: Our model suggests that HSV has an antagonist interaction with *S aureus* that is either unaffected or partially reversed dependent on the herpes virus tested and fungal morphologic form. Future research needs to be conducted to further understand their interactions.

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B14—Chronic Diseases & Conditions

Methyl-Accepting Chemotactic Proteins' (MCPs) Role in *Escherichia coli* Human Insulin Receptor Expression and Chemotaxis

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Hypothesis: Previously reported methyl-accepting chemotaxis proteins (MCPs) function as the receptor for human insulin on *Escherichia coli* cells.

Introduction: Insulin is conserved in function, structure, chemical properties, and bioavailability across the taxonomic kingdoms. Both glucose and insulin can be present in the urine of individuals with diabetes mellitus. Previous studies have shown that human insulin coordinates with glucose the expression of directional movement and biofilm formation in *E coli*. As a significant cause of urinary tract infections, understanding the mechanisms involved in *E coli* translocation from the colon to the bladder could aid in development of new strategies in the prevention of urinary tract infections. The cell signaling pathway(s) for insulin in *E coli* is still unknown. We have previously shown that insulin, in the absence of glucose, binds at the poles of *E coli* cells in proximity to reported chemotaxis receptor proteins, the MCPs. The focus of this study is to determine the MCP to which insulin binds.

Methods: The hypothesis was addressed using a 2-pronged approach.

FITC-insulin staining: Overnight cultures of E coli strains RP437 (parent), UU1250 (MCP null – *Δaer, tar-tap, trs, trg*), and UU2612 (MCP null – *Δaer, tar-tap, trs, trg*) were grown in yeast nitrogen base with 1% peptone (YNBP) to mid-logarithmic and stationary growth phases in the absence or presence of 0.5% glucose. At mid-logarithmic and stationary growth phases, samples for microscopy were removed, fixed (methanol), and stained with fluorescein isothiocyanate (FITC)-insulin and DAPI

(FITC-insulin, 25 µg/mL; DAPI, 20 µg/mL; 30 minutes, 37°C; Sigma-Aldrich). FITC-insulin/DAPI-stained cells were examined by epi-fluorescent microscopy (Nikon). Cells were rated on a scale of +1 to +4 for degree of fluorescence and bipolar, punctate, or even for pattern of insulin binding. Triplicate samples were examined and results expressed as percentages of total number of cells examined (minimum 300 cells examined per sample).

Chemotactic Capillary Assays: Responses of RP437 and UU1250 to reported peak chemotactic glucose concentration (10-3 M) and insulin (2, 20, or 200 µU/mL Humulin R insulin) were determined by the standard chemotactic capillary assay. Strains grown in YNBP to mid-logarithmic growth phase (shaken at 37°C, O.D. = 0.2) were harvested and washed twice (1750 rpm; 30 minutes; chemotaxis buffer, 10^{-2} M K_2HPO_4, 10^{-3} M $MgSO_4$, 10^{-3} M $(NH_4)_2SO_4$, and 10^{-4} M EDTA, pH 7). The final cell pellet was suspended in chemotaxis buffer to an absorbance600nm of 0.14. Capillary tubes (10 µL) filled with either chemotaxis buffer alone or with glucose and/or insulin were placed in 0.5 mL of the washed cell suspension. After incubation (30 minutes; 37°C) capillary tubes were washed, crushed, and number of CFU/capillary determined by standard plate count.

Data Analysis. All assays were performed with an n=8 and repeated at least once. Data were analyzed by ANOVA with post-hoc analysis by Student-Newman-Keuls Multiple Comparisons Test where appropriate (GraphPad InStat).

Results: FITC-insulin staining: Growth in the presence of glucose resulted in the majority of RP437, UU1250, and UU2612 cells displaying an even to punctate pattern of FITC-insulin binding, regardless of growth stage (mid-logarithmic growth stage, 97%, 97%, and 98%, respectively; stationary growth stage, 85%, 94%, and 94%, respectively). In the absence of glucose, this pattern of FITC-insulin binding was also observed for mid-logarithmic phase RP437, UU1250, and UU2612 cells (93%, 91%, and 93%, respectively). However, RP437, UU1250, and UU2612 stationary phase cells grown in YNBP alone displayed a predominantly bipolar pattern of FITC-insulin binding (62%, 65%, and 68%, respectively).

Chemotaxis Determination: The behavioral response of RP437 (parent) and UU1250 (universal MCP deletion strain) was that of significant (P<.01) chemoattraction toward the positive control, ie, glucose (2334 + 141.2 and 3740 + 295.7 CFU/capillary, respectively) as compared with the buffer control (170 + 22.9 and 2,670 + 89.4 CFU/capillary, respectively). However, the response to all concentrations of insulin tested (2, 20, or 200 µU/mL) for RP437 (173.3 + 43.1, 166.7 + 30.4, 213.3 + 44.9 CFU/capillary, respectively) and UU1250 (2428 + 184.2, 3028 + 165.9, 2893.3 + 121.4 CFU/capillary, respectively) was similar to that measured for capillary tubes containing buffer alone. Thus, neither the parent nor MCP null strain were able to chemotactically respond to insulin, a chemorepellent in wild type *E coli*.

Conclusions: Similar to *E coli*'s response to glucose, these findings indicate that expression of insulin receptors and chemotactic reaction to insulin are independent of each other. Furthermore, these results provide indirect evidence that the insulin receptor in *E coli* is distinct from the known MCPs. Further studies are ongoing to characterize the human insulin binding site(s) on *E coli*.

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B15—Chronic Diseases & Conditions

The Role of Insulin and Glucose on *Escherichia coli* Survival and Development of Persister Populations

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Hypothesis: We hypothesize that insulin with glucose affects *Escherichia coli* persister population development and survival.

Introduction: Formation of persister cells in a microbial population is a survival mechanism. Microbial persister cells are a dormant phenotype physiologically programed for enhanced survival in the absence of a carbon source and/or the presence of antibiotics. Glucose depletion can promote the formation of the *E coli* persister phenotype. Our previous studies have shown that human insulin and glucose together affect *E coli* metabolism and behavior. The focus of this study is to determine whether insulin affects glucose promotion of the persister phenotype.

Methods: *E coli* survival was measured over time (days) after growth (37°C, shaking incubation) in LB medium alone or with glucose 220 mg/dL and/or insulin (Humulin R; 20 and 200 µU/mL). Survival was measured by standard plate count (CFU/mL). The levels of antibiotic-resistant persister cells present were determined. *E coli* grown for 9 days under the various conditions was exposed to MIC (minimum inhibitory concentration) levels of Bactrim antibiotic (4/76 µg/mL sulfamethoxazole:trimethoprim ratio; 108 CFU/mL PBS initial concentration). After addition of drug, cell viability (CFU/mL) was determined by standard plate count over time. Controls consisted of cell viability over time in antibiotic-free PBS.

Data Analysis: Assays were performed in triplicate and repeated once. Data were analyzed by ANOVA with post-hoc analysis by Student-Newman-Keuls Multiple Comparisons Test where appropriate (GraphPad InStat).

Results: By day 3, growth in LB media alone resulted in a 10% decline in the number of viable bacteria, which was similar to that measured for glucose supplement alone (14% decline CFU/mL). The presence of insulin, with or without glucose from day 0 to day 3 resulted in the largest decline in viable bacteria ranging from an 18% decline in viable bacteria (insulin 20 µU/mL) to 39% decline in viability (insulin 200 µU/mL and glucose 220 mg/dL). From day 3 to day 9, the presence of glucose alone significantly protected *E coli* from viability loss (5% decrease in viability) as compared with insulin alone (18% to 19% viability decrease; 20 and 200 µU, respectively) or LB medium alone (28% decline in CFU/mL). Glucose also significantly ameliorated loss of viability in presence of insulin (20 and 200 µU/mL; 9% loss of viability). In addition, the combination of glucose and insulin resulted in a resuscitation of the population from days 7 to 9 with a 1.4- and 1.6-fold increase in cell population (glucose and insulin, 200 and 20 µU/mL, respectively).Bactrim resistance, an indicator of the presence of persister cells, was also affected by the presence of glucose and/or insulin. At day 9 of growth, antibiotic killing of *E coli* was enhanced by the combination of glucose and insulin (20 µU/mL, 85%; 200 µU/mL, 75% population decline at 6 hours exposure to drug, respectively) as compare to glucose alone (61% population decline), insulin alone (61%, 20 µU/mL; 64%, 200 µU/mL, population decline, respectively), or LB alone control (55% population decline). After 24 hours antibiotic exposure, significantly more 9-day-old bacteria remained in the population grown in the presence of glucose alone (17% of T_0 CFU/mL), as compared with all other growth conditions (<1% of cells present at T_0).

Conclusion: Insulin is protective against the development of persister cells in an aerobic planktonic population. In contrast, glucose at a physiologically relevant concentration can overcome some of these protective effects. These findings may begin to ex-

plain the occurrence of treatment failures, as evidenced by relapses in urinary tract infections for individuals with diabetes.

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B16—Chronic Diseases & Conditions

Vaginal Estrogen Delivery in a Rodent Model of Vulvovaginal Atrophy With Menopause

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Introduction: Menopausal women experience many bodily changes, including vulvovaginal atrophy, as their estrogen levels decrease. These changes can have a profoundly negative impact on a woman's physical, mental, and sexual health. Vaginal delivery of estrogen is currently recommended for treating vulvovaginal atrophy with menopause to avoid systemic hormone exposure. Although it has been demonstrated that local delivery has a restorative effect on the vaginal mucosa, little is known about its effect on other aspects of vaginal physiology. Furthermore, the effect of local estrogen delivery on peripheral tissues is incompletely understood.

Objective: This is a preliminary study to develop a protocol for vaginal estrogen delivery in a rodent model of menopause. The goals of this study are to determine the following: (1) the effect of local estrogen delivery on vaginal structure and function and (2) if vaginal estrogen delivery results in systemic estrogen exposure.

Materials and Methods: Three-month-old female Sprague-Dawley rats were ordered from a commercial supplier as either bilaterally ovariectomized (OVX) or sham ovariectomized (SH). SH rats were given vaginal vehicle cream and OVX rats were given vaginal vehicle cream (VV), vaginal 0.002% (low estrogen, LE) or 0.004% (high estrogen, HE) 17- β estradiol cream, or no vaginal treatment for a period of 17 days; n=3 for each group. Treatment groups were designated OVX receiving LE (OVXLE), OVX receiving HE (OVXHE), OVX receiving VV (OVXVV), OVX receiving no treatment (OVX), and SH receiving VV (SHVV). Weights were recorded daily and vaginal smears were obtained approximately every 3 days in each animal to track their estrus cycle and epithelial cell changes. Once the treatment period concluded the uterus and vagina were harvested, weighed, and paraffin embedded for subsequent histochemical and immunohistochemical analysis. Vaginal tissue slices were stained using Masson's Trichrome Stain (MTS) and hematoxylin and eosin stain (HE stain). Slides also underwent immunohistochemical (IHC) staining of α-actin, a smooth muscle marker.

Data Analysis: Data were analyzed utilizing SigmaPlot software. One way analysis of variance (ANOVA) tests were performed and if significance was found ($P<.05$), post hoc pairwise multiple comparisons were made between groups utilizing the Tukey test of mean separation. One way analysis of variance on rank (ANOVA on Rank) tests were performed on data that failed to pass the normality or equal variance test. A mean separation test (Tukey test) was performed if significance was indicated in the ANOVA on Rank test.

Results: Vaginal estrogen delivery resulted in dose-dependent changes in body weight over the treatment period between OVXHE- and OVXLE-treated animals ($P<.05$). Significant differences were also found when comparing total body weight changes between the following groups: OVXHE vs OVX ($P<.001$); OVXHE vs OVXVV ($P<.001$); OVXLE vs OVX ($P<.02$); and OVXLE vs OVXVV ($P<.01$). No significant differences were found between OVX and OVXVV treated animals ($P>.65$). Additionally, body weight changes were significantly different between SHVV and OVX treated animals with or without VV administration

($P<.004$). Significant differences in uterine weight at termination were noted when comparing the following groups: OVXHE vs OVX ($P<.001$); OVXHE vs OVXVV ($P<.001$); OVXLE vs OVX ($P<.001$); and OVXLE vs OVXVV ($P<.001$). No significant differences occurred when comparing OVXHE vs OVXLE ($P>.20$) or OVXVV vs OVX ($P>.61$). Furthermore, there was a significant difference in uterine weight between SHVV and OVX treatment groups ($P<.05$), but not between SHVV and OVXVV ($P>.05$) or OVXVV and OVX treatment groups ($P>.05$). Preliminary visual examination of vaginal smears indicate that estrogen administration altered the mucosal environment toward that of an SH-treated animal, with estrogen levels trending toward a dose-dependent behavior.

Conclusion: Uterine and body weight differences suggest that our protocol of vaginal estrogen delivery results in systemic exposure to hormone. Additionally, preliminary findings indicate that delivery of vaginal estrogen cream in our rodent model was effective at reversing atrophy of the vaginal mucosa.

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B17—Impact of OMM & OMT

Analysis of Tissue Hysteresis of Contracted vs Relaxed Muscles

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Background: Tissue texture abnormality is one of the primary characteristics that clinicians palpate to identify somatic dysfunction. While palpation for tissue texture is commonly performed, it is difficult to objectify. Hysteresis is a phenomenon where tissues change in length or tension as a result of loading over time. The purpose of this study was to find a relationship between increasing muscle contraction and muscle tissue hysteresis as measured by the SA-201 (Sigma Instruments), an FDA-approved durometer and treatment device. If such a relationship is found, it would be hopeful that this instrument would help identify changes in muscle tension that can occur with manipulative treatment.

Hypotheses: (1) Tissue hysteresis, as measured by the SA-201, will differ significantly between relaxed and contracted muscles, and also between sexes. (2) The SA-201 will produce consistent, comparable hysteresis waveforms over repeated measurements with strong intraexaminer reliability.

Methods: Six male and 7 female volunteers, aged 21-71 years with a body mass index <25.5 and with no symptoms in the testing sites, participated in the study following institutional reviewbBoard approval. Durometer measurements were made in 5 different skeletal muscle tissues: right bicep brachii, left lateral deltoid, left gastrocnemius, right vastus medialis, and left erector spinae. Durometer measurements consist of 4 unitless values to describe those curves: fixation, mobility, frequency, and motoricity. Fixation is a measure of the peak of the curve and is inversely related to tissue resistance. Mobility is the time to peak divided by the total time and shows relative time of deformation. Frequency represents the total time for tissue deformation and reformation. Motoricity summarizes the integral of the curve. Each muscle was tested under 3 conditions: relaxed, light contraction (LC), and moderate contraction (MC). Different weight machines were used to stimulate contraction for each of the 5 target muscles. Participants were asked to find and report a maximum lifting capacity (MLC) at each machine. Approximately 25% of the MLC was used for the LC condition and 50% of the MLC was used for the MC condition. For each condition, participants were asked to perform an isometric exercise while 1 of the 2 examiners collected 10 repeated measurements using the SA-201.

Data Analysis: To reduce some of the operator-caused variation in measurement, the 2 most extreme of the 10 repeated measurements were

excluded from analysis. Mixed models were used to estimate main and simple interaction effects of muscle and condition on fixation, mobility, frequency, and motoricity. Where significant sex differences existed, further comparisons by sex were conducted. A random effect for participant's muscle was included to allow for correlation among these measurements. Intraclass correlation coefficients (ICCs) were used to estimate the intraexaminer reliability of the 4 durometer measurements among the 8 repeated measurements in unique participant-muscle-condition combinations. Each estimate is reported with its standard error (SE).

Results: In most instances, relaxed muscles revealed significantly higher values for the 4 durometer measurements compared with lightly or moderately contracted muscles (all $P<.05$). Exceptions included mobility in the erector spinae (LC only) and vastus medialis, frequency in bicep and vastus medialis (LC only), and motoricity in erector spinae and vastus medialis (all $P>.10$). When LC and MC conditions were compared, there were only 2 significant differences found; LC fixation was 3.0 (SE 1.1) units greater in bicep and LC frequency was 1.5 (SE 0.6) units less in erector spinae (both $P=.02$). There were no differences in any of the 4 durometer measurements between sexes, with the exception of the erector spinae at MC. Males were 8.3 (SE 2.8), 14.4 (SE 6.1), 3.7 (SE 1.9), and 13.5 (SE 6.3) units greater than females in fixation, mobility, frequency, and motoricity, respectively (all $P<.02$). ICCs were 0.95 (SE 0.01) for fixation, 0.89 (SE 0.01) for mobility, 0.94 (SE 0.01) for frequency, and 0.82 (SE 0.02) for motoricity.

Conclusion: Muscle contraction was shown to influence muscle tissue hysteresis as measured by the SA-201 between most relaxed and contracted muscles but not between muscles with 2 different contraction levels. For the most part, tissue hysteresis curves were not significantly different between sexes. The sex difference in the erector spinae at MC across all 4 durometer measurements was notable. One possible explanation for this difference is that females have greater variation in average muscle fiber size, a trait unique to the erector spinae. Limitations of the study include subjectivity in the estimation of participants' MLCs, human error stemming from variability in preload pressure and angle when using the SA-201, and variability in body composition from the use of a body mass index as an exclusion criterion. Based on the observation that there were no significant changes in the hysteresis curves between the LC and MC condition, it is uncertain whether the SA-201 will be able to identify partial improvement in hypertonicity when tissues respond to manipulative techniques. Further research is needed to clarify this issue. Since the ICC data indicated that the instrumentation had some inconsistency, future studies may be able to improve the instrument's reliability by including better ways to standardize muscle contraction, possibly by using electromyography, reducing human measurement error by using stabilizing equipment to improve consistency in measurements, possibly by using a robotic arm to consistently activate the device, and better defining the study population using body fat percentage rather than body mass index.

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B18—Chronic Diseases & Conditions

Scavenging Reactive Carbonyls After TBI-Induced Lipid Peroxidation: Repurposing an FDA-Approved Drug as an Antioxidant

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Introduction/ Clinical Relevance: Traumatic brain injury (TBI) is diagnosed in 1.7 million civilians

each year in the United States. The military subset-populations have experienced an exacerbated 3-fold increase of TBI diagnoses since the onset of wars in Iraq and Afghanistan. Due to the complex pathophysiology and increasing cost of medical care, the Centers for Disease Control and Prevention (CDC) classified TBI injury as a "major public health epidemic" with costs surging over $16 billion each year and an estimated $56 billion deficit since 2004. Despite multiple clinical trials, no pharmacologic compounds have demonstrated clinically efficacy. The economic burden, devastating morbidity, and limited drug efficacy highlights a profound unmet need in the clinical treatment of TBI. Our intention is to investigate the feasibility of a previously FDA-approved drug for the management of TBI.

Background: Traumatic brain injury is divided into primary and secondary injury. Primary injury is characterized as the initial blunt, mechanical, or sheering force on the brain. Secondary injury cascades act as the major contributing source of brain pathology. Secondary injury cascades can ensue immediately or onset days, weeks, or in some cases, years after trauma. The cascade itself is complex, however, the majority of secondary trauma is either elicited or exacerbated by the generation of free radicals. Free radicals eg, •OH, •NO2, and CO3•- induce the lipid peroxidation (LP) of polyunsaturated fatty acids (PUFA) within cell and organellar membranes. Traditional clinical antioxidant therapies are intended to scavenge the free radicals responsible for either the initiation or propagation of lipid peroxidation (LP). However, targeting free radicals after TBI is difficult due to rapid reaction with other cellular macromolecules, and the resulting limited post-injury time window in which they may be intercepted by a radical scavenging agent. In contrast, our laboratory has begun testing an antioxidant approach that scavenges the final stages of LP (ie, formation of carbonyl-containing breakdown products). By scavenging breakdown products such as the highly reactive and neurotoxic aldehydes (often referred to as "carbonyls") 4-hydroxynonenal (4-HNE) and acrolein (ACR), we are able to prevent the covalent modification of cellular proteins that are largely responsible for posttraumatic neurodegeneration. Without intervention, carbonyl additions render cellular proteins non-functional, which initiates the loss of ionic homeostasis, mitochondrial failure, and subsequent neuronal death. The aldehyde-scavenging compound, Phenelzine (PZ), is an FDA-approved monoamine oxidase inhibitor for clinical treatment of depression and possesses a hydrazine functional group capable of covalently binding neurotoxic carbonyls.

Hypothesis: The hypothesis of this project is that carbonyl scavenging with PZ will exert an antioxidant neuroprotective effect in the traumatically injured rat brain mechanistically related to PZ's hydrazine moiety reacting with the lipid peroxidation (LP)-derived reactive aldehydes 4-hydroxynonenal (4-HNE) and acrolein (ACR).

Methods/Analysis: This project consists of 2 components: in vitro and in vivo experiments. The in vitro experiments explore a proof of principle approach to determine if exogenously applied 4-HNE and ACR are able to inhibit mitochondrial function. Mitochondria were isolated from the cortex of healthy, young adult rat brains and exposed to increasing concentrations of exogenously applied 4-HNE or ACR to determine the suboptimal concentration that can inhibit mitochondrial respiratory function. A PZ pretreatment paradigm was used to determine the concentration that maximally prevents mitochondrial dysfunction and oxidative damage accumulation. The mechanism of PZ function was also explored by testing PZ alongside another MAO-inhibitor: pargyline (PG), which does not possess the scavenging hydrazine moiety. In vitro experiments were essential in determining if PZ is able to scavenge reactive aldehydes and preempt a mitochondrial dysfunction in a quantifiable way. Mitochondrial cohorts exposed to insult, treatment, or both were compared with

non-treatment controls by way of ANOVA. Statistical significance was set at $P<.5$. Our in vitro experiments established proof-of-principle justification to investigate the feasibility of PZ in vivo. In vivo experiments were designed to test the efficacy of a PZ to protect various markers of mitochondrial function and cortical tissue sparing when administered in rats after an actual brain injury. In these experiments, the TBI pathology was the source of the aldehydes 4-HNE and ACR as opposed to in vitro exogenous exposure. The pneumatic piston of the CCI device deformed brain tissue to a depth of 2.2 mm at a velocity of 3.5 m/sec in anesthetized rats stabilized in a stereotactic frame. PZ was administered as either a single subcutaneous injection 15 minutes after injury (10 mg/kg) or as a repeated dosing paradigm. The repeated dosing paradigm extended for 72 hours to match the accumulation time course of 4-HNE and ACR after TBI. Cortical rat mitochondria was isolated and assessed for oxidative damage marker accumulation, mitochondrial respiratory dysfunction, calcium buffering capacity, histological tissue sparing, and cytoskeletal degradation assays. Injury cohorts were compared with non-injury control rats by ANOVA. Statistical significance was set at $P<.05$. In all experiments the sample size was dictated by an a priori power analysis.

Results: Data from our ex vivo experiments demonstrate that the exogenous application of 4-HNE or ACR significantly reduced respiratory function and increased markers of oxidative damage in isolated non-injured rat cortical mitochondria, whereas PZ pretreatment significantly prevented mitochondrial dysfunction and oxidative modification of mitochondrial proteins in a concentration-related manner. Additionally, PZ's neuroprotective scavenging mechanism was confirmed to require the presence of a hydrazine moiety based on experiments with a structurally similar MAO inhibitor, pargyline, which lacks the hydrazine group and did not protect the isolated mitochondria from 4-HNE and ACR. Additionally, our in vivo work demonstrated that subcutaneous injections of PZ after TBI in the rat are able to significantly protect brain mitochondrial respiratory function, decrease markers of oxidative damage, protect mitochondrial calcium buffering capacity, and increase cortical tissue sparing without decreasing neuronal cytoskeletal spectrin degradation.

Conclusions: These results affirm that PZ is capable of protecting mitochondrial function and providing neuroprotection after experimental TBI related to scavenging of neurotoxic LP degradation products. These results are the first to investigate the feasibility of the FDA-approved drug PZ as a clinically appropriate drug for the treatment of TBI. Further work is necessary to explore potential limitations such as determining the appropriate dose to optimally scavenge reactive aldehydes, but not increase possibility deleteriously increasing intersynaptic catecholamine levels.

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B19—Osteopathic Philosophy

Roles of APC N-Terminal and Central Domains in Optic Axon Pathfinding and Arborization In Vivo

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Background: Formation of neuronal circuits involves axons navigating specific paths to their targets in the brain, where they then elaborate terminal arbors required for functional visual connectivity. Defects in axon pathfinding and connectivity have been implicated in a number of neurodevelopmental and neurodegenerative diseases, such as Down's Syndrome and Alzheimer Disease. Wnt ligands regulate axon pathfinding and arborization, but the mechanisms of their downstream factors are not well defined. *Adeno-*

matous Polyposis Coli (APC) is 1 important downstream factor of Wnt signaling that can regulate B-catenin stability as well as microtubule and actin organization. By understanding the structures of axonal pathfinding in the developing brain, we can better understand the mechanisms underlying neurologic diseases and apply more rational treatments to patients.

Hypothesis and Aims: We hypothesized that the *APC* regions that bind B-catenin (central repeat region) and that regulate the cytoskeleton (N-terminal domain) differentially sculpt growth cones of optic axons in the optic tract, and shape their developing arbors within the optic tectum, thereby modulating visual connectivity.

Methods and Data Analysis: We overexpressed a truncation of *APC* that binds to B-catenin together with a GFP marker, or for a control just the GFP construct, in small numbers of optic neurons in developing eyebuds of Xenopus laevis embryos. Using in situ and in vivo fluorescence imaging (Nikon E800 microscope, Nikon DS-5M camera) and morphometric analysis (NIH Image J), we determined the effects of this mutant on the organization of optic axons (dispersion and crossing), the shape of their growth cones (aspect ratio) in the optic tract, as well as the complexity of their nascent arbors (number of branches, aspect ratio) within the optic tectum in intact young tadpoles. We also constructed a mutant of the N-terminal domain of APC that can regulate microtubule organization. Statistical analysis used a student's *t* test with 2 tails (Excel).

Results: Quantitative analysis showed that overexpression of the *APC* truncation that can bind B-catenin (APCB-cat) but not microtubules resulted in more dispersed and disordered optic axons in the optic tract. Growth cones of these optic axons were also malformed, with smaller, narrower shapes and very long filopodia compared with control optic axons. In addition, in the optic tectum at a later stage, APCB-cat expressing optic axons developed arbors with significantly fewer branches than control arbors.

Conclusions: These data suggest that the *APC* binding domain for B-catenin regulates pathfinding and arborization of optic axons required to establish functional visual connectivity in situ. Future work will examine the function of the N-terminal domain of B-catenin on these dimensions of optic axons, growth cones, and their arbors in vivo. These studies will define distinct roles for binding domains of *APC* in establishing optic axon connectivity and visual function. By clarifying mechanisms of normal development, these studies can also define possible processes underlying neurologic diseases.

B21—Chronic Diseases & Conditions

Interaction of HERG and EAG With β-Catenin in an Oocyte Expression System

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Background: The HERG (human *ether-à-go-go* gene) channel is a potassium selective voltage gated ion channel important in the repolarization of ventricular cardiac myocytes. Studies have shown that drug-induced blockade of HERG or mutations in the HERG channel are associated with delayed cardiac repolarization, which can lead to Long QT syndrome and the development of the potentially lethal ventricular arrhythmias, Torsades de Pointes. EAG is another K+ channel from the same family as HERG and is selectively expressed in the brain and placenta of rats and humans. β-Catenin is a multifaceted protein that is involved in cell-to-cell adhesion, signal transduction, cancer, and neuronal development. In a recent study, β-catenin was shown to upregulate the amount of HERG K+ channels in the plasma membrane of Xenopus oocytes.

Interaction between β-catenin and HERG could have implications for establishment of connectivity and function in the developing nervous system.

Hypothesis and Aims: The goal of this research is to determine if the gating properties of HERG and EAG (ie, channel open and closing and channel inactivation and recovery from inactivation) are altered by β-catenin.

Methods: Electrical recordings to assess channel function were performed using 2-electrode voltage clamping of Xenopus oocytes expressing either HERG alone, EAG alone, β-catenin alone, HERG coinjected with β-catenin, or EAG coinjected with β-catenin. cRNA was injected into enzymatically defolliculated oocytes and currents recorded under different voltage protocols 3-4 days after injection. Control experiments were done using uninjected and water-injected oocytes.

Data Analysis: Generation of normalized conductance vs voltage curve (GV curve)

G-V curves were generated using a 2-step voltage protocol in which the voltage was stepped first to a series of voltages and then to -60 mV. G-V curves were obtained by plotting the current at the beginning of the step to -60 mV as a function of the voltage of the preceding pulse. The resulting GV curve was fit with a standard Boltzman function which gave the voltage at which half of the channels open (V_{mid}).

Measuring the rate of channel closing: The rate of deactivation was measured using a 2-step protocol in which the voltage was initially stepped to +20 mV and then stepped to a range of voltages. The rate of channel deactivation was obtained by fitting the current at each voltage to a double exponential, thus giving 2 time constants (Tau_{fast} and Tau_{slow}).

Measuring the fraction of inactive channels: The fraction of inactive channels was measured using a 3-step protocol in which the oocyte was initially stepped to a range of voltages to open and then inactivate channels, then stepped to a negative voltage to reopen the inactivated channels, and then finally stepped again to the same range of voltages as in the first pulse to allow the channel to inactivate. Steady state inactivation can be calculated from the ratio of the current at the beginning of the third pulse (which gives an estimate of the total number of open channels) to the current at the end of the first pulse (which gives an estimate of the number of channels that did not inactivate).

Measuring the rate of inactivation: The rate of inactivation was measured using the same 3-step protocol used to measure steady state inactivation by fitting the 3rd step to a single exponential.

Statistical analysis: A standard 2-tailed student's *t* test was used to compare oocytes injected with either HERG or EAG alone and oocytes injected with either HERG or EAG and β-catenin.

Results: Coexpression of HERG with β-catenin showed no statistical difference in any parameter measured (V_{mid}, rate of channel closing, rate of channel inactivation, steady state inactivation). However, β-catenin increased the rate of EAG deactivation at most voltages tested.

Conclusions: β-catenin did not alter any of the gating properties of HERG tested in this study, but did slow the rate of EAG channel deactivation. Future work will examine the physiological relevance of β-catenin modification of EAG gating properties in neuronal development, specifically on the establishment of axonal connectivity in the developing nervous system. One major limitation of this study is that the experiments were performed in Xenopus oocytes, as opposed to neuronal tissue.

B22—Chronic Diseases & Conditions

Effects of Inhaled Anesthetics and Aging on the Blood-Brain Barrier and Blood-Retina Barrier: Implications for a Mechanism of Post-Operative Delirium

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Research Question(s)/Hypotheses: Postoperative Delirium (POD) is characterized by an acute phase of cognitive impairment, and many patients aged 65 years or older exhibit POD when they are subjected to general anesthesia. Many of these patients develop a chronic phase of cognitive impairment characterized as postoperative cognitive dysfunction (POCD) and subsequently dementia. Furthermore, POCD consequent to delirium may increase the rate of cognitive decline in Alzheimer disease. Little is known about the pathology and mechanisms that cause POD and POCD, but advanced age and inhaled anesthetics (IAs) are predisposing factors. Current literature disputes the pathophysiologic connection between IAs and POD, but several models exist. Previous studies from our laboratory have reported that POD is associated with a transient and abrupt, anesthesia-induced breakdown of the blood-brain barrier (BBB). The resulting disruption of brain homeostasis and altered neuronal functioning plays a crucial role in the phenomenology of the delirious state. We tested the hypothesis that IAs directly affect brain vascular endothelial cells, leading to an increase in BBB permeability and an influx of plasma components into the brain, including IgG antibodies. We expanded upon this hypothesis by adding the retina and its vasculature, containing another physiologic blood-tissue barrier, to assess for concomitant changes in this system on going with BBB dysfunction. Current literature has shown the endothelial lining of the inner blood retina barrier (BRB) to be analogous in structure and function to the endothelial lining of the BBB. This comparison allowed us to build upon past results by investigating the impact of IAs and age on the BRB. We explored this hypothesis by using rat models to determine if commonly used IAs, specifically Sevoflurane or Isoflurane, can increase BRB permeability, and if this phenomenon was synergistically enhanced with age.

Methods: Sprague Dawley rats at various ages were treated with Sevoflurane or Isoflurane for 3 hours and then either sacrificed immediately or first allowed to recover for 24 hours. Tissue was processed for scanning electron microscopy (SEM) to monitor structural changes in the luminal surfaces of brain vascular endothelial cells, and immunohistochemistry (IHC) to monitor the extent of BBB and BRB permeability. The 3 treatment groups used were young (3-6 months), middle-aged (9-12 months) and older (18 months) rats. IHC was used to detect IgG leakage reflective of endothelial cell damage and barrier function in either the retina or the brain, respectively. Furthermore, we used a Nikon FXA microscope to take images of the BBB and BRB respectively.

Data Analysis: Both inhaled anesthetics caused disruption of BBB- and BRB-associated tight junctions at cell margins, and this was further proved by the enhanced immunoglobulin G (IgG) positive immunostaining of retinal interstitial spaces and local neurons. We used IgG as a tissue biomarker indicating BBB leak. Results revealed that the binding of IgGs was increased in the middle-aged and older rat group when compared with the younger group, thus corroborating our hypothesis. However, there were noted differences between IAs with Sevoflurane causing greater disruption of cell ultrastructure as evidenced by an increased IgG extravasation. Using a Nikon FXA microscope we were able to take images from each group and analyze the data. Quantitative IHC demonstrated increased BBB permeability in Sevoflurane-treated rats compared with that of controls, and older rats were more severely affected. Retinas were further

immunostained with GFAP, a marker of Muller cell activation significant for cellular debris clearance and tissue damage and maintenance. Initial analysis of these images did not reveal any appreciable differences between control and any treatment groups, even though Muller cell activation is a hallmark for many retinopathies. Given the short window of time we are assaying for the disruption of tissue integrity, it may be too short to be telling of the lasting impact chronic or repeated exposure to IAs may actually have on the retinal structure. Lastly, eosin staining for tissue architecture may reveal similar findings to that of GFAP, even though it is well established that layers change in thickness in many disease states, again owing to the short time frame in which we are addressing this IA administration. Extravasated IgG had a selective affinity for pyramidal neurons in the brain and ganglion neurons in the ganglion cell layer of the retina.

Results: Results suggest that the BBB pathology is correlated to BRB disruption in the ganglion cell layer with coincident immunolabeling of IgG in a tissue otherwise devoid of antibody presence to any appreciable extent. Furthermore, preliminary data indicate that surgical-plane Sevoflurane or Isoflurane anesthesia causes structural changes that directly increase the permeability of the BRB. The results were exacerbated in older rat models, thus supporting our previous hypothesis.

Conclusion: We propose that this may be used as a model that achieves surrogacy status to the BBB. These 2 seemingly distinct systems have shown analogous effects from IA exposure, and thus have diagnostic, therapeutic, and overall far-reaching clinical implications for future directions of research. We propose that the resulting loss of brain homeostasis disrupts neuronal function, thus leading to the manifestation of POD. Furthermore, selective binding of extravasated IgG to neurons, a feature consistently observed in Alzheimer disease, may contribute to neuronal dysfunction and lead to POCD and dementia.

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B23—Impact of OMM & OMT

Use of Model Assay to Identify Object Properties That Influence Detection by Palpation

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Context: Palpation serves both diagnostic and therapeutic functions in the practice of osteopathic medicine. Palpation is the process of feeling an object, in or on the body, to determine size, shape or location. The information obtained is used to determine the condition of the underlying tissue. However, there is little information about which parameters of a physical structure affect a practitioner's ability to discern information about that palpated structure.

Objective: To use a model palpation assay to provide insight into the parameters that influence the location and identification of an object by palpation. This study examines the effects of object shape and size on performance in the model palpation assay.

Methods: Subjects were first-year, second-term osteopathic medical students. Informed consent was obtained from all subjects. Objects of various size (shape held constant) and shape (dimensions held constant) were produced in plastic using a 3D printer. For the model palpation assay, an object was placed under layers (superficial – 2 layers, deep – 4 layers) of felt sheets. The top felt sheet was divided into a 3 × 3 matrix with 9 equal area sectors. The object was randomly placed in the center of one sector. The subject was then asked to (a) locate and (b) identify the object. The subject performed 2 tests

at a superficial depth and 2 tests at a deep depth. This procedure was repeated with each subject under conditions of no blindfold and with blindfold for a total of 8 trials per subject. Object size was varied, diameter and thickness independently, using the dime as the basic size. Object shapes included circle, triangle, square, pentagon, hexagon, and octagon maintaining the dimensions (diameter and thickness) similar to a dime. A random number generator program was used to assign the location of the object under the felt sheets. A random number generator was also used to determine which object was included in the trial.

Data Analysis: Statistical analysis was performed using SPSS. Comparisons of location by parameter were performed using the McNemars test. Comparisons of shape identification were performed using the χ^2 test. The study was classified as exempt by the New York Institute of Technology Institutional Review Board.

Results: A total of 129 subjects completed the model palpation assay tests. Since each testing condition was repeated twice on every subject, the total number of observations is 258.

Object Location: In aggregate, subjects were significantly better able to locate an object at the superficial as compared with the deep depth when varying object size ($P<.02$). Location of objects of increased size was significantly better than location of objects of reduced size ($P<.02$). In contrast, there was no significant difference in the ability of subjects to locate different- shaped objects between the superficial and deep depth ($P>.05$). The presence or absence of a blindfold did not significantly affect the overall results.

Object Identification: In the aggregate, subjects were significantly better able to identify the object shape at the superficial as compared with the deep depth ($P<.01$). Shape identification was inversely correlated with shape "complexity" (the number of angles in the shape – triangle < square < pentagon < hexagon < octagon < circle). Greater complexity was correlated with poorer identification. The presence or absence of a blindfold did not significantly affect those results.

Conclusion: Using a well-defined model assay, these results demonstrate that multiple parameters affect the information content of an object obtained through palpation. These parameters include object location, object size and object shape. The results suggest that information content obtained by palpating a body structure will be inversely correlated with depth from the body surface. For example, structures at greater depth will be associated with less information content obtained through palpation. A recent study reported that a subject's ability to view him or herself while palpating decreased his or her ability to correctly identify complex shapes. This was attributed to an overload of short-term memory capacity from increased sensory input. Since our findings do not show a significant difference performing the trials with vs without a blindfold, it suggests that the information content being obtained in our study was not large enough to overload the subjects' short-term memory capacity. This study highlights the complexities involved in using palpation to obtain information about subsurface structures. Further work is needed to determine if the conclusions reached using this model palpation assay can be translated to palpation of the human body. There are 2 limitations of the current study. First, the subject population is relatively homogeneous with regard to age and previous experience with palpation. This may limit the applicability of the study to the general population but is likely appropriate for the target practitioner population. Second, the data for the χ^2 analysis contain a small number of dependent measurements, which violates the assumption of independence for this analysis.

B24—Chronic Diseases & Conditions

Attenuation of Dilated Cardiomyopathy in DMD Mice Expressing Retinal Dystrophin in Muscle

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Introduction: Duchenne muscular dystrophy (DMD) is an X-linked progressive neuromuscular disease that affects approximately 1 in every 3500 male births. It is caused by the lack of a muscular protein called dystrophin. Patients require the use of wheelchairs by age 12 years followed by death in the third decade of life from cardiac or pulmonary complications. Almost all patients with DMD develop dilated cardiomyopathy. Treatment is mostly centered on palliative care and slowing the disease process; however, currently there is no cure for DMD. Disease progression studies of DMD have traditionally been completed on the mdx model mouse, which is a good genetic model of DMD but presents limited opportunities to study the phenotypic effects of DMD due to the mild impact on muscle disease of the mdx mutation. In mdx mice, a protein called utrophin compensates for the lack of dystrophin protein in the muscle, allowing for a milder phenotype than would occur in a human affected by DMD. A better DMD mouse model to study involves the production of double mutant mice with the mdx mutation and utrophin knockout such that there is no compensatory protein to replace dystrophin. This double mutant exhibits severe muscle degeneration and kyphosis, in addition to premature death around age 4 months. This mouse model displays a phenotype similar to human DMD patients. Our laboratory has made a transgene that was inserted into the mouse genome to allow expression in skeletal muscle of an isoform called retinal dystrophin, which is not normally expressed in muscle but is similar enough to muscle dystrophin to suggest that it may compensate for muscle dystrophin and improve the clinical presentation of DMD patients. Breeding mice to generate DMD model mice with and without this transgene for retinal dystrophin (Dp260; dystrophin protein 260 kDa) shows that expression of retinal dystrophin attenuates skeletal muscle disease in these DMD model mice.

Hypothesis: We hypothesize that expression of retinal dystrophin in cardiac muscle will attenuate the dilated cardiomyopathy observed in DMD mice. This work would suggest a potential novel therapy of inducing expression of retinal dystrophin in DMD patients to accomplish the same outcomes.

Methods: The generation of DMD model mice with and without the retinal dystrophin transgene requires 3 generations of breeding. Tail DNA extraction from the final product of this breeding strategy, followed by genotyping PCR for mdx, utrophin knockout, and the presence of the retinal dystrophin transgene (Tg+), is required for identification of DM vs DM, Tg+ mice. Once classified the following experimental studies were conducted: (1) Evidence of retinal dystrophin expression in cardiac muscle was achieved by western blotting; (2) After identification of the mice, they were transported to Idexx Inc in Columbia, Missouri, for histopathology of trichrome stain of whole heart cross-section; (3) Mice were also transported to Cardiovascular Mouse Phenotyping Laboratory at Washington University in St. Louis to obtain functional EKG data; and (4) Impact on lifespan of DM, Tg+ vs DM mice was calculated.

Data Analysis: Analysis of results included the following: (1) Qualitative assessment of expression of retinal dystrophin from the transgene was completed by western blotting; (2) Qualitative assessment of histopathology of heart muscle was performed. Impact of expressing retinal dystrophin in cardiac muscle of DMD, Tg+ mice vs DM mice was assessed by histopathology with trichrome staining; (3) SPSS statistical analysis was conducted

for the EKG data, which included heart rate, left ventricular mass, and fractional shortening; and (4) Impact on lifespan by expressing retinal dystrophin in DMD model mice was calculated as a percent survivorship of a population of affected control and experimental mice.

Results: Experimental analyses in this study have indicated the following: (1) Western blot analysis indicated that retinal dystrophin is expressed and detected in protein extracts from heart tissue of retinal dystrophin transgene mice (including DM, Tg+ mice). However, the expression of retinal dystrophin is absent in the hearts of DM mice; (2) Histopathology shows thinning of the left ventricular wall with extensive fibrosis typical of dilated cardiomyopathy, while DM, Tg+ hearts showed normal phenotype; (3) EKG data showed significant decrease in heart rate, left ventricular mass, and fractional shortening in DM mice vs DM, Tg+ mice, similar to control mice; and (4) The impact on lifespan is that DM, Tg+ mice survive a normal lifespan as compared with control mice, whereas the DM mice are dead by age 5 months with 80% dead by age 3 months.

Conclusion: Dilated cardiomyopathy is vastly improved by expression of retinal dystrophin in cardiac muscle of DMD mice. This suggests that a novel therapy involving the expression of retinal dystrophin in skeletal and cardiac muscle would be beneficial to DMD patients.

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B25—Impact of OMM & OMT

Is Accuracy of Diagnosis Dependent on the Positioning of the Patient During an Osteopathic Evaluation?

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Context: Students at colleges of osteopathic medicine perform lumbar spine diagnosis in a variety of patient positions. Little evidence exists to support whether patient position influences accuracy of identifying positional asymmetry of transverse processes of the lumbar spine.

Hypothesis: Osteopathic medical students will demonstrate a difference in accuracy when assessing positional asymmetry of transverse processes of lumbar models oriented to simulate a seated patient or a prone patient.

Methods: The local institutional review board considered the current study exempt. Sixteen second-year osteopathic medical students participated in a 20-hour elective course that focused on providing objective palpation feedback. Students were divided into quartiles based on previous performance on first-year objective palpatory model assessments. Four students were selected from each quartile for participation in the course. The transverse processes (TP) of 4 foam-covered, bronze static lumbar spine models were set with asymmetries of 2-6 mm in the transverse plane. Two vertical models (VM) simulated a seated patient, and 2 horizontal models (HM) simulated a prone patient; the VM and HM had corresponding asymmetries. All students palpated all 4 models using a sequence randomized by model orientation and student quartile ranking. Students recorded whether the right TP was anterior or posterior compared with the left.

Data Analysis: A random intercept logistic regression model was fit to the data to determine the difference in probability of correctly determining the direction of asymmetry between horizontal and

vertical models while accounting for quartile ranking of the student, direction, and absolute value of the asymmetries of the models. Different interactions were studied as well.

Results: No significant difference was found in accuracy between the VM and HM (P=.06). The probability of being correct was 0.83 (SE 0.03) for the VM and 0.91 (SE 0.02) for the HM. Only direction and absolute value of asymmetry were significant (P<.001 and P<.001, respectively). The probability of correctly determining the direction of asymmetry in anterior and posterior models was 0.95 (SE 0.02) and 0.72 (SE 0.04), respectively. The odds of correctly determining the positional asymmetry of the TPs were 1.7 (SE 1.13) times greater for each 1 mm increase in absolute value of model asymmetry. The accuracy of diagnosis in both VM and HM increased as the model asymmetry increased: 63% (VM) and 78% (HM) at 2 mm, 74% (VM) and 86% (HM) at 3 mm, 83% (VM) and 91% (HM) at 4 mm, 89% (VM) and 95% (HM) at 5 mm, and 94% (VM) and 97% (HM) at 6 mm. No significant interaction was found between VM and HM for anterior and posterior models (P=.39). For VM, the probability of correct diagnosis was 0.91 when the right TP was anterior and .68 when posterior. For HM, the probability of correct diagnosis was 0.97 when the right TP was anterior and 0.76 when posterior. Quartile ranking of students had no significant relationship with the probability of correctly determining the direction of asymmetry (P=.77). The probability of correctly determining the direction of asymmetry was 0.88, 0.85, 0.90, and 0.86 in quartiles I, II , III, and IV, respectively.

Conclusion: In the current study, second-year osteopathic medical students showed greater accuracy when palpating HMs simulating the prone position, but the difference was not statistically significant. As expected, accuracy of diagnosis improved as asymmetry increased. Students were more accurate when the right TP was anterior. Future research should investigate whether results may be confounded by hand or eye dominance (VM and HM) or what side of the table an examiner stands on (HM only).

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B26—Musculoskeletal Injuries and Prevention

Kinetics of Vertical Locomotion in Nonhuman Primates: Variation in Muscle Morphology and Implications for Human Movement

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Introduction: The task of climbing is an important aspect of life for all non-human primates. Climbing requires muscle recruitment and enough energy to suspend an animal and carry it upward. During climbing, the forelimb and the hindlimb may function differently; it is thought these differences led to the shifting of weight posteriorly, which gradually brought forth the reliance on the hindlimb as the major source of propulsion and weight bearing during locomotion. The reliance on the hindlimbs for weight bearing is unusual among most mammals and thought to be basal to primates. Eventually in primates, the forelimbs were freed up from any locomotor function and bipedalism evolved. However, it still remains unclear how the work done by the muscles of the different limbs during climbing relates to primate muscle anatomy. Many past studies have focused their attention on the force differences between the limbs during quadrupedal, bipedal, and manual locomotion in a horizontal plane. However, few data exist on primate movement during vertical climbing, and even fewer force data exist describing primate climbing mechanics. Thus,

our goal was to explore vertical movement in primates to better understand the relationship between primate anatomy and the function of their limbs during climbing. Understanding the form-function relationships of varied hindlimb anatomy in nonhuman primates during vertical movement may provide insight about how humans with various differences in lower limb form (eg, due to disease processes or natural variation) are able to climb stairs or mountains, improve strength, and avoid injury. We predicted the following: (1) primates that climb more regularly will exhibit a greater reliance on the hindlimb during climbing and (2) primates with hindlimb morphology similar to humans will rely more heavily on the hindlimb.

Methods: Sample: Seven species of primate were examined on the basis of these hypotheses: (1) regular climbers, ascending and descending from 31%-50% of their time (Loris tardigradus, Nycticebus pygmaeus), (2) hindlimb anatomy with features similar to humans (Loris tardigradus, Nycticebus pygmaeus), and (3) general arboreal quadrupeds for comparison (Cheirogaleus medius, Saimiri sciureus, Aotus trivrigatus, Eulemur mongoz, Macaca fascicularis). This sample spanned an order of magnitude in body size, from 190 g to 8 kg.

Data Collection & Instruments: Multiple replicates of at least 2 subjects from each species were video recorded during voluntary climbing of a stationary pole over the course of several days. The middle section of the stationary pole was instrumented to an AMTI force transducer that recorded the forces exerted by the limbs when it contacted the instrumented section. The reaction forces were examined as the 3 principle components, with a focus on the peak propulsive force (that moving the body upwards) and the peak tangential force (that pushing into or pulling away from the pole).

Data Analysis: Climbing speed was calculated from the video records. Comparisons between limbs were made for each force component, as a ratio to body weight, and taking speed into account. In the cases in which speed had a significant effect on peak limb forces, an analysis of covariance (ANCOVA) was calculated to compare limbs. In the cases in which speed was not a significant factor, a 2-sample *t* test was calculated to compare limb forces.

Results: Cheirogaleus medius, Eulemur mongoz and Saimiri sciureus exhibited a significant correlation between speed and peak propulsive force (P=.0054, <.0001 and .0004, respectively). All 3 of these species propelled themselves upward more with their hindlimbs than with their forelimbs (P<.0001 in all cases). Aotus trivrigatus and Macaca fascicularis exhibit a similar pattern, irrespective of speed (both P=<.0001). However, Loris tardigradus and Nycticebus pygmaeus species, which have similar hindlimb anatomy to humans, exhibit greater peak propulsive forces with their forelimbs than with their hindlimbs (P=.0379. and P=.0051). These 2 patterns mimic the patterns associated with horizontal locomotion for these particular species. In terms of peak tangential forces, no species exhibited a relationship with speed. The majority of species used their forelimbs in tension (ie, pulled away from the substrate) and their hindlimbs in compression (pushed into the substrate). The difference in limb use was significant for these species (P<.0001 in all cases). However, Loris tardigradus and Saimiri sciureus did not use their limbs for opposite purposes during climbing, and they tended to utilize both limbs in compression. However, when the absolute magnitude of the peak tangential forces were examined, there were no significant differences between hindlimb and forelimb force for any of the species except for the Loris tardigradus (P=.0191).

Conclusions: Lorises (Loris tardigradus and Nycticebus pygmaeus) share certain hindlimb muscle morphology with apes, including humans, that appear to be associated with climbing and/or significant propulsion with the hindlimb. For example, lorises have a large soleus and small plantaris muscles, which is unusual among primates except for apes (however, Aotus may also exhibit this

anatomy), whereas most quadrupedal animals have a small soleus and large plantaris muscle. Additionally, lorises have gluteal musculature similar to humans, with a broad origin of gluteus superficialis (ie, maximus), and a separate tensor of the fascia latae muscle. These, and additional similarities between loris and ape/human morphology, suggest that the hindlimb is well suited for extension and propulsion. Thus, this study provides more evidence that climbing may have pre-adapted our earliest ancestors to bipedal locomotion. It is strange, therefore, that the hindlimbs of lorises do not exhibit greater peak propulsive forces than the forelimbs, nor do the limbs of lorises exhibit opposing tangential functions. There are several possible explanations, which we will explore with additional data. First, lorises are notoriously slow moving. While they can move quickly, their preferred locomotor mode is a slow, cryptic hunting, much like chameleons. At such slow speeds, it may be that there is no need for the limbs to perform differently during climbing. Second, peak forces may not fully explain the function of the limbs during the entire stride. A more holistic measure of limb function may be impulse forces, which is the force over the entire contact period. This measure is analogous to the work performed by the muscles, whereas peak force is analogous to the maximum exertion of the limb. Finally, the position of the body relative to the substrate may also impact the distribution of forces across the limbs. Qualitatively, lorises appear to hold themselves away from the substrate differently than the other species. We are examining this quantitatively to determine whether limb and body positioning affects the peak forces during climbing. Understanding about how primate species climb with different morphologies provides insight to how differences in human bipedal complex relates to differences in climbing ability and propulsion in general.

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B27—Chronic Diseases & Conditions

Prednisone and Fluoxetine Prevent Exercise-Induced Rapid Exhaustion in *Caenorhabditis elegans* Duchenne Muscular Dystrophy Mutants

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Research Question(s)/Hypotheses: Duchene muscular dystrophy (DMD) is an incurable genetic disease, and those who have it typically die in their second decade. The disease is currently incurable. To facilitate cost-effective, high-throughput drug screening for DMD, we previously developed a worm treadmill platform. The worm treadmill reveals a unique phenotype for dys-1 mutants comparable to DMD mouse model. Briefly, *Caenorhabditis elegans* displays a specific locomotion response to various stimuli including food, chemicals, and electricity. *C elegans*' response to electricity has been well described and dubbed electrotaxis—the repeatable behavior of crawling toward the negative pole when subjected to an electric field of sufficiently low power so as not to interfere with muscle contraction (Gabel et al, 2007). We used this behavior to initiate and maintain locomotion to perform exhaustion tests. Using this approach we have previously observed that the time to exhaustion and distance traveled, when compared with wild type worms, was decreased in dys-1 mutants. The aim of this study was to evaluate whether prednisone, currently the only available therapy for DMD, and fluoxetine—known to prevent *C elegans* muscle damage (Carre-Pierrat et al, 2006), or a combination of the 2 drugs can improve time to exhaustion and/or distance traveled in dys-1 mutants.

Methods: Treatment with prednisone and fluoxetine can prevent muscle damage, improve time to

exhaustion, and distance traveled in force exercised dys-1 mutants. In addition, the combination of these 2 drugs might provide a synergistic effect and show better results than single compounds.

Data Analysis: *C elegans* strains were maintained at 25°C under standard conditions (Brenner, 1974). The worm treadmill consists of a specially formulated agar-based gel and buffer placed in a classic DNA-electrophoresis box, a power source, a microscope camera, and an infrared thermometer to monitor gel temperature. Groups of 50-150 hypochlorite synchronized young adult worms were transferred to the gel, and a voltage of ≥4 v/cm was applied to initiate locomotion toward the anode. The poles of the electric field were alternated as the worms reached the end of the gel. The distance and disposition of crawling *C elegans* was continuously tracked. The goal was to run the worms to a state of exhaustion – defined as a state when at least 75% of the worms ceased locomotion toward the anode. Hypochlorite synchronized wild type, as well as dys-1 eggs were placed on plates with no drugs added and used as controls. Hypochlorite synchronized dys-1 mutant eggs were placed on plates with 0.5 mg/mL prednisone, 0.05 mg/mL fluoxetine, or a combination of the 2; all drugs were mixed into OP50 bacterial lawn (food) at the given concentrations. After reaching the point of exhaustion the worms' actin filaments were stained with rhodamine phalloidin and visualized with a fluorescent microscope to observe muscle damage.

Results: We collected both the time and distance ran data from multiple repeated experiments (2-13 experiments for each drug/control condition). The experiments were performed by 3 independent researchers. We plotted and analyzed the data using GraphPad Prism 6 software. To assess statistical significance of the data, we used a 1-way ANOVA followed by Tukey's multiple comparison test. *P* values lower than .05 were considered significant.

Conclusion: As we observed previously, wild type worms ran significantly longer and farther than dys-1 mutants. Now we can report that dys-1 mutants treated with prednisone, fluoxetine, and a combination of both drugs ran statistically significantly longer (up to 90 minutes) and farther than untreated dys-1 mutants. The results of treated dys-1 mutants were comparable or better then wild type controls. In addition, postexercise dys-1 mutants exposed to prednisone had significantly less muscle damage than was observed in untreated postexercise dys-1 mutants; additionally, they ran significantly longer and farther than unexposed dys-1 mutants. Postexercise dys-1 mutants treated with fluoxetine ran significantly longer than wild type and untreated dys-1 worms and ran significantly farther than untreated dys-1 mutants. The greatest improvement was observed in the dys-1 mutants exposed to prednisone and fluoxetine; these worms ran significantly longer than all other groups, as well as significantly farther than untreated dys-1 mutants or dys-1 mutants exposed to prednisone or fluoxetine alone.

Acknowledgment/Funding Source: This study demonstrates that treatment with prednisone, fluoxetine, and especially a combination of the 2 drugs confers progressively improved running distance and time to dys-1 mutants. As expected, based on animal models and previously established prednisone effects in other *C elegans* mutants (Gaud et al, 2004), prednisone has shown therapeutic effects. However, this was the first time this has been shown in forcefully exercised dys-1 (dystrophin) mutants. The greatest improvement observed with a single drug treatment was with fluoxetine, indicating serotonergic transmission may represent a novel therapeutic target for DMD. The greatest overall improvement was observed with simultaneous fluoxetine and prednisone treatment. This finding provides initial data suggesting that synergistic drug effects should be strongly considered in future screenings for potential DMD therapeutics.

B28—Chronic Diseases & Conditions

Prednisone Improves *Caenorhabditis elegans* Duchene Muscular Dystrophy Mutant Biomechanics

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Introduction: The nematode *Caenorhabditis elegans* has been shown to have skeletal muscle cells functionally orthologues to human skeletal muscle and has been widely used as a model for neuromuscular disorders. Duchene Muscular Dystrophy (DMD), a severe neuromuscular disorder, is currently incurable and those who have it rarely live past their 20s. The *C elegans* dys-1 mutant carries mutations in the dystrophin gene (Bessou et al, 1998). Mutations in human dystrophin gene are the cause of DMD. These orthologous features make the dys-1 mutant a potentially ideal candidate for rapid and cost-effective high-throughput DMD drug screening platform. Locomotion is a fundamental phenotypic metric in *C elegans*. Previously, to fully characterize locomotory phenotypes, we have integrated noninvasive video microscopy, MATLAB-based image analysis algorithms, and fluid mechanics principles into a Biomechanical Profiling Platform (BMP) to quantify *C elegans* locomotion (Krajacic et al, 2012). In the current study, using BMP, we quantified 18 distinct features that describe *C elegans* body shape, swimming patterns (kinematics) and tissue material properties (biomechanics) and compared wild type, dys-1 mutant worms and dys-1 mutant worms treated with prednisone—a drug known to have beneficial effects on *C elegans* muscle (Gaud et al, 2004), and currently the only drug widely used in DMD patients. In mdx mouse model for DMD, mice undergoing chronic exercise on a treadmill are known to have more severe dystrophy progression (De Luca et al, 2003). Previously, we developed the worm treadmill apparatus and have shown that dys-1 mutant worms have lower exercise tolerance than wild type worms. In this study, we used the worm treadmill platform to assess dys-1 biomechanics before and after enforced exercise. The goal of this study is to, for the first time, determine the effects of potential muscle damage sustained during enforced exercise on the dys-1 mutant's biomechanical profile. Additionally, this study aims to discover whether prednisone, a drug known to reduce *C elegans* muscle damage (Gaud et al, 2004), will have a beneficial effect on these mutant worms.

Hypothesis: Prednisone will protect dys-1 mutant worms from potential exercise-induced muscle damage and improve the biomechanic profile parameters of the post exercise dys-1 mutant worms. including power generated while swimming, force output, as well as worm swimming speed.

Methods: *C elegans* strains were maintained at 25°C under standard conditions (Brenner, 1974). To enforce locomotion, >150 worms per experiment were exercised on the worm treadmill. The worm treadmill consists of a specially formulated agar gel and buffer placed in a classic DNA-electrophoresis box, a power source, a microscope camera, and an infrared thermometer to monitor gel temperature. Hypochlorite-synchronized young adult worms were transferred to the gel, and a voltage of ≥4 v/cm was applied. To induce continuous locomotion, the poles of the electric field were alternated as the worms reached the end of the gel. The distance and disposition of crawling *C elegans* was continuously tracked. The goal was to run the worms to a state of exhaustion – defined as a state when at least 75% of the worms ceased locomotion toward the anode. The worms were then collected and allowed to recuperate for 24 hours. Individual worms were transferred into a 50-µL drop of M9 buffer in the recording chamber and, after 1 minute of acclimation, covered with a cover glass. Image series of swimming nematodes where then acquired on a standard transmitted light stereo microscope at

19.33 frames per second. Exported image series were then analyzed using BMP script in MATLAB 2010b (Krajacic et al, 2012).The recordings were made for 10-15 worms for each strain: wild type worms (used as control), untreated dys-1 worms, and treated dys-1 mutant worms grown on bacterial lawns (food) containing .05 mg/mL prednisone. In all groups, the recordings were obtained for pre- and postexercised worms. All experiments were repeated at least twice.

Data Analysis: To analyze the obtained image series, a MATLAB-based image analysis and biomechanics algorithm (BMP) was used to quantify 18 distinct features of *C elegans* motility (Sznitman et al, 2010; Krajacic et al, 2012). Statistical significance for single components of the biomechanical profile (eg, force, power, speed, frequency) was determined using unpaired *t* test or 1-way ANOVA with Tukey's multiple comparison test. P values lower than .05 were considered significant.

Results: The biomechanics of postexercised worms were compared to see how wild type, dys-1, and dys-1 treated with prednisone compared with each other after being exercised to exhaustion. We show that dys-1 mutant worms grown on prednisone can produce statistically significantly more force and power and can swim faster after recovering from exhaustion than untreated worms. Dys-1 worms treated with prednisone had a statistically significant increase in power and force, as well as swimming speed produced in comparison to dys-1 worms that were not treated. Other components of the biomechanical profile (eg, trashing frequency) showed an improving trend, however, not statistically significant. As expected, we have also shown that wild type worms recover much better after exhaustion and were statistically significantly higher in power, force and speed when compared with dys-1 with or without prednisone treatment.

Conclusion: Our study shows that prednisone treatment can statistically significantly improve several key biomechanical parameters in dys-1 mutant worms. Most importantly, the force outputs, power outputs, and swimming speed are all significantly improved after treatment, revealing the potential of using BMP and the worm treadmill as a cost-effective screening tool for potential novel therapeutics for Duchenne Muscular Dystrophy. In addition, our findings further contribute to establishing *C elegans* dys-1 mutant as a novel DMD drug screening model.

♦ Abstract that won first or second place in the 2014 SOMA Student Poster Competition.

♦B29—Impact of OMM & OMT

Does Pulmonary Function Change With External or Internal Rotation of the Extremities?

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Research Question(s): There is limited literature regarding the role of myofascial tension and extremity position on pulmonary function. The goal of this research is to determine if external or internal rotation of the extremities can change tidal volume and vital capacity, secondary to a change in chest compliance. If myofascial restrictions of the extremities can change pulmonary function, pulmonary patients with extremity injuries, or somatic dysfunction, may need to be treated differently than the standard of care. Clinically, by optimizing body position and treating somatic dysfunction, osteopathic physicians could enhance (1) respiratory therapies, (2) athletic performance, and (3) quality of life in patients with limited cardiac or respiratory function.

Hypothesis: External rotation of the upper and lower extremities will increase lung volumes and pulmonary function.

Methods: Midwestern University IRB approval was obtained to measure range of motion and pulmonary function in healthy subjects, aged 21-40 years, nonsmokers. Strict height limitations were used to mini-

mize anatomical differences in lung volumes (Females: 61-67", Males 66-72"). Patient history and systemic vitals were obtained upon arrival. Active range of motion of the shoulder and hip were measured with a goniometer. As a control, each subject was tested in an upright neutral position with their feet shoulder-width apart, upper extremities comfortably at their sides with palms facing medially. To measure the effects of external rotation of the extremities, heels were kept together and shoulders were externally rotated maximally to the end of their physiologic barrier. For internal rotation, toes were kept together as upper and lower extremities were taken fully into their barrier. As a measure of chest compliance, upper and lower thoracic excursion were measured in neutral, external, and internal rotation. Additionally, 3 pulmonary function tests were obtained in each position for a total of 9 tests. Subjects were allowed to rest for 5-15 minutes between tests to prevent fatigue. The sequence of body position for pulmonary function testing was varied to prevent repetition and fatigue testing bias. Because fascial restrictions increase with age, as preliminary data, the effect of body position on pulmonary function was measured in a 50-year-old male subject with chronic somatic dysfunction as compared with the young healthy controls.

Data Analysis: All data were de-identified, summarized in Excel worksheets, and presented as mean ± SEM. Raw data were graphed and statistically analyzed using Sigma Plot (12.5). *T* tests and a 1-way ANOVA with a Duncan post-hoc analysis were used to determine significance ($P<.05$).

Results: To date, 21 subjects have been recruited (12 females, 9 males, age: 25 ± 1 y, height: 169.7 ± 2.1 cm, weight: 69.0 ± 3.4 kg, BMI: 24.0 ± 1.0), with an average resting heart rate of 65 ± 4 BPM, and a blood pressure 115/75 mm Hg. Right vs left range of motion for upper or lower extremities did not differ. Average external and internal hip rotations were 34 ± 2° and 37± 1° respectively; and external and internal shoulder rotations were 82 ± 2° and 72 ± 3°, respectively. Upper and lower chest excursion did not change with external or internal rotation of the extremities. Tidal volume was (0.79, 0.78 and 0.79 L) in neutral, external and internal rotation, with no significant changes with external ($P=.85$) or internal ($P=.96$) rotation. Similarly, vital capacity and forced vital capacity did not change with body position. In the older subject, shoulder range of motion was decreased with external rotation limited to 70° and internal rotation to 55°. Additionally, tidal volumes changed from 1.39 to 1.47 and 1.14 L in neutral, external, and internal rotations, respectively (N =1).

Conclusion: These data suggest that pulmonary function is unaffected with external and internal rotation of the extremities in healthy young adults. However, future studies will include older subjects with chronic somatic dysfunction. This initial study was designed to obtain baseline data and is limited in the scope of clinically relevant subjects.

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♦B30—Chronic Diseases & Conditions

Hyperglycemia Limits Autophagy Via Inhibition of Nuclear Translocation of Transcription Factor EB

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Cardiovascular disease is the major consequence resulting in morbidity and mortality amongst diabetic patients. Hyperglycemia is a known independent risk factor associated with diabetic heart failure. However, the mechanisms that mediate hy-

♦ Abstract that won first or second place in the 2014 SOMA Student Poster Competition.

perglycemia-induced cardiac damage remain poorly understood. Previous literature show that generation of reactive oxygen species (ROS) and lack of cell maintenance compromise cellular sustainability. Autophagy is the principle pathway via lysosomal degradation of proteins and organelles to maintain cellular homeostasis. We previously showed that the inhibition of autophagy is a protective response in hyperglycemia-induced cardiac injury. Transcription Factor EB (TFEB), known as a master regulator of the autophagy-lysosome pathway, controls the expression of autophagy-related proteins and lysosomal proteins. In the present study, we determined whether high levels of glucose could affect the expression and the nuclear localization of TFEB, and thus autophagic activity, in cultured cardiac cells. Western blotting results suggest that the total protein expression level of TFEB remains consistent under both high (30 mM) and physiologic (5.5 mM) glucose conditions. However, the nuclear localization of TFEB is markedly reduced in cardiac myocytes cultured under high glucose, as shown by immunofluorescence staining and confocal microscopy, indicating that high glucose inhibits the nuclear translocation of TFEB. In addition, the inhibition of TFEB nuclear localization is accompanied by a reduction of lysosomal-associated membrane protein 1 (LAMP-1), suggesting reduced autophagy-lysosome activity. Indeed, we show that high glucose inhibits autophagy and induces cell death. However, restoration of autophagic activity by treatment with Rapamycin, a known inducer of autophagy, exacerbates high glucose-induced cell death, further suggesting that the inhibition of autophagy is an adaptive response that protects against high glucose toxicity. Interestingly, Rapamycin treatment increases the nuclear translocation of TFEB as shown by increased co-localization of TFEB and 4',6-diamidino-2-phenylindole (DAPI), a DNA dye that stains nuclei. Rapamycin also reverses the expression level of LAMP-1. Collectively, these findings suggest that high glucose conditions suppress the nuclear translocation of TFEB, which may be responsible for the protective role of inhibited autophagy in hyperglycemia-induced cardiac damage. Future studies are warranted to investigate the precise molecular mechanism inhibiting nuclear translocation of TFEB in high glucose and to determine whether TFEB overexpression or knockdown can directly regulate autophagic activity, thereby affecting hyperglycemia-induced cardiac injury.

♦ Abstract that won first or second place in the 2014 SOMA Student Poster Competition.

♦B31—Chronic Diseases & Conditions

Effect of Neonatal MSG Exposure on Cerebellar Nuclei

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Introduction: Monosodium Glutamate (MSG) is a natural occurring sodium salt of glutamic acid and is used as a food enhancer in many processed foods. Glutamate is the most abundant excitatory neurotransmitter in the central nervous system and is stored and released by both neurons and astrocytes. MSG administration during postnatal development (in rodents) results in neurodegeneration in several forebrain regions, characterized by neuronal loss and neuroendocrine abnormalities (Olney, 1969; Zhang et al, 1994; Beas-Zárate et al, 2001; Gonzalez-Burgos et al, 2001). Herein, we describe the results of neonatal MSG exposure on cerebellar circuitry in rodents.

Methods: All procedures were approved by the Lake Erie College of Osteopathic Medicine (LECOM) IACUC, and animals were housed at the LECOM Animal Facility. At postnatal day 4 (P4) male rat pups were divided into 2 groups: MSG and unexposed controls. Animals were injected subcutaneously to MSG (4 mg/kg) or handled by the experimenters daily from P4 through P10. Animals were then permitted to develop normally (weened at P21) until P28 when they were euthanized (pentobarbital, 80 mg/kg;

ip), perfused through the ascending aorta with saline and fixed with 4% paraformaldehyde in 0.1M sodium phosphate buffer, pH 7.2. Brains were sectioned on a freezing microtome at a thickness of 40 microns, mounted onto glass slides from cresyl gelatin, and stained for Nissl substance with Giemsa. Neurons were reconstructed with the use of a drawing tube and an Olympus BX45 microscope. Reconstructed neurons were analyzed with ImageJ software. All data sets were checked for a normal distribution and analyzed using GraphPad Software.

Results: Animals exposed to MSG had noticeably lower body weights. At P28, control animals weighed significantly more than MSG exposed animals (*t* test, $P=.03$) and had shorter nose-to-tail lengths (*t* test, $P=.009$), but there was no difference in brain weights at P28 ($P=.94$). In the cerebellar vermis, Purkinje cell (PC) bodies were significantly smaller (Mann-Whitney, $P<.0001$). These PC had characteristic round cell body morphologies in both control and MSG-exposed groups and there was no difference in cell body shape between these groups (Mann-Whitney, $P=.39$). Finally, there was a statistically lower density of PC in MSG-exposed animals (Mann-Whitney, $P<.0001$). We additionally examined the nuclei of the inferior olive (IO) as these neurons provide excitatory climbing fibers to cerebellar PC. In the IO complex, the ventral lateral principle olive (POvl), the medial accessory olive (MAO), and the dorsal accessory olive (DAO) all had significantly larger neurons compared with controls (Mann-Whitney, each $P<.005$). In the MAO, there were significantly fewer round neurons and more stellate neurons (χ^2, $P=.0008$). Finally, there appeared to be hypoplasia in the DAO and MAO. In the DAO, the lateral extension was not observed in MSG-exposed animals and in the PO, the ventrolateral and dorsolateral limbs are connected by arch in control animals, but this was not observed in MSG-exposed animals.

Discussion: The cerebellar vermis maintains muscle and postural control over truncal and proximal muscles. The inferior olive is a major source of input to parts of the cerebellum, including the vermis. Dysfunction of PC or any parts of the IO could be postulated to cause gait ataxia, disequilibrium, and intention tremor.

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B32—Chronic Diseases & Conditions

TNFa and IL-10 Cytokines in Bladder and Kidney of Mice With Increased Uropathogenesis

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Introduction: Proinflammatory TNFα and anti-inflammatory interleukin (IL)-10 cytokines play an important role in innate immune responses during uropathogenesis. However, early cytokine activation events that occur in the bladder immediately after urinary tract infection (UTI) are poorly understood. Recent evidence from our laboratory shows that estrogen and estrogen receptor α (ERα) deficiency are important susceptibility factors in UTI pathogenesis as observed in ERα gene knock-out (KO) mice. We hypothesized that ERα disruption alters TNFα and IL-10 induction in the bladder contributing to adverse UTI outcome. We studied the kinetics of TNFα and IL-10 in the bladder and kidney of ERα KO and wild-type (WT) mice at 2 and 7 days after UTI by Dr*E coli*.

Methods: Protein immunohistochemistry was performed in paraffin-embedded kidney and bladder tissue sections from infected mice using HRP-DAB system.

Results: TNFα was predominantly seen in the cells of transitional epithelium of the bladder and IL-10 expression was found in both bladder

smooth muscles and uroepithelium. TNFα and IL-10 were expressed in kidney tubules as well in glomeruli. Compared with ERα WT, ERα KO mice showed delayed induction of proinflammatory cytokine TNFα but increased anti-inflammatory IL-10 production in both bladder and kidney at the early time point resulting in adverse UTI outcome in these mice.

Conclusions: Timely induction of both TNFα and IL-10 at the early onset of UTI may play an important role for favorable disease outcome. Therapeutic modulation of TNFα and IL-10 may serve as important targets in the future for UTI management.

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B33—Chronic Diseases & Conditions

Mechanism of Cerebellar Ataxia Treatment by Transcranial Direct Current Stimulation Is Associated With the Modulation of Purkinje Cell Activity: An In Vivo Study Using Rats

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Introduction: Transcranial direct current stimulation (tDCS) has been shown to be an effective treatment method for cerebellar ataxia in humans. However, the changes in the cerebellar cortical neurons have not been studied as potential contributing factors in the mechanism of the treatment. The focus of this study is to monitor activity changes in rat cerebellar Purkinje cells due to the application of tDCS.

Hypothesis: tDCS used for cerebellar ataxia treatment changes the cerebellar output to the motor cortex by increasing Purkinje cell activity.

Methods: The protocol used in this project was approved by the IACUC of PCOM. Ten adult female Sprague-Dawley rats were used in this study. The animal was anesthetized using Isoflurane followed by Ketamine/Xylazine/Acepromazine cocktail. The animal was kept on a heating pad to prevent hypothermia and the heart rate was monitored by a vital sign monitor. The animal was then placed on a stereotaxic apparatus. Surgery was performed to expose the surface of the cerebellar cortex to allow the use of recording electrodes. The recording electrode was lowered by a manipulator into the cerebellar cortex. The skin posterior to the cerebellum was kept intact for tDCS. To generate tDCS, a metal wire/plate was attached to the skin immediately posterior to the hole prepared for the cerebellar neuron recordings. An anodal current (100 or 200 μA) was delivered using stimulus isolator for 20 minutes, which is comparable to the treatment to human cerebellar ataxia. Neural signals were collected in 3 segments: before stimulation (10-minute control), during stimulation (20 minutes), and after stimulation (10 minutes). Data were then analyzed using MatLab Software.

Results: Fourteen Purkinje cells were recorded from Crus I or II regions in the cerebellar cortex. Eight cells showed a significant increase in average firing rate (22.76%, P=.0038). One cell showed no change through all 3 stages, and rest 5 cells showed a decrease in the average firing rate (41.8%, P=.084). For 5 cells local field potentials were analyzed using power spectrum in which no significant change was observed to the main peak at 2 Hz. In 1 case (tDCS with 200 μA), the amplitude of the second peak between 7 and 8 Hz increased.

Conclusions: The majority of the Purkinje cells (8 out of 14) showed an increase in average firing rate after the application of tCDS with anodal current. This change is not dependent on the intensity of the

stimulation. The changes in the local field potential reflect the activity changes in all the types of the cerebellar neuronal structures including those interneurons, parallel fibers, and even climbing fibers. Taking together the changes in both Purkinje cell and local field potential activities in response to tDCS, the variability in the activity changes of the cerebellar cortex may involve other cellular components in the circuitry.

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B34—Chronic Diseases & Conditions

Publication Bias Evaluations Are Not Routinely Conducted in Clinical Oncology Systematic Reviews

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Research Question: Publication bias (PB) may lead to exaggerated estimates of summary effects in systematic reviews (SR). The extent of PB assessment by SRs within oncology journals is unknown.

Methods: This study examined SRs from high impact factor oncology journals between 2007 and 2015 using a PubMed search. SRs were screened and coded for relevant PB study characteristics. A re-analysis of SRs not initially evaluating PB was performed using Egger's regression and the trim-and-fill method.

Data Analysis and Results: Of 182 included SRs, 52 performed a PB assessment. The most common form of evaluation was a funnel plot supplemented by Egger's regression or Begg's test (23 of 52 [44%]). PB was found in a subset of these SRs (10 of 52 [19%]). SRs that stated adherence to a reporting guideline frequently failed to address PB. Based on re-analysis of meta-analytic data, the magnitude of effect sizes generally decreased when conducting our evaluations of PB among non-reporting SRs in our sample.

Conclusion: Our study shows that there is an underutilization of PB assessments in oncology SRs. Furthermore, SRs not reporting PB evidence were likely to have at least some degree of PB. PB could be improved by adhering to reporting guidelines and through grey literature and clinical trials registries searches.

Funding: No funding source.

B35—Chronic Diseases & Conditions

Heat Shock Protein Protects Against Diet-Induced Obesity: Stabilization of Total Intestinal Bacterial Content

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Introduction: The gut microbiota has a critical role in nutrient acquisition and metabolic balance. Changes in total bacterial content, bacterial diversity, or shifts in major bacterial phyla or in individual species may influence calorie extraction and gastrointestinal inflammation. While knowledge regarding the influence of intestinal bacteria in the development of obesity has exponentially increased, little is known about how host anti-inflammatory mediators such as heat shock protein 70 (HSP70) expressed in the gut may alter the gut microbiota and prevent obesity. Henstridge et al, 2014, showed that the expression of Hsp70 in the intestinal lumen results in the prevention of an inflammatory response in the gut. Our study explored the effect of transgenic (TG) overexpression of Hsp70 specifically in the villin-expressing epithelial cells in modifying total bacterial content as a mean of preventing diet-induced obesity (DIO).

Hypothesis: We hypothesized that Hsp70 over-expression prevents DIO in part by stabilizing the total bacterial content in the intestinal microbiota, thus

preventing the dysbiosis induced by high fat diets.

Methods: Fecal pellets were collected from non-transgenic (NTG) and TG Hsp70 littermates after 14 weeks on a low fat (LF; 10 kcal%) or high fat (HF; 60 kcal%) diet. TG Hsp70 mice expressed Hsp70 via a villin-driven promoter. Bacterial DNA was isolated from the fecal pellets, quantified by nanodrop, and analyzed using the Femto Bacterial DNA Quantification Kit (Zymo Research). Results were analyzed by 2-way ANOVA with a Sidak post-hoc test. Results are presented as mean ± SD and significance was determined at $P<.05$. The protocol was approved by the Midwestern University Institutional Animal Care and Use Committee.

Results: Quantification of fecal Hsp70 content demonstrated undetectable levels in the NTG mice, but significant levels in TG mice (38.8 pg Hsp70/mg of feces, $P<.05$). Two-way ANOVA showed a diet effect ($P<.05$) and total fecal bacterial DNA was significantly reduced by a HF diet (0.50 ± 0.16 vs 0.20 ± 0.01 ng bacteria/ng total DNA in the LF compared with HF diet fed mice, respectively). Villin-promoter driven Hsp70 expression in the TG mice demonstrated protection against the HF-induced reduction in total fecal bacterial content (0.42 ± 0.13 vs 0.36 ± 0.09 ng bacterial DNA/ng total DNA in LF compared with HF diet fed mice, respectively). Sequencing analysis of fecal bacterial DNA indicates that 5 taxonomic groups were altered by overexpression of HSP70.

Clinical Significance: Little is known about the effect of diet on the total bacterial content of the GI tract. Total bacterial load may be important in the development of DIO and altering total bacteria may be exploited as a strategy to reduce obesity. These results indicate that HF diets reduce total bacteria and may predisposition to loss of protective bacteria, leading to a pro-inflammatory state. Up-regulation of colonic Hsp70, stabilizing the intestinal bacterial load and preserving protective bacterial groups, may offer 1 way to prevent or treat obesity. Further research is needed to fully understand the role of total intestinal bacteria in DIO and the role of Hsp70 in protection from obesity.

Clinical Studies

C1—Impact of OMM & OMT

Cardiovascular Responses to Selected Cranial Osteopathic Manipulation in Healthy Young Women

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Background and Purpose: The principle of osteopathic medicine is based on the understanding that a person is a dynamic unit of function, and any alterations in structure will subsequently affects its function. Osteopathic manipulation in the cranial field is aimed to influence biomechanics and autonomic nervous system function, as well as improve circulatory functions. However, there are not many published studies demonstrating the physiological responses to selected cranial techniques. The purpose of this study was to measure changes in heart rate (HR), stroke volume index (SI), and cardiac index (CI) in response to selected cranial techniques and sham manipulation.

Methods: Osteopathic manipulation in the cranial field and sham manipulation were performed by the same osteopathic physician on healthy women aged 20-35 years. Cranial techniques performed were occipital-atlantal decompression, occipital-mastoid decompression, and fourth ventricle compression. Sham manipulation was performed on the control group by the osteopathic physician placing his hands on the skull of the subject without influencing cranial motion. Cardiac parameters were measured by impedance cardiography. The changes before and after manipulation were compared. BIOPAC Systems equipment and software were utilized to record and analyze the data.

Results: Following osteopathic manipulation in the cranial field, but not sham manipulation, there were significant decreases in HR (94%± 6.2%, *P*=.003) and CI (90%±16.2%, *P*=.019) without significant changes in SI at the end of treatment.

Conclusion: The data collected have validated that occipital-atlantal decompression, occipital-mastoid decompression, and fourth ventricle compression decreased cardiac index, by decreasing heart rate without significant impacts on cardiac contractility. Future studies will be focused on the responses of cardiac patients to the selected cranial techniques.

Support: This project was supported by TUN Research Grant Award.

C2—Chronic Diseases & Conditions

WHO vs CDC: Anthropometric Discrepancy of Peruvian Children

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Research Question(s)/Hypotheses: The Centers for Disease Control and Prevention (CDC) holds a greater pediatric standard for healthy weight compared with the World Health Organization (WHO). Studies have shown a discrepancy between the WHO criteria of malnutrition vs the CDC criteria (Phillips, Shulman 2014). The Michigan State University College of Osteopathic Medicine has been collecting pediatric information from various regions throughout Peru from 2011-2014. The purpose of this study was to investigate the aforementioned discrepancy by applying both the WHO and CDC criteria of malnutrition to a large population of Peruvian children. It was predicted that more children would be deemed underweight by the CDC guidelines.

Methods: The CDC uses the standard of body mass index (BMI) to measure the weight to height ratio and, therefore, the weight status of children. According to this definition, any child with a BMI less than the fifth percentile for their age on a national growth curve is considered "underweight." The WHO measures weight status using Z-score: a measure of standard deviation based on height, weight, and age. Any individual with a Z-score lower than -2 is considered to be in the category of "thinness." In this retrospective cross-sectional study, pediatric population data collected in 2011 from Huamachuco, Peru, in 2012 from Mala, Peru, and in 2013-2014 from Iquitos, Peru, was used to calculate and compare the percentage of underweight children.

Data Analysis: For this study, a preprogrammed Microsoft Excel file, readily accessible at http://www.cdc.gov/healthyweight/ was used to calculate percentile scores for the CDC. Z-score was calculated according to WHO guidelines by using the LMS model. L, M, and S values were used according to WHO guidelines found at http://www.who.int/childgrowth/en/.

Results: Over 4 years, a total of n=897 (excluding n=29) Peruvian children were surveyed, ranging from ages 2-19 years. It was concluded that the CDC criteria categorized more pediatric patients as underweight. In 2011, the average percent of children underweight was 0.6% as defined by the CDC criteria, and 0% according to the WHO criteria. In 2012, the average percent of children underweight was 0.72% according to the CDC and 0% according to the WHO. In 2013, the average percent of children underweight was 3.01% by the CDC criteria and 1.2% based off WHO criteria. Data from 2014 showed 4.29% underweight by CDC standards and 1.77% by WHO standards. More females were underweight than males, 3.02% vs 2.51%, respectively, for the CDC, and 1.16% vs 0.91% for the WHO. More children aged 2-4 years were classified underweight relative to children aged 5-19 years.

Conclusion: Overall, the difference between the CDC classification of malnutrition, compared with the WHO definition, is relevant. Unlike the CDC standard, the WHO standard is meant to be appli-

cable to children with a wide variety of diets and from all socioeconomic backgrounds (Phillips, Shulman 2014). As it applies to international medicine, it is important for American physicians to recognize the differences between the parameters used to measure children of healthy weight living in America and children living in other parts of the world. The standard for what constitutes a healthy child in America, greater than the 5th percentile on an average American growth curve, is shifted much higher relative to other countries, eg, greater than the 2.3% on a worldwide scale. These varying definitions have impacts clinically, as a child classified "underweight" or in the category of "thinness" should be evaluated for malnourishment, or could have a variety of underlying conditions such as chronic illness, hormonal imbalances, or psychosocial neglect (Garfunkel, Tanski 2010). Labeling a child as such is a responsibility and, although other clinical factors are also considered, it is important to know the tools one is using to evaluate and treat patients. In summary, the definition of a healthy weight child varies cross culturally and needs to be taken into account when evaluating pediatric patients no matter where the setting may be.

C3—Osteopathic Philosophy

Knowledge of Osteopathic Medical Education in the Canadian Undergraduate Premedical Population

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Introduction: Osteopathic physicians (ie, DOs) represent one of the fastest growing segments of health care professionals in the United States. By 2015, it is anticipated that 1 out of every 5 graduating medical students in the United States will be a DO. This rapid expansion has also been paralleled in Canada. In this novel study, we examine the role of seminars run by osteopathic medical students (OMS) in spreading awareness about osteopathic medical education in undergraduate universities throughout Canada.

Hypothesis: We hypothesized that Canadian premedical students would find OMS-led seminars to be useful in learning about osteopathic medicine and would play an important role in fostering the growth of osteopathic medicine in Canada.

Methods: A total of 181 students from Canadian premedical schools, spanning 5 provinces and 11 institutions, were surveyed after attendance at OMS- and physician-run seminars about osteopathic medical education. Seminar attendees were provided with an anonymous multiple-choice survey at the end of the presentation.

Results: Results from our study indicate that 174 of 181 surveyed students (96%) found the OMS-led seminars useful in raising awareness about the DO degree and that they would recommend the seminar to others. One hundred thirteen of 181 Canadian students (62%) were aware that US-trained DOs were fully qualified physicians. Furthermore, 109 of 181 students (60%) had initially heard of osteopathic medical education through Facebook, through premedical forums, or from these seminars. In contrast, 59 of 181 (33%) heard about osteopathic education via word of mouth, 11 (6%) from experience working with DOs, and 2 (2%) from the AOA/AACOM or osteopathic medical school websites. In addition, 77 of 180 students (43%) viewed DO underrepresentation in Canada as the largest challenge for the profession.

Data Analysis: The collected survey data reveals that the 96% of the 181 surveyed students found the seminars useful in raising awareness about osteopathic medicine; this finding supports our hypothesis that OMS-led seminars would serve as a useful learning tool for Canadian premedical students.

Furthermore, 23 of 181 students (13%) first heard of the DO degree at an OMS-led seminar, supporting our hypothesis that the seminars would help spread awareness of the DO degree in Canada. 145 of 181 (80%) Canadian pre-medical students learned of the DO degree through unofficial channels, such as Facebook, word of mouth, and online premedical forums. Conversely, only 2 of 181 students (2%) learned of the DO degree through an official channel, such as the AOA, AACOM, or an osteopathic medical school website. The American osteopathic medical community could take a number of steps to further foster the growth of Canadian applicants to osteopathic medical schools, including increasing outreach to Canadian students through official OMS-led presentations at Canadian universities. This approach could help Canadian premedical students receive information on the DO degree through official channels, rather than relying on word of mouth or other unofficial online sources, which could contain misinformation.

Conclusion: Overall, virtually all participants felt the seminars were helpful in raising osteopathic awareness amongst Canadian students, thus supporting our hypothesis. This study provides preliminary evidence to support the notion that hosting increased numbers of OMS-led seminars at Canadian universities is an effective way to increase awareness of osteopathic medical education in Canada, and to ensure that the information is delivered through an AOA- or AACOM-approved channel. This first of its kind study provides new insight into the Canadian premedical population. In addition to validating the approach of OMS-led seminars, the findings from this investigation into Canadian pre-medical students' views on osteopathic medicine can be used to further identify effective tools for generating awareness of osteopathic medical education in Canada and beyond.

C4—Chronic Diseases & Conditions

Dosage Range of Post-Implant Intrathecal Baclofen: A Retrospective Study

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Introduction: This is a descriptive study of the management of 33 patients with spasticity using an intrathecal (IT) baclofen pump. These patients had spasticity due to traumatic brain injury (TBI), spinal cord injury (SCI), cerebral palsy (CP), multiple sclerosis (MS), paraplegia, quadriplegia, lower back pain, and Fredricks Ataxin. Spasticity is a "motor control disorder that is characterized by tight or stiff muscles and an inability to control those muscles." This can be caused by damage to the spinal cord or brain by either injury or disease. IT baclofen has been shown to reduce motor tone by inhibiting both monosynaptic and polysynaptic reflexes at the spinal level by possibly decreasing the excitatory neurotransmitter release from primary afferent terminals. A study by Borowski et al concluded that IT baclofen therapy is a safe and effective treatment for children with spasticity. These positive effects have also been shown in other studies. Baclofen appears to be effective in treating both cerebral- and spinal-associated spasticity. The primary objective of this study was to examine the relationship of a patient's ideal dose of IT baclofen with their age, sex, and diagnosis. The overall goal is to be able to use this data to formulate the dosing for IT baclofen recipients in a more standardized manner and in less of the "trial and error" method that is typically used currently.

Methods: This is a retrospective chart review of IT baclofen management of 33 active patients in an office setting. The patients included in this review had to have an IT baclofen pump for 6 months or longer and were being dosed therapeutically with IT baclofen. The data included daily IT baclofen con-

centration and dose, other current medications and dosages, age (by year born), sex, and diagnosis specific to spasticity. Statistical analysis was done with a program through Excel with significance threshold at P=.05.

Results: Patients were dosed with IT baclofen ranging from 23 mcg/d to 1250 mcg/d. The dose of IT baclofen did not demonstrate a significant correlation with age (P=.20) or sex (P=.50). There were, however, significant differences in dosages between patients by specific diagnoses. Significant dosage differences were found in patients diagnosed with MS vs CP (P=.01); and SCI paraplegia vs CP (P=.0005). Not all dosages were significantly different by diagnosis, such as paraplegia and MS (P=.12) or paraplegia and quadriplegia (P=.77). This means that there was no significant difference between IT baclofen dosages in these diagnoses. The origin of the spasticity, central (cerebral) or spinal, also did not show a significant difference (P=.08). The results also show that patients who are taking other medications along with IT baclofen were not significantly different than those who were not (P=.25).

Discussion: This study sheds light on the dose of IT baclofen specific to a patient's diagnosis, as well as its lack of relation to a patient's age or sex. Based on our data, we are able to conclude that there is a significant difference between IT baclofen dose in patients with CP and those with MS. The study shows that the mean IT baclofen dose given to patients with CP (mean, 874.35 mcg/d; range, 566.4 mcg/d) is significantly higher than the dosage for patients diagnosed with MS (mean, 245.81 mcg/d; range, 503.14 mcg/d). This might imply that patients with CP tend to need higher doses of IT baclofen than patients with MS. In contrast to our study, Santamato et al showed that after a 6-month period, patients diagnosed with MS had significant increases in their IT baclofen dose compared with those with other spasticity etiologies. This increase in dose might be due to MS patients having a quicker tolerance to baclofen, a progression of the disease and spasticity, or other variables. A significant difference was found between those with SCI paraplegia and CP (P=.0005). Patients diagnosed with paraplegia showed a mean dosage of 317.7588889 mcg/d and a range of 613.12.75 mcg/d, but patients diagnosed with CP showed an average dose of 874.35 mcg/d and a range of 566.4 mcg/d. This indicates that patients with CP typically require more IT baclofen than patients diagnosed with SCI paraplegia. The origin of spasticity (central or spinal) was not found to cause a significant difference in IT baclofen dosage in our study (P=.079). This agrees with the study by Saval and Chiodo that found no significant dose, concentration, dose change, or mode of delivery differences between patients with spinal or central origins of spasticity. Although the catheter tip location was not taken into account for this study, a prospective cohort study by Sivakumar et al found that the location of the catheter tip did not have a statistically significant effect on patients' clinical responses to spasticity. The range was calculated by subtracting the lowest IT baclofen dose from the highest IT baclofen dose. It should be noted that there was a range value above 500 mcg/d in patients with the same diagnostic cause of spasticity. This large of a range could be due to the varying severity of the specific diseases, misdiagnoses, or individual variations of the patients.

Conclusion: Our data indicate that patients with CP required significantly higher amounts of IT baclofen than those diagnosed with SCI paraplegia or MS. We can also infer from our data that there is no significant difference in dose of IT baclofen with regard to age or sex. This data can be helpful for clinicians managing spasticity with IT baclofen in the outpatient office setting. If a patient's dosage requirement is significantly higher than the dosages in this study, this could be an indicator of such problems as misdiagnosis, pump malfunction, broken catheter, or catheter displacement from the IT space.

This could signal the need for further evaluation of the patient, the pump, and the catheter system. Future studies should compare the dosage with catheter tip location, infusion rates, baclofen concentration, and functional outcomes. This could lead to a better understanding of the optimal dose range, as well as improved functional outcomes for individuals with spasticity. The limitations of this study include relatively low population size, relatively short length of time that the patient had the pump, lack of a formal spasticity assessment, and lack of functional outcome assessment. This should be viewed as a pilot study, and additional studies are needed to delineate a standardized and optimal dosage plan for patients using IT baclofen.

C5—Impact of OMM & OMT

Efficacy of Osteopathic Manipulative Medicine and Phototherapy for Patients With Chronic Low Back Pain

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Introduction: The research has demonstrated separately that phototherapy and osteopathic manipulative medicine (OMM) are effective in reducing chronic low back pain. However, there has not been any research to evaluate whether the interaction of the 2 treatment approaches together can provide enhanced pain relief. Osteopathic physicians utilize an approach to the treatment of patients called osteopathic manipulative medicine (OMM). The osteopathic physician will diagnose and then treat the somatic dysfunctions found with 1 or more of several OMM treatment approaches. Research has shown this approach to be beneficial for back pain reduction. Physical therapists may utilize phototherapy, or low level laser therapy (LLLT), for the management of low back pain. Research has shown that this modality can be effective for both tissue repair and pain relief.

Hypothesis: The combined treatment with both osteopathic manipulative medicine (OMM) and phototherapy will provide greater pain relief for patients with chronic lower back pain than standard medical management or either treatment alone.

Methods: Fifteen subjects (aged >18 to <65 years) with chronic low back pain greater than 3 months duration, who met the inclusion criteria, were randomly assigned to 1 of 4 groups: (1) control group receiving standard medical treatment only, (2) phototherapy group with subjects receiving phototherapy twice weekly for 8 weeks, (3) OMM group with subjects receiving OMM twice weekly for 8 weeks, or (4) combination group with subjects receiving combined phototherapy and OMM each twice weekly for 8 weeks. All subjects were to complete 3 questionnaires, which were the Visual Analog Scale (VAS), the Oswestry questionnaire for measuring the level of pain, and the Medical Outcomes Study (MOS) 36-Item Short-Form (SF) Health Survey, also known as the SF-36 Health Survey, for measuring the quality of life (QOL) associated with the pain, at 3 points in time (before the intervention, halfway through the intervention, and after the intervention). The phototherapy machine utilized for this study is manufactured by Dynatronic Solaris Phototherapy Unit. The red/infrared probe has 4 red diodes emitting 660 nm wavelength and 32 infrared diodes emitting 880 nm wavelength. Osteopathic manipulative treatment (OMT) was provided by osteopathic physicians with teaching experience in OMT, and no high-velocity techniques were utilized. The entire body, with attention to the lumbar spine, sacrum, and pelvis, was included in the evaluation and treatment. To detect any existing patterns or trends in the changes of pain scores from before to after intervention across different treatment groups, extensive exploratory data analysis was performed in both quantitative and visual manners, followed by the analysis of covari-

ance (ANCOVA) in a confirmatory manner. The data set analyzed includes those subjects consenting to participate, including those with incomplete data sets, through July of 2015. This continues to be an active, publically registered clinical study, and recruitment is ongoing. Future analysis will include all subjects data obtained up to the study closure. NYIT IRB-approved BHS-740.

Results: The preliminary results show that the mean (SD) VAS pain score was 3.3 (2.5) before treatment, 3.6 (2.7) in mid-treatment, 2.6 (2.6) after treatment, and the mean (SD) Oswestry pain score was 16.5 (7.7) before treatment, 13.1 (7.5) in mid-treatment, and 12.5 (7.7) after treatment. The combination group showed more noticeable drops in both VAS and Oswestry pain scales from before to after treatment compared with the groups of either standard treatment only, OMM only, or phototherapy only (VAS: -3.4 [4.4] vs 0.1 [3.9]; Oswestry: -10.7 [8.1] vs -2.0 [6.9], for combination vs the others, respectively), though it did not reach statistical significance probably due to a combination of limited sample size and incomplete surveys. The combination group showed better improvement in the SF-36 subsections of role limitations due to physical health (12.5 [17.7] vs 0 [0.0]), bodily pain (21.3 [30.1] vs 4.4 [27.6]), and general health perceptions (5.0 [7.1] vs -.3 [9.5]), and equal improvement in the rest of the subsections compared with the other groups.

Conclusion: At this time, the data from this pilot study does not provide statistically significant results to support our hypothesis that there is a synergistic effect of OMM and phototherapy for subjects with chronic lower back pain. However, there were identifiable trends and patterns present, which pointed to improvement in scores between the pre-treatment and post-treatment data. Our original hypothesis may be better supported as we approach our requisite sample size. A larger sample size may enable us to further differentiate the singular and combined effects of the interventions. Understanding the effects of each treatment approach alone, and then in combination, can guide practitioners to work collaboratively for more patient-centered and effective treatment plans, whether for chronic lower back pain or for other physical pain conditions.

Registered: ClinicalTrials.gov (1/8/2013)

C6—Chronic Diseases & Conditions

Effect of Oral Re-esterified Omega-3 Nutrition on Dry Eye Syndrome

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Background: Dry eye disease (DED) is the number 1 reason why patients seek an eye consultation. According to Medicare data, 37% of visits to an eye doctor are due to dry eyes. Dry eye disease is a common yet complex and multifactorial condition that can lead to visual loss, damage to the ocular surface, discomfort, and overall reduction in quality of life. Omega-3 supplementation has been recommended as part of the management of aqueous deficient and evaporative dry eye disease in both the International Dry Eye Workshop (DEWS) and International Workshop on Meibomian Gland Dysfunction.

Objective: The purpose of this study was to assess the effect of oral re-esterified omega-3 fatty acids on tear osmolarity, matrix metallopeptidase-9 enzyme (MMP-9), Ocular Surface Disease Index Questionnaire (OSDI), tear break-up time (TBUT), Schirmer's score, corneal staining and Omega index.

Methods: This was a multicenter, prospective, interventional, randomized, double-masked, placebo-controlled, IRB-approved study (Western IRB). Patients with dry eyes and confirmed Meibomian Gland dysfunction were randomly assigned to re-

ceive either placebo or 1680 mg of eicosapentaenoic acid (EPA) and 560 mg docosahexaenoic acid (DHA) for 12 weeks (Dry Eye Omega Benefits, PRN Physician Recommended Nutriceuticals). All patients underwent a screening, baseline, 6-week and 12-week visit.

Results: A total of 105 patients with dry eyes completed the study. The eye with higher tear osmolarity was determined as the worse eye. Mean tear osmolarity at baseline and 12 weeks was 326.0 and 317.7 mOsm/L in placebo group; compared with 326.2 and 306.9 mOsm/L in omega-3 group (P=.004). OSDI at baseline and 12 weeks was 27.1 and 22.0 in placebo group; compared with 32.4 and 15.5 in the omega-3 group (P=.002). Tear break-up time at baseline and 12 weeks was 4.61 and 5.81 seconds in placebo group; compared with 4.78 and 8.25 seconds in the omega-3 group (P=.002). Omega-3 index levels statistically improved in 12 weeks in the omega group vs placebo (P<.001). There was a statistically significant (P<.05) improvement in tear osmolarity, OSDI, tear break-up time, MMP-9 biomarker enzyme, and omega index levels as observed over 12 weeks.

Conclusions: This study demonstrated that oral supplementation with re-esterified (second generation) Omega-3s improved both subjective and objective signs and symptoms of DED over a 12-week period. This adds to the growing volume of data suggesting a correlation between Omega-3 levels and DED. Prior studies show that tear osmolarity exhibits the strongest correlation to DED and severity and can be effectively used to track therapy. The findings from this study are strongly suggestive of a therapeutic effect from the re-esterified omega-3 compound. Currently there is no recommended dosage for the consumption of omega-3s in the treatment of dry eyes. This study demonstrates that re-esterified omega-3 fatty acids consumed in a dose of 1680 mg EPA and 560 mg DHA once daily for 12 weeks improved both subjective and objective improvement of signs and symptoms of dry eyes. Additional studies are however necessary.

C9—Musculoskeletal Injuries and Prevention

Evaluation of Musculoskeletal Competency in Osteopathic Medical Students and Their Faculty

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Background/Hypotheses: In 1998, Freedman et al suggested that medical school graduates in the United States failed to achieve a basic level of musculoskeletal competence. Studies have confirmed this in medical students, residents, and physicians at institutions in the United States and abroad. In 2006, Stockard et al reported marginally higher pass rates among osteopathic medical students over their allopathic counterparts, most likely due to their musculoskeletal curriculum emphasis. The authors hypothesized that A.T. Still University–School of Osteopathic Medicine in Arizona (ATSU-SOMA) medical student class cohorts would show an increasing mean score, with third- and fourth-year students demonstrating a basic level of musculoskeletal competence; furthermore, that the musculoskeletal teaching faculty would show a basic level of musculoskeletal competence. To our knowledge, this is the first study to date to examine faculty teaching in any part of the musculoskeletal curriculum, at an accredited US osteopathic medical school.

Methods: With institutional review board approval, we sent the Basic Competency Examination in Musculoskeletal Medicine (BCEMM) survey instrument electronically to all enrolled students and musculoskeletal related faculty at ATSU–SOMA. This survey has been previously validated by 124 orthopedic and 240 internal medicine US residency program directors. The student and faculty e-mail list was gener-

ated by the registrar's office. Faculty teaching anatomy, medical skills, osteopathic manipulative medicine (OMM), and regional directors of medical education (RDME) for first-, second-, third- and fourth-year medical students were included. All other faculty were excluded. The survey was sent 2 times per week for 4 weeks during May 2014. Responses were collected and de-identified using Qualtrics database. The BCEMM survey contains a fill-in-the-blank, 25-item questionnaire. The survey responses were graded by 2 authors independently. Per exclusion criteria, any survey that had 19 or more questions consecutively unanswered was excluded. A passing score was designated greater than or equal to 70% correct, per previous studies. Four-hundred-and-seventy-eight e-mail addresses were collected, and surveys were sent out accordingly.

Data Analysis: Data are reported as mean percentage test scores (SD) with 95% CI.

Results: Of the 478 surveys sent, 437 were to students and 41 were to faculty. One-hundred-and-one student responses were collected, 14 of which were excluded per criteria. Eighty-seven student responses met the inclusion criteria: 26 from first-year, 21 from second-year, 23 from third-year, and 17 from fourth-year medical students. Thirty-two faculty member responses were collected and 18 were included per criteria: 3 from the anatomy department, 3 from the medical skills department, 2 from the OMM department, and 10 from the RDME department. The mean percentage test scores for first-, second-, third-, and fourth-year medical students whose responses met inclusion criteria were 46% (0.16; 95% CI, 40%, 52%), 53% (0.15; 95% CI, 46%, 60%), 64% (0.12; 95% CI, 59%, 69%), and 58% (0.12; 95% CI, 52%, 64%), respectively. The mean percentage test scores for faculty in anatomy, medical skills, OMM, and RDME were 67% (0.06; 95% CI, 51%, 82%), 71% (0.22; 95% CI, 16%, 125%), 90% (0.08; 95% CI, 14%, 166%), and 56% (0.17; 95% CI, 44%, 69%), respectively. Fifteen percent (13 of 87) of students passed: 12% (3 of 26) in first year, 10% (2 of 21) in second year, 17% (4 of 23) in third year, and 24% (4 of 17) in fourth year. Forty-four percent (8 of 18) of faculty whose responses met inclusion criteria passed: 1 of 3 in anatomy, 2 of 3 in medical skills, 2 of 2 in OMM, and 3 of 10 in RDME. The students' mean score was 55%. The faculty mean score was 64%.

Conclusion: The results suggest that the majority of responding osteopathic medical students (85%) and about half of musculoskeletal teaching faculty (56%) whose responses met inclusion criteria failed to demonstrate a basic level of musculoskeletal competence. Stockard et al reported their fourth-year osteopathic medical students' mean score was 65.65%. This is higher than what we found (58%). In 2007, Day et al. reported the mean scores of 43%, 56%, and 66% for second-, third-, and fourth- year allopathic medical students respectively. ATSU–SOMA second- and third- year students' mean scores and pass rates were higher than those reported by Day et al. In 2012, Skelley et al reported the overall mean test score as 51.1% and the individual class test score mean as 37%, 52%, 54%, and 59% of first-, second-, third-, and fourth-year allopathic medical students, respectively. The overall mean score for ATSU-SOMA and the mean score of first-, second-, and third-year osteopathic medical students were higher than what Skelley et al reported. These results suggest a marginal advantage of osteopathic medical students' musculoskeletal competence over their allopathic counterparts. ATSU–SOMA faculty are well-respected, competent clinicians and educators, and yet collectively, their mean score was 64%. However, medical skills and OMM faculty groups both demonstrated a basic level of musculoskeletal competence. While the pass rate of faculty (44%) was higher than any of the student groups (24%), it warrants further investigation. Faculty within the anatomy department are comprised of both clinicians and basic scientists who have little to no clinical experience. This could account for their 67% mean score. While the BCEMM survey was originally

validated by 124 orthopedic and later by 240 internal medicine US residency program directors, the internal medicine program directors assigned a mean importance score of 7.4 (of 10) to the questions on the examination compared with a mean score of 7.0 assigned by the orthopedic program directors; thus, the BCEMM survey may not reflect the didactic knowledge necessary to perform well in all aspects of primary care, which is the focus of ATSU-SOMA. Our study was limited by a low student and faculty response rate. Future research should elucidate the etiology and repercussions of a lack of basic musculoskeletal competence, not only nationally, but also globally. Also, future research should seek to verify that the validated 25-question BCEMM survey is truly the best assessment of a medical student's musculoskeletal competence.

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C11—Chronic Diseases & Conditions

Descriptive Study of Mohs Surgical Wounds Managed With a Collagen ECM Dressing or Standard Wound Care

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Skin cancer is the most common malignancy in humans with over 1 million cases detected per year. Mohs micrographic surgery is the preferred method of treatment, and although most Mohs wounds are closed primarily, some are left open to heal by secondary intention. Wound healing, comfort, and the aesthetic appearance of the healed wound are of concern to patients and providers. In this study, we prospectively evaluated the effect of a dermal template with collagen extracellular matrix dressing (CECM) on individuals with Mohs wounds healing by secondary intention. The primary objective was to characterize the healing time of Mohs surgical wounds when managed with CECM in addition to standard wound care. Twelve subjects from 3 sites were enrolled and randomly assigned to control or treatment in this IRB-approved study. Subjects were enrolled and randomly assigned to treatment the day of surgery and followed weekly for 4 complete weeks, for a total of 5 visits. Control wounds (n=7) were managed with silver contact layer. Treatment wounds (n=5) were managed with silver contact layer plus CECM dressing. Wounds were measured, photographed, and dressed at each study visit. Patient reported outcomes were collected along with overall patient satisfaction scores at the final visit. Data were analyzed using means ± SD, ranges, and medians. Average initial wound size and subject demographics were similar between groups. Forty percent of the treatment group and 28% of the control group were completely healed at 4 weeks. Interestingly, excessive granulation of tissue was noted with 2 subjects (40%) in the treatment group compared with 4 subjects (57%) in the control group. Between 86% and 100% of all subjects were satisfied or very satisfied with both treatments.

Funding: This study was funded by Hollister Incorporated.

C13—Chronic Diseases & Conditions

Medication Adherence in Persons With Chronic Conditions in Medically Underserved Regions of Ecuador

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Introduction: In Ecuador, where chronic illness is a relatively new phenomenon, cultural models for patient care are still very much in the making. Elucidation of noncommunicable chronic conditions (NCC) and medication adherence in medically underserved areas of Ecuador has yet to be achieved and remains a priority for the World Health Organization. Anecdotal data indicate that developing countries in South America are experiencing increases in chronic illnesses and that there is an expanding need for interventions that target improved health and management of these conditions. The primary goal of this study was to advance the understanding of medication adherence in rural Ecuadorians living with chronic conditions.

Methods: A cross-sectional, correlational study was conducted to evaluate NCC in the Milpe region of Ecuador. A convenience sample of 31 patients aged 18 or older currently taking medications for chronic illness who received medical care during a university-based medical outreach trip completed an anonymous pen-and-paper questionnaire. The survey collected data on medication adherence, health literacy (re: medications), perception of personal health status, and access to medical care. The survey, offered in Spanish, took about 20 minutes to complete. χ^2 analyses were computed to assess the relationship between medication knowledge and medication adherence behaviors in rural Ecuadorians using SPSS statistical software. This study was approved by the researchers' university's institutional review board.

Results: The majority (n=29; 93.5%) of the participants reported a net income of less than $5000 per year and 84% reported having less than a high school education. Sixty-five percent of participants rated their health as fair or poor. The most commonly reported conditions were diabetes, hypertension, high cholesterol, and heart disease; 45.2% (n=14) participants reported having multimorbid chronic conditions. Nearly one-fifth (n=6; 19.4%) had no health care provider and reported there was no clinic or hospital to go to for their chronic conditions. Fifty-five percent (n=17) reported it was hard or very hard to get medication refills on time, and 58.1% (n=19) reported they sometimes or often put off getting refills because they were unable to get to the pharmacy. Analyses revealed no statistically significant relationship between knowledge and behaviors with regard to medication adherence. While many participants understood the benefits of and how to take their medications, medication adherence behaviors were still suboptimal (M=2; possible total score range 1 to 4, low numbers represent less adherence).

Conclusion: This is the first study to our knowledge that examined medication adherence behaviors in Ecuadorians with chronic conditions living in rural, medically underserved areas. Data from this study will assist in determining which treatment strategies will be most beneficial when considering the development of health care services and generate guidance protocols to improve medication adherence among this understudied group and for whom interventions have not yet been developed.

C14—Chronic Diseases & Conditions

Determinants of Tissue Contact Using the 8mm Equipped With Mini Electrode Technology

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Introduction: The current large tip ablation catheters are limited in their ability to accurately assess tissue contact. We tested the hypothesis that focal electrogram (EGM) voltage and pace thresholds (TH) utilizing 3 × 0.8 mm mini electrodes (ME) radially distributed 1.5 mm from the tip of an 8 mm ablation catheter allow differentiation between good and poor contact.

Methods: The catheter was inserted into a 9F deflectable sheath equipped with 11F 14 mm long perforated tubing. The 8 mm tip was extended outside the tubing for good contact, and retracted inside allowing only 1 mm to protrude for poor contact. RF lesions were placed under fluoroscopic and St. Jude NavX guidance followed by recording of pace TH and EGM amplitudes for good (73) and poor contact lesions (31). RF application was titrated to the nadir of the ME EGM reduction. The hearts were stained in Tetrazolium blue and lesions matched to electrical recordings.

Results: 8 mm-Ring data revealed minimal differentiation between preablation good and poor contact in the atria (A) and ventricle (V), whereas ME data exhibited marked differences in both pace TH and EGM amplitude. Only 55% of poor contact lesions in the A were transmural compared with 94% of good contact. Poor contact lesion depth in the V was 49% that of good contact.

Conclusions: (1) The MEs placed on the 8 mm ablation catheter are useful for defining pre-ablation catheter to tissue contact. (2) Poor tissue contact significantly reduces ME EGM amplitude and increases ME pace TH, resulting in decreased A and V lesion depth and an increased number of non-transmural lesions in the A.

C15—Pain Management

Improving Response to Treatment for Patients With DDD by the Use of Molecular Markers

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Research Question(s)/Hypotheses: Protein biomarkers associated with lumbar disk disease have been studied as diagnostic indicators and therapeutic targets. A cartilage degradation product, the Fibronectin-Aggrecan complex (FAC) identified in the epidural space, has been shown to predict response to lumbar epidural steroid injection in patients with radiculopathy from herniated nucleus pulposus (HNP) and identified in patients with DDD. A therapeutic agent that prevents the formation of the G3 domain of aggrecan will reduce the fibronectin-aggrecan G3 complex and accordingly may be an efficacious treatment. Because the production of G3 domain of aggrecan is catalyzed by different known classes of proteases, a common inhibitor of all of these proteases could be an ideal therapeutic agent. Such a protease inhibitor is found in plasma and synovial fluid, alpha-2-macroglobulin (A2M). The purpose is to determine the ability of FAC to predict response to biologic therapy with concentrated autologous A2M for patients with LBP from DDD

Methods: Twenty-four patients with LBP and MRI positive for DDD. Patients underwent lavage for molecular discography and FAC analysis and injection of platelet poor plasma rich in A2M. Oswestry disability index (ODI) and visual analog scores (VAS) were noted at baseline and at 3 months. Clinical improvement was defined as patients with

both a decrease in VAS of at least 3 points and ODI >20 points.

Data Analysis: ANOVA

Results: 13M/11F. Aged 24-62 years (average 44.3 years). 12 disks were FAC + in 10 pts, out of 40 disks total. 11 patients improved, 13 did not. Mean VAS improvement in FAC-positive patients was 4.9 ± 0.9, vs 1.5 ± 1.2. FAC negative (P< .0001; ANOVA). ODI improved 37 ± 9.3 in FACT-positive vs 9.4 ± 11.9 in FAC-negative (P<.0001; ANOVA).

Conclusion: "FAC+" patients are more likely to demonstrate improvement after autologous A2M injection. This suggests that not only is FAC an important biomarker in identifying who will improve, but also that A2M is an important biologic treatment in discogenic diseases, a true theranostic. The current study bridges the gap between the presence of a biomarker and clinical outcomes.

♦C16—Chronic Diseases & Conditions

Intra-Individual Variability in Salivary Uric Acid and Insulin Levels

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Research Question(s)/Hypotheses: Salivary uric acid and insulin have been identified as potential noninvasive biomarkers of systemic diseases including type 2 diabetes and metabolic syndrome. However, the degree to which salivary levels of these molecules fluctuate over time has not been determined. The goal of this study was to characterize the within-subject variability in salivary uric acid and insulin concentration. This information should help to establish the viability of these biomarkers as candidates for further clinical development. It was hypothesized that there would be greater variability in fasting salivary uric acid levels than insulin levels within subjects.

Methods: This study was approved by the West Virginia School of Osteopathic Medicine Institutional Review Board. Subjects were recruited through local distribution of flyers. Volunteers who were aged at least 5 years and capable of providing consent/assent and following instructions for saliva collection were eligible for the study. Exclusion criteria were a history of gout, diabetes, or Sjorgren's syndrome or current pregnancy. Unstimulated fasting saliva samples were collected on site from each subject twice per week for 4 weeks. The passive drool method was used and flow rates were calculated. Mucins were removed from saliva using centrifugation.

Data Analysis: Salivary uric acid concentration was determined using the Stanbio enzymatic assay. Salivary insulin concentration was determined using the Mercodia ultrasensitive insulin ELISA kit. Statistical analysis was performed using IBM SPSS statistics 22. Intraclass correlation coefficients (ICC) were calculated to assess the variability in repeated measurements from individual subjects.

Results: Eight subjects participated in the study. The average age of participants was 29 years, and 5 participants were female. Six of the volunteers provided all 8 saliva samples and all volunteers provided at least 5 samples. The average salivary uric acid concentration was 211.6 + 83.6 mM (range, 66.3 – 456.8). The average within-subject range over repeated collections was 161.5 + 60.9 mM. Salivary insulin could be reliably detected in 4 of the 8 subjects. The average insulin concentration was 3.7 + 1.9 mU/L (range, 0.8 – 7.9) and average within-subject range was 2.8 + 1.3 mU/L. ICCs calculated using the first 5 samples from each subject demonstrated only moderate intra-subject correlation over repeated samples for both uric acid (0.478) and insulin (0.653). Variability remained high even with correction for salivary flow rate.

Conclusion: These results suggest that salivary levels of both uric acid and insulin fluctuate significantly over time within individuals. This variability may limit their use as noninvasive tools for screening and diagnosis.

♦ Abstract that won first or second place in the 2014 SOMA Student Poster Competition.

C17—Chronic Diseases & Conditions

Prevalence of Cardiometabolic Abnormalities in Obese and Overweight Children in a Rural Clinic

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Overview: Pediatric obesity is associated with an increased risk of developing cardiovascular disease and type 2 diabetes at a young age. Identifying children with early signs of these diseases is an important step in the prevention of future complications. The goal of this study was to investigate the prevalence of cardiometabolic abnormalities in obese and overweight children in a primary care clinic located in rural West Virginia, a state with one of the highest rates of pediatric obesity in the nation.

Hypothesis: It was hypothesized that the prevalence of hypertension, dyslipidemia, hyperinsulinemia, and impaired fasting glucose would be higher in obese children than in overweight children.

Methods: This study was approved by the West Virginia School of Osteopathic Medicine Institutional Review Board. De-identified data were obtained from pediatric electronic medical records available at the Robert C. Byrd Clinic in Lewisburg, West Virginia. All obese and overweight patients younger than 18 years who received fasting insulin, glucose, and lipid panel screening in a 2-year period (2012-2014) were included in the sample. The extracted data included patient age, gender, body mass index percentile, hypertension diagnosis, and results of fasting insulin, glucose, and lipid testing. Cutoffs used to define hyperinsulinemia, impaired fasting glucose, and dyslipidemia were those recommended by the American Diabetes Association and Expert Panel Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents.

Data Analysis: Data analysis was done using IBM SPSS 22. Exploratory analysis was performed to examine distribution of continuous variables. Means were compared using the Mann-Whitney U test. The χ^2 test was used to compare categorical variables.

Results: Data were available for 223 patients (124 female and 99 male). The average age of the population was 13.4 years (range, 10-17 years) and 79% were obese. Seventy percent of the population had at least 1 cardiometabolic abnormality and 16% had 3 or more. Obese children were significantly more likely to have low HDL-cholesterol than overweight children (44% vs 22%) and hypertension was only seen in the obese children (13%). However, there were no significant differences in the prevalence of hyperinsulinemia, impaired fasting glucose, hypercholesterolemia, or hypertriglyceridemia between the 2 groups.

Conclusions: Although hypertension was only seen in obese patients, dyslipidemia, hyperinsulinemia, and impaired fasting glucose were equally prevalent in both groups. These findings suggest that screening for changes in lipid and glucose metabolism in our rural Appalachian population should be done in children who are overweight, not only in those who are obese.

C20—Chronic Diseases & Conditions

Paraoxonase 1 Lactonase Activity in Familial Hypercholesterolemia: A Pilot Study

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Background: The beneficial effects of paraoxonase 1 (PON1) on the inhibition of atherosclerosis might be more pronounced in a population that is prone to develop the disease than the general population. For this reason, we studied the status of PON1 in patients with familial hypercholesterolemia (FH). These patients are characterized by substantially increased serum low density lipoprotein-cholesterol (LDL-C)

concentrations and sharply increased cardiovascular disease risk. The few studies in the literature concentrate on polymorphisms, and those that measured activity did not compare with a polygenic hyperlipidemia control population, nor did they measure the physiological lactonase activity of PON1. We hypothesized that PON1 activity is increased in FH to compensate for excess oxidative stress on LDL-C.

Aims: To investigate PON1 esterase and lactonase activity and its distribution in HDL subclasses in a population of FH patients treated with statins.

Methods: Heterozygous FH patients (n=19) and age-matched hyperlipidemic subjects (n=21) also treated with statins were recruited at the lipidology clinic in Jichi Medical School. PON1 arylesterase and lactonase activities were analyzed using phenylacetate or dihydrocoumarin as the substrate, respectively. Lipid profiles were measured using standard methods. PON1 distribution in HDL subclasses was analyzed with our recently published method (1-2): native lipoproteins from serum were separated in a 4-12% gradient gel and PON1 activity was detected in situ using para-nitro-phenylacetate, scanning and densitometry. The study was approved by the Ethics Committee of Jichi and Touro University.

Results: Controls and case did not differ in their TC,. LDL-C, HDL-C, or TG values due to effective treatment. PON1 arylesterase was on average 13% higher and lactonase was 79% higher in FH patients than in controls. The zymogram did not show a different distribution of PON1 in HDL subclasses.

Conclusions: Our pilot data show FH patients seem to have increased levels of a PON1 protein and even higher of its activity: they have more PON1 and it is far more active. Indeed our pilot data suggest that enhanced lipoperoxidation in this condition induces PON1 expression and activity, probably as a protective measure. This difference is not due to statin treatment nor to redistribution within HDL subclasses.

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C21—Impact of OMM & OMT

Response of Tinnitus to Osteopathic Manipulation

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Research Question(s)/Hypotheses: Tinnitus is a perception of sound when no stimulus is present. It affects 16% of Americans and is fairly treatment resistant. Until recently, tinnitus was thought to be a disease of the cochlea. Evidence suggests the pathophysiology is far more complex, with involvement of the central and peripheral nervous systems, and the musculoskeletal system. Tinnitus is most commonly due to sensorineural hearing loss but other subtypes exist. Tinnitus that is modulated by musculoskeletal dysfunction is called somatosensory tinnitus. The involvement of the musculoskeletal system suggests that treatments of this system may reduce tinnitus. Indeed, limited studies of massage suggest therapeutic benefit. Osteopathic manipulative treatment (OMT) manages musculoskeletal dysfunction, yet treatment of somatosensory tinnitus has not been described. There is a case report of a patient responding to OMT after head injury, but the tinnitus subtype is not clear. This study explores the use of osteopathic manipulation as a treatment for tinnitus. Our specific aim is to describe characteristics of tinnitus patients who respond to treatment with osteopathic manipulation. Our hypothesis is that patients with musculoskeletal dysfunction that modulates their tinnitus respond to OMT.

Methods: Tinnitus patients (ICD-9 338.30, 338.31, 338.32) from the osteopathic medicine clinics in

Neurology and the Family Medicine Center for Integrative Medicine were identified through a retrospective design using a diagnosis search of the electronic medical record from January 2010 to May 2014. All tinnitus patients seen in those clinics who were treated with OMT were included. Tinnitus patients who did not have OMT were excluded. Patients who did not follow up after OMT were excluded because there was no data on response. A standardized structured data abstraction form was used to collect data. One osteopathic physician performed data abstraction. The history and examination sections were reviewed for symptom characteristics, subjective severity, treatment response, total treatments, physical examination findings, and treatment with osteopathic manipulation. Patients were divided into those who responded to manipulation and those who did not. Response was defined as having a subjective decrease in perceived tinnitus severity.

Data Analysis: Contingency tables were established for the data. Characteristics of those who responded to OMT were compared with non-responders in the following categories: age, sex, exacerbating factors, physical examination findings, and treatment response. Fisher's exact test was used to determine variance and significance for the small sample size.

Results: Nineteen of 20 tinnitus patients met inclusion criteria (average age, 57.6 years; 57.9% white). Responders comprise 52.6%. The mean responder is 58.5 years compared with 56.7. Females comprised 40% of the responsive group and 67% of non-responders (P=.37, Fisher's exact). Eighty percent of the treatment responsive patients endorsed worsening of tinnitus with musculoskeletal activity (head turning, cervical flexion, cervical side bending, chewing), whereas none of the unresponsive patients reported this (P=.0007). All responders had osteopathic examinations showing somatic dysfunction of the head and neck, while only 33.3% of non-responders had these findings (P=.003). Patients who responded did so after an average of 3.25 treatments and were treated an average total of 5.89 times. Sixty percent of the treatment responsive group rated their tinnitus volume severity on a scale of 0 to 10 with 10 being the loudest volume. Tinnitus severity ranged from 4 to 10 prior to treatment and 0 to 2 after treatment, showing an average reduction of 76.9%. Scored data were not available for the other treatment responsive patients. Instead they noted qualitative improvement. Unlike the treatment responsive group, non-responders did not have historical elements that supported a diagnosis of somatosensory tinnitus. Tinnitus patients who responded to manipulation were more likely to report worsening of tinnitus with head or neck movement (Fisher exact 0.000714; P<.05).

Conclusion: Tinnitus patients who respond to osteopathic manipulation overwhelmingly report aggravation from musculoskeletal activity and have somatic dysfunction of the head and neck on examination as compared with those who do not respond. This group likely has somatosensory tinnitus; thus, the data suggest that somatosensory tinnitus responds to osteopathic manipulation. However, this study was limited by the small sample size, which reflects a low number of referrals to OMT for tinnitus. This may be linked to the experience that tinnitus is treatment refractory. It was further limited by the retrospective design which did not allow for uniform measures of the impact of tinnitus and treatment. The data from this review are being used to prepare for a clinical trial to evaluate OMT for the treatment of somatosensory tinnitus.

♦C23—Chronic Diseases & Conditions

Assessment of Respiratory Syncytial Virus Hospitalizations After Implementation of Updated Palivizumab Treatment Recommendations

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Background: Respiratory syncytial virus (RSV) is the most common cause of infection of the lower respiratory tract in infants and young children and is the leading cause of hospitalization and death due to viral illness during the first year of life. Prophylaxis with palivizumab is effective in preventing RSV infections and decreasing hospitalizations in high-risk infants. In 2014, the American Academy of Pediatrics issued updated recommendations for the administration of palivizumab excluding subgroups of patients that previously qualified for administration. Although these more restrictive guidelines recommend prophylaxis for infants and children at the highest risk of RSV-related complications, many patients are excluded who are still at a higher risk of such complications than the general pediatric population.

Methods: A retrospective observational chart review was performed on all patients hospitalized with RSV infection between November 1, 2013-March 31, 2014 (Season 1), and November 1, 2014-March 31, 2015 (Season 2). Patients were screened for inclusion or exclusion from analysis. The primary endpoint is to compare RSV-related hospitalization rates before and after implementation of the 2014 palivizumab prophylaxis recommendations (season 1 vs season 2). Multiple secondary endpoints were also assessed for the 2 study groups, including pediatric intensive care unit (PICU) admission rates, severity of disease, and length of stay (LOS) across the aforementioned RSV seasons. IRB approval was granted for Spartanburg Regional Medical Center.

Results: Two hundred ten study participants were analyzed across both RSV seasons; 108 were sampled from season 2 and 102 from season 2. A statistically significant difference in hospitalization rates was observed between the 2 seasons with 1 patient excluded from season 1 (0.93%) and 8 patients excluded from season 2 (7.84%); $P<.05$. However, there was no statistically significant difference in PICU admission rates, severity of disease, or LOS between the 2 study populations.

Conclusion: Across both seasons, a statistically significant increase in RSV-related hospitalizations was noted in the patient population that was no longer eligible for RSV prophylaxis. It can be deduced that this difference is a result of the change in palivizumab eligibility requirements per the more stringent 2014 guidelines compared with the 2009 recommendations. Future studies aim to expand the population size to include other potentially affected RSV seasons, which we anticipate will further increase the power of the study.

C24—Impact of OMM & OMT

Assessing the Efficacy of Objective Feedback on Palpatory Skill Development in Osteopathic Medical Students

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Introduction: Palpatory skills are taught at all colleges of osteopathic medicine through a variety of methods; however, limited objective feedback and assessment are incorporated into curricula regarding skill acquisition, such as assessment of asymmetry. The level of objective feedback necessary for sig-

♦ Abstract that won first or second place in the 2014 SOMA Student Poster Competition.

nificant improvement in palpatory accuracy in osteopathic medical students is unknown.

Hypothesis: Increasing palpatory training with objective feedback, in addition to the standard 180 hours of the osteopathic principles and practice curriculum (OPPc), will improve palpatory assessment performance in second-year osteopathic medical students compared with OPPc alone.

Methods: A retrospective longitudinal observational study, with institutional review board exemption status, was performed using 2 comparison groups of second-year osteopathic medical students. The elective group (N=16) was given 10 hours of additional training with immediate objective feedback using a Photoshop overlay of the examiner palpating the landmark. The overlay was captured using a digital camera measuring system triggered by the examiner when localizing the landmark. This system allowed for adjustment of the students' landmark localization if necessary. The nonelective group (N=144) did not receive this additional training. All students evaluated coronal plane asymmetry of pelvis bony landmarks and sagittal plane asymmetry of transverse processes using palpation of calibrated, adjustable, foam-covered pelvic and lumbar spine models, respectively, at the end of their first and second year of medical school. The following pelvic landmarks were palpated by all participants: anterior superior iliac spines, posterior superior iliac spines, and pubic tubercles.

Data Analysis: Student palpatory assessment performance was determined according to the calibrated model asymmetry. To assess the impact of objective feedback on palpatory assessment performance in the elective group, random intercepts logistic regression analyses were used to test for differences between elective and non-elective groups in their accuracy on the examination at the end of the second-year examination for both pelvic and lumbar models while controlling for examination accuracy from the end of the first year. The class rank of each student was determined according to their examination performance, and low class rank indicated better performance. Wilcoxon signed rank tests assessed the significance in the shift in class rank of students in the elective group from the first year to the second year for both pelvic and lumbar model performances.

Results: In the pelvic examination, there was no evidence that the elective group performed significantly differently from the nonelective group (P=.39) or that difference was dependent on the type of pelvic landmark (P=.79). In the lumbar examination, the elective group mean (SE) performance (0.90 [0.028]) was not significantly greater compared with the nonelective group mean (SE) performance (0.86 [0.013]; P=.18). There was no significant improvement in class rank for the elective group for either pelvic model performance (median decrease=10, P=.49) or lumbar model performance (median decrease=18, P=.13).

Conclusions: Although there were trends indicating better performance in the elective group, the current study showed no statistically significant improvement between the students with the additional 10 hours of training with objective feedback and the students with the standard 180 hours of OPPc. However, because of these trends and our small sample size, additional research in this area is warranted. Future studies should investigate whether the number of hours were adequate to make a substantive change in test performance and whether the timing for this training was ideal. Some students may have difficulty making changes to their palpatory techniques after developing motor patterns or habits during their first year. Therefore, having objective feedback when the students are first learning palpatory skills may have greater effects on performance than those seen in the current study. Future studies should also investigate how much additional training is needed to significantly increase palpatory accuracy among osteopathic medical students.

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C26—Chronic Diseases & Conditions

Effect of Osteopathic Manipulative Medicine on Motor Function and Balance in Parkinson Disease

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Introduction: Parkinson disease (PD) is a progressive disorder of the nervous system that affects mobility, balance, and cognition. Tremor, bradykinesia, and rigidity are physical symptoms that contribute to postural instability and gait abnormalities in many individuals with PD. Levodopa is the current mainstay of treatment and can be effective for these symptoms. Over time, however, PD medications lose their effectiveness and individuals will experience fluctuations in motor function, dyskinesia, and dystonia. Additional treatment options are needed. Osteopathic manipulative medicine (OMM), a treatment of manual forces directed to improve function and homeostasis, has been shown to improve postural instability in the elderly, improve balance in individuals with dizziness, and improve gait in patients with PD. To date, it remains unclear if repeated OMM treatments can improve motor function and balance in individuals with PD.

Hypothesis: We hypothesize that biweekly OMM treatments over a 6-week period using a predefined protocol will lead to improvement in motor function and balance in subjects with PD as compared with a 6-week controlled counseling period.

Methods: This study was approved by the NYITCOM institutional review board (BHS-975) and is registered at clinicaltrials.gov (NCT02107638) and Fox Trial Finder. Our inclusion criteria include individuals older than 40 years with a diagnosis of PD by a neurologist who fit 1 of the following criteria: (1) Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III score of >30, (2) Sensory Organization Test (SOT) score of <75, or (3) Mini-Balance Evaluation Systems Test (Mini-BESTest) score of <19. Subjects who have a history of other neurologic conditions or who were unable to complete the assessment tools were excluded. Subjects received biweekly OMM treatments using a predefined protocol for 6 weeks, followed by a 4-week washout period. The subjects then entered a crossover arm with weekly counseling sessions from a medical provider for 6 weeks as a placebo control. Balance and motor function were measured by the MiniBESTest, SOT, and MDS-UPDRS at various points throughout the study: befire OMM, week 6 (after completion of the OMM protocol), week 10 (pre-counseling and after a 4-week washout from the OMM intervention), and week 15 (at the end of counseling).

Data Analysis: Five subjects were included in this analysis. A paired-samples *t* test was performed to compare the MiniBESTest (n=4), SOT (n=3), and UPDRS (n=4) scores before and after OMM (week 6) to before counseling (week 10) and after counseling (week 15). A paired-samples *t* test was also used to analyze the MiniBESTest scores from the OMM intervention alone at week 6 (n=5), and week 10 (n=5). All statistical analyses were performed with an alpha of α=0.05.

Results: The MiniBESTest scores before and after 6 weeks of OMM improved by an average of 4.50, as compared with the scores before and after 6 weeks of counseling, which decreased by an average of 2.50. This finding was statistically significant (*P*=.007; CI, -10.44, -3.56). The comparison of MDS-UPDRS and SOT scores before and after

OMM to before and after counseling were not statistically significant (MDS-UPDRS P=.799; CI, -21.77, 18.27; SOT P=.15; CI, -37.84, 11.84). When analyzing the data from the OMM intervention alone, the MiniBESTest scores before OMM to week 6 showed that there was an improvement of 4.00. This finding was statistically significant (P=.037; CI, -7.62, -0.38). The MiniBESTest scores before OMM to week 10 improved by 5.4, which was also statistically significant (P=0.014; CI, -8.98, -1.82). The MiniBESTest scores from week 6 to 10 improved by an average of 1.40 (P=0.48; CI, -6.41, 3.61). This was not statistically significant.

Conclusion: The data from this pilot study support our hypothesis that OMM may improve motor function and balance in patients with PD but counseling may not. The MDS-UPDRS and SOT scores did not improve statistically; however, the MiniBESTest scores did show a significant improvement when compared with counseling. On further investigation into the MiniBESTest scores during the OMM intervention alone, there was significant improvement seen in the overall pre- and post-OMM treatment scores. To our knowledge, there are no studies that have investigated the effects of OMM on motor function and balance in PD over an extended period. The data demonstrate that there was a continuous improvement over 6 weeks of OMM treatment, with a continued effect for another 4 weeks after treatment had ended. This suggests that long-term treatment with OMM in individuals with PD may lead to an improvement in balance and that these effects may last up to 4 weeks after the completion of therapy. A limitation to the current project is the small sample size. It is also uncertain whether these results equate to a clinical significance, such as fall reduction. This is an ongoing study and we hope to address these limitations through continued accrual and data collection. Future research should be considered to further investigate the application of OMM in improving balance and motor function in PD. By doing so, we may be able to offer an additional treatment option to help improve not only function and balance, but also quality of life for individuals suffering from PD.

Acknowledgment: We would like to thank all of the subjects, faculty, staff, and medical student volunteers for their contributions to this study.

C27—Chronic Diseases & Conditions

Patient Preferences for Diabetes Education

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Aims: To explore patient preferences for receiving diabetes education materials.

Methods: A survey was provided to a convenience samples of adults with type 1, type 2, and gestational diabetes at a diabetes specialty center.

Data Analysis: Descriptive analysis was performed and correlational analysis was done using SSPS software. χ^2 analyses were used to evaluate demographic data on preferences.

Results: Ninety-nine people completed the survey. They were evenly spread between male (47) and female (52). Of the respondents, 58 had type 2 diabetes, 28 had type 1, and 9 had gestational diabetes. The age range was 18-91 years. The least preferred method of getting diabetes education was in-person meetings in a group (<5%). The most preferred was a combination of diabetes education approaches that focused on Web-based training as the first step (43%). χ^2 analyses revealed no significant effect of the demographic data on preferences. Men preferred Web-based private training while women preferred a combination of Web-based and in-person training.

Conclusion: The most current models used for diabetes education—in-person private and in-person group—may not be patient centered. Health care teams may need to expand/change the format of diabetes education to improve the ability to reach more patients.

Acknowledgments: The authors would like to thank the Diabetes Endocrine Center and the Ohio University Diabetes Institute for their partnership in this project.

C28—Osteopathic Philosophy

Education Level and Knowledge of Infectious Disease Transmission in Rural El Salvador

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Introduction: Infectious diseases are a major cause of disease in developing countries such as El Salvador, where chikungunya and dengue are highly prevalent. While mortality from these diseases is not a major concern, their morbidity has a substantial impact on quality of life and health. Furthermore, though by law children are required to complete at least 9 years of education in El Salvador, the average number of school years completed in rural areas was 4.1 as of 2010. Thus, the current lack in education and the heightened prevalence of various infectious diseases in El Salvador drive the importance in exploring the existence of a possible relationship between the 2. The purpose of this study is to examine the association between the highest level of education completed in individuals and self-reported knowledge of infectious disease transmission in rural El Salvador.

Hypothesis: It was hypothesized that the completion of a higher grade level of education would indicate an increased knowledge of modes of transmission of infectious disease prevalent to the area.

Methods: Prior institutional review board approval was acquired for all methods of this study. During an Edward Via College of Osteopathic Medicine outreach trip in October 2014, medical students verbally administered questionnaires in Spanish to each head of the household before being seen as patients in the clinic. Research was conducted in the following 3 sites in rural El Salvador: Santa Agueda School: Sonsonate, Asociacion Amigos para Lationamerica (AMILAT) Community Clinic: Santiago Texicuangos, and Village Clinic: El Tremedal. Medical students explained the research to 149 patients, who provided informed consent before participating. Each participant was asked questions regarding transmission modes of various infectious diseases, living conditions (environmental factors), and education. Data were analyzed via Statistical Package for the Social Sciences (SPSS).

Data Analysis: Bivariate analyses were performed through SPSS to assess the differences between those who answered the questions correctly and those who answered the questions incorrectly, against the highest level of education completed. Statistical analysis by way of *t* test were ran and found to be statistically significant for several diseases.

Results: Survey participants who answered transmission knowledge questions correctly had, on average, higher education levels when compared with those who answered them incorrectly or who reported not knowing the answer. The association of education (grade level) in predicting the correct answers to questions about disease transmission was found as follows through data analysis: chikungunya (P=.000), tuberculosis (P=.004), rabies (P=.000), dengue (P=.000), and HIV (P=.001).

Conclusion: Based on the results obtained, it is evident that education plays an important role in the knowledge of infectious disease transmission. The positive correlation found supports the reasoning that schooling provides individuals with the insight necessary to understand how the prevalent diseases in their area are transmitted. It is pre-

sumed that awareness of transmission modes provides the individual with ways to avoid the disease. The need to educate the citizens about infectious disease prevalence in their area is therefore vital, whether it be through schools, a health promoter, or other sources. Limitations of the study include a small sample size, language barriers, and time constraints. Future studies should incorporate more sites, both rural and urban, to thoroughly explore the education differences in each setting.

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C29—Osteopathic Philosophy

Teaching the Teachers: Role-Playing and Its Effect on Precepting Osteopathic Manipulative Treatment in the Clinical Setting

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Research Question/Hypothesis: Currently there is little consensus on the best teaching practices for osteopathic manipulative treatment (OMT) in the setting of continuing medical education (CME). We hypothesized that role-playing is an effective way to teach OMT to preceptors in the clinical field, and we investigated this using a survey study after 4 of our CME training events. Role-playing is a form of simulation-based exercises meant to place the participants in real-life situations in which appropriate responses and actions may be rehearsed. Involving participants in these simulated clinical precepting scenarios can potentially be an effective teaching method. In our survey study, we also aimed to determine the efficacy of role-playing in CME training for MD and DO preceptors in supervising the application of osteopathic manipulative treatment. There are many allopathic preceptors in osteopathic training programs, and with the impending merger of graduate medical education, it is important to assess the best practices in educating allopathic physicians to be confident with supervising OMT in the clinical setting.

Methods: This study was approved by the NYIT IRB (# BHS-1058). A survey study was conducted by the New York Institute of Technology College of Osteopathic Medicine (NYITCOM) Department of Osteopathic Manipulative Medicine (OMM) during CME events, in which the OMM faculty trained MD and DO program directors and chief residents, all of whom came from the school's teaching hospital affiliates. Forty-six attendees from the CME training sessions participated in the survey study. Pre- and post-training event surveys were administered to assess the efficacy of role-playing. Physician preceptors from various specialties attended the training events. During the CME training, clinical cases were presented to the participants, and third-year osteopathic medical students played the role of osteopathic medical students (OMS) in the case scenarios. Students were asked to role-play approaching volunteer participants, requesting the use of OMT techniques on the patients in the case scenarios. The OMS discussed the integration of OMT into the cases including indications, contraindications, and how and why they would perform the selected techniques. The preceptors were then encouraged to ask questions and interact with the OMS as they would do in a real clinical scenario, asking questions of the OMS regarding the OMT and any explanations the students may or may not have given. Through the surveys, demographic data were collected, including attending or resident status, type of medical degree, years in practice, and previous use of OMT. A 5-point Likert Scale was utilized to assess self-reported changes in the following areas: (1) overall perception of OMT, (2)

ability to discuss OMT, (3) ability to precept OMT, (4) utilization of OMT, and (5) understanding of the clinical applications of OMT. The participants also ranked the effectiveness of role-playing as a part of the CME event.

Data Analysis: The participants' responses in the Likert scale were analyzed at the interval measurement scale by calculating the mean rank from 5 choices (1=very poor; 2=poor; 3=fair; 4=good; 5=very good). A paired sample *t* test was used to assess the changes in their evaluations on the given questions from pre- to post-training sessions.

Results: This study involved 46 survey participants from 4 CME training events. Of the participants, 14 (30%) were residents and 32 (70%) were attending physicians, of whom 31 (67%) were osteopathic physicians (ie, DOs) and 15 (33%) were allopathic physicians (MDs). The mean number of years in medical practice was 12.6 (SD 11.0). Thirty-one participants (69%) reported use of OMT before the training event, while 14 (31%) reported not using OMT prior to the training event. The mean rank of all participants for their overall perception of OMT changed from 3.96 (SD 1.19) in the presession survey to 4.57 (SD 0.54) in the postsession survey, showing a statistically significant improvement ($P<.001$). The mean rank of all participants for their overall ability to discuss OMT changed from 3.36 (SD 1.37) in the presession survey to 4.24 (SD 0.68) in the postsession survey, showing a statistically significant improvement ($P<.001$). The mean rank of all participants for their overall ability to precept OMT changed from 2.8 (SD 1.18) in the presession survey to 3.92 (SD 0.87) in the postsession survey, showing a statistically significant improvement ($P<.001$). The mean rank of all participants for their overall utilization of OMT changed from 2.77 (SD 1.26) in the presession survey to 3.93 (SD 0.73) in the postsession survey, showing a statistically significant improvement ($P<.001$). The mean rank of all participants for their overall understanding of the clinical applications of OMT changed from 3.33 (SD 1.24) in the presession survey to 4.27 (SD 0.62) in the postsession survey, showing a statistically significant improvement ($P<.001$). For the effectiveness of role-playing, 1 participant (2.2%) answered very poor, 0 (0.0%) answered poor, 4 (8.7%) answered fair, 20 (43.5%) answered good, and 21 (45.7%) answered very good, which culminated in the mean rank of 4.3 (SD 0.81). For the overall educational quality of the training event 1 (2.2%) answered very poor, 0 (0.0%) answered poor, 0 (0.0%) answered very poor, 15 (32.6%) answered good, and 30 (65.2%) answered very good, which culminated in the mean rank of 4.59 (SD 0.72).

Conclusion: Role-playing appears to be a favorable method for training attending physicians to teach trainees in the use of OMT. All CME participants reported improvements in their understanding, comfort level, and ability to perform and precept others using OMT after attending the training program. The largest changes included the ability to utilize and precept OMT. It was demonstrated that role-playing is potentially an effective training modality for a physician audience comprised of multiple specialties. One limitation of the study is that we did not investigate role-playing in comparison to other teaching modalities. Other limitations include a small sample size and potential bias as participants attended with the intention to learn about OMT. Future studies should be done to assess the effectiveness of other teaching modalities.

Acknowledgment: NYITCOM Department of OMM, Keith Rivera, MS.

C30—Chronic Diseases & Conditions

Identification of Clinical Characteristics of Hotspotters in Oncology to Control Rising Health Care Costs

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Introduction: Due to rising health care costs, Accountable Care Organizations (ACOs) have been established to align providers and health systems. ACOs can leverage opportunities to avoid wasteful and redundant care. Collaborative mining of integrated health cost data and clinical chart reviews for cancer patients can identify areas where operational changes can reduce oncology costs. Across health care, like all specialties, costs in oncology have been increasing over the past 5 years. This has occurred during an unparalleled period of major improvements in treatment efficacy and toxicity reduction. Additionally across health care, the highest cost 5% of patients are responsible for 50% of expenditures. Within oncology, we hypothesize that studying the clinical profile of these "hotspotters" can identify areas to optimize care and reduce cost.

Methods: One year of Medicare claims data were interrogated for 31,336 ACO Medicare beneficiaries. 3,942 Medicare recipients with a cancer diagnosis were identified from their CMS Hierarchical Condition Categories (HCCs). Three cohorts were defined within this group: (1) low cost (55%) had annual claims totaling less than the ACO mean; (2) intermediate cost (29%) incurred claims exceeding the ACO mean; and (3) hotspotters (5%) incurred claims totaling more than $50,000. In the hotspotter cohort of 216 patients, the study was limited to 70 active oncology subjects with 3 or more ambulatory cancer center visits. The medical characteristics of this group were recorded through a chart audit and expenditures were tracked.

Analysis: Instead of postulating the highest cost factors specific in cancer patients, a thorough chart review was conducted. From these patients, diagnoses were categorized based on factors such as primary tumor location, treatments received, staging, body mass index, and primary medical oncologists. These data along with Medicare claims data were looked at using statistical analysis to identify significant disparities.

Results: The active oncology hotspotters had a median of 4 major medical HCC comorbidities (max=11). The most common comorbidities were congestive heart failure (27.1%), disorders of immunity (24.3%), specified arrhythmias (24.3%), and COPD (22.9%). By way of comparison between the 3 overall cohorts, the low, intermediate, and hotspotter cost cohorts had a median of 2, 3, and 6 comorbid HCCs respectively. Logistic regression analysis demonstrated which comorbidities were statistically significant for predicting hotspotters. In terms of utilization, 63 of 70 (90%) had ED visits. There were a median of 4.5 ED visits (max=20). 42 of 70 (60%) were hospitalized with a median of 1 hospitalization (max=9). The hotspotters had a median of 11 ambulatory oncology visits (max=35). On logistic regression analysis, number of ED visits and hospitalizations were predictive of being a hotspotter. Primary tumor location was relatively evenly distributed showing blood/lymph (34%), lung (23%), breast (16%), gastrointestinal (13%), genitourinary (11%), and brain (3%). Analysis of treatments received showed 31 of 70 patients (44.3%) received surgery, 32 (45.7%) received radiation treatment, 61 (87.1%) received chemotherapy, and 39 (55.7%) received immunotherapy. Cancer staging of patients was documented as I (7.1%), II (14.3%), III (17.1%), IV (32.9%), and unknown/unstageable (28.6%). Body mass index for patients were 15-19.9 (8.6%), 20-24.9 (28.6%), 25-29.9 (28.6%), 30-34.9 (20%), 35-39.9% (5.7%), 40-44.9% (1.4%), and 45-49.9 (4.3%). Ad-

ditionally, primary medical oncologists were pulled to see if any disparities were seen among individual providers; none were found to be significant.

Conclusions: Mining claims with clinical data opens an opportunity to characterize hotspotter patient care in oncology. The current ongoing study suggests that the costs of care for oncology patients are largely influenced by medical comorbidities. Future study appears warranted on whether patients who meet criteria as likely hotspotters will benefit from more intensive outpatient optimization of their medical comorbidities to avoid ED visits and hospitalizations. These findings suggest that rising costs in oncology could be substantially reduced through avoidance of redundant or wasteful care in hotspotters without sacrificing the quality or complexity of novel cancer therapies achieved in recent years. Multidisciplinary conferences and clinics with pathology, radiology, surgery, radiation oncology, and oncology are common to manage cancer. This study suggests that similar multidisciplinary models for patients with multiple medical diagnoses may be used to reduce costs. For example, patients with a cancer diagnosis, congestive heart failure, and COPD could be identified and referred to a multidisciplinary conference and clinic with representatives from oncology, cardiology, pulmonology, and palliative care.

C31—Chronic Diseases & Conditions

Comparison Between Fried Frailty Score and Serum Albumin Levels in Taiwanese Patients With ESRD on Hemodialysis

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Research Question: The incidences of end stage renal diseases (ESRD) continue to rise in many countries and impose significant disease burden to patients and countries. According to the United States Renal Data System (USRD), the prevalence of ESRD is the highest in Taiwan, followed by Japan and the United States. Hemodialysis is the most common therapy for ESRD in most of the reported countries, while peritoneal dialysis is inappropriate for aged patients who need assistance and appears to be only more commonly used in Hong Kong and Mexico. In contrast, renal transplant rates for ESRD patients vary widely among countries and appear to depend on the health care system and cultural diversities. Considering the health burden in ESRD patients who receive life-time hemodialysis and the financial burden for patients and countries, it is of great interest for clinicians to effectively assess treatment options for better use of limited resources. Indeed, such a health issue is particularly important in countries with universal health care, including Taiwan. Past studies have shown that hypoalbuminemia, a measure of nutritional status, is an independent predictor of mortality in dialysis patients. In this study, we explored the validity of Fried Frailty Score as an additional prognostic factor in determining mortality, adverse outcomes, and quality of life in ESRD patients undergoing hemodialysis. Frailty is recognized as increased vulnerability and declined physiological function. The Fried Frailty Score is commonly used to measure health status in geriatric populations. It determines patient's quality of life and is an independent, highly sensitive predictor of mortality and morbidity in comparison to old age. By exploring the validity of the Fried Frailty Score as a prognostic factor in ESRD patients, this study thus upholds the osteopathic principles of viewing the body as a single dynamic unit of function. It is anticipated that results obtained from this study will help lead to more effective management of ESRD patients.

Hypothesis: We hypothesized that the Fried Frailty Score would inversely correlate with plasma albumin level in ESRD patients undergoing hemodialysis.

Methods: We surveyed and calculated the Fried Frailty Score for 151 patients undergoing hemodialysis 3 times per week at TIHTC Taipei Hospital Hemodialysis Center using 5 criteria established by Fried et al: (1) unintentional weight loss, (2) weakness, (3) slow walking speed, (4) low physical activity, and (5) self-reported exhaustion. A frail patient is defined as having at least 3 of the 5 criteria, pre-fail having at least 2, non-frail having less than 2, and robust as having none. We obtained electronic data for Karnofsky Score, age, sex, serum albumin, serum creatinine, hemodialysis initiation date, and number of comorbidities. Comparison of these data were made by graphing serum albumin levels of patients, categorized by a frailty score from 0 to 5, and also categorized by frail, pre-frail, non-frail, or robust. Robust patients specifically were then analyzed based on age and albumin levels to explain why they have the frailty score they do.

Results and Data Analysis: Out of 151 patients, 60 had a frailty score of 0, 38 had a score of 1, 18 had a score of 2, 15 had a score of 3, 18 had a score of 4, and 2 had a score of 5. The average serum albumin level for patients with a frailty score of 0 (n=60) is 3.56 ± 0.28, score of 1 (n=37) is 3.51 ± 0.40, score of 2 (n=18) is 3.29 ± 0.35, score of 3 (n=14) is 3.03 ± 0.56, score of 4 (n=17) is 3.07 ± 0.34, and score of 5 (n=2) is 3.00 ± 0.20. The median serum albumin level for patients with a frailty score of 0 is 3.6, score of 1 is 3.5, score of 2 is 3.2, score of 3 is 3.05, score of 4 is 3.1, and score of 5 is 3. There is a clear decline in the number of patients with normal albumin levels as frailty score increases. The ratio of those with normal albumin to those with hypoalbuminemia for a frailty score of 0 is 1.73, score of 1 is 1.31, score of 2 is 0.5, score of 3 is 0.27, score of 4 is 0.13, and score of 5 is 0. The data show that as the score increases, the ratio decreases, suggesting the score has powerful prognostic value in the outcome of patients with advanced kidney disease. Looked differently, for patients with hypoalbuminemia (albumin levels less than 3.5 g/dl), 28.21% had frailty score of 0, 20.51% had score of 1, 15.38% had score of 2, 14.10% had score of 3, 19.23% had score of 4, and 2.56% had score of 5. In those with normal albumin levels, 54.29% had frailty score of 0, 30.00% had score of 1, 8.57% had score of 2, 4.29% had score of 3, 2.86% had score of 4, and 0% had score of 5. Twenty-two of 60, or 36.7% of patients, with a frailty score of 0 have hypoalbuminemia. On further investigation, 14 of these 22 patients, or 63.6%, are younger than 60 years. The younger age of these patients explains why they have a frailty score of 0 even with hypoalbuminemia.

Conclusions: The data show that as Fried Frailty Score increases, the level of serum albumin decreases in ESRD patients undergoing hemodialysis at TIHTC Taiwan Hospital. This finding strongly suggests that Fried Frailty Score has powerful prognostic value in the outcome of ESRD patients. The score does not only determine mortality but also describes the quality of life of patients. In this regard, such information can further assist the medical team in providing appropriate and effective services and interventions, as well as influence patient's decision in choosing the treatment modality, such as peritoneal dialysis (which is suitable for younger patients), renal transplantation, or starting hospice.

C32—Chronic Diseases & Conditions

Osteophytic Lipping in Response to BMI in the Tibio-femoral and Tibio-talar Joints

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Research Question(s)/Hypotheses: Osteophytes are bony outgrowths that develop along joint margins, often as a compensatory mechanism for joint degeneration caused by osteoarthritis. Developed as

a way to limit joint motion and compensate for cartilage degeneration, osteophytic lipping is the body's unsuccessful attempt to heal itself. Obese and overweight individuals are at a higher risk of developing osteoarthritis due to greater force on load-bearing joints. Increasing articular surface area dissipates the pressure associated with the increased load (Pressure=Force/Surface Area). Osteoarthritis is a highly prevalent disorder, affecting approximately 27 million Americans today. Obesity is an ever-growing epidemic and it is estimated that 1 in every 3 adults in America are obese. Combining osteoarthritis and obesity, roughly $200 billion US dollars were spent on medical costs in 2014. Little research has been done on obesity-related osteoarthritis, although this is likely the primary reason for the high rate of knee replacements in obese individuals. This study examines the effects of age and body mass index (BMI) on osteophytic lipping in the tibio-femoral and tibio-talar joints. Due to the load bearing nature of these joints, they are ideal to study the effects of osteophytic lipping. The hypothesis is that obese individuals will exhibit a greater degree of lipping in both joints than normal BMI individuals, regardless of age.

Methods: Skeletal remains from the University of Tennessee W.M. Bass Donated Collection with known age and BMI were sampled (n=247). Low bone density and osteoporosis are confounding variables for osteophytic lipping; therefore, bones displaying characteristics such as chipped periosteum, micro fractures, decreased cortical thickness and increased porosity were excluded upon gross inspection. Females were excluded due to the prevalence of osteoporosis. In addition, bones containing fractures, trauma, knee and hip replacements were also excluded due to bone remodeling. Carrera Precision CP9806-TF Titanium sliding calipers were used to record maximum lipping of the distal femoral condyles, proximal tibial condyles and tibiotalar articulating surfaces. Maximum lipping values were obtained by measuring osteophytes from the edge of an articulating surface to the end of a bony outgrowth. The greatest value along the perimeter of the joint surface was recorded. Each lipping measurement was taken 3 times and averaged to control for intra-observer error. BMI was classified as normal (18-24, n=82), overweight (25-29, n=82), or obese (≥30, n=83); age was classified into 3 categories: 23-40 (n=30), 41-65 (n=153), and 66-90 (n=64) years. Medical history of the donors was not obtainable and is therefore a limitation in this study.
Data Analysis: Paired *t* tests were used to evaluate asymmetry in joint lipping. A 2-way MANOVA was run to investigate effects of age and BMI on lipping. Bonferroni post-hoc tests were run to evaluate between-group means for each variable. In addition, Pearson correlation coefficients were calculated to evaluate the strength of correlation between age & lipping and between BMI & lipping.

Results: Paired *t* tests found no significant asymmetry in lipping of the knee joint and distal tibia. However, significant asymmetry was present on the talus (P=.015), with more lipping on the right side. The 2-factor MANOVA showed that BMI has a significant effect on the degree of lipping on all joint surfaces examined (P<.01). Age has a significant effect on lipping in the knee joint (P<.05), but not in the ankle joint. Pearson correlations between BMI and lipping (r=.23−.41) were greater for both joints than the correlation between age and lipping (r=.01-.23). The correlation between age and lipping on the ankle joint was nearly 0 (r=.01−.03) compared with BMI and ankle lipping (r=.27−.41).

Conclusion: This study shows that BMI plays a greater role than age in the degree of osteophytic lipping at the knee joint, and it appears to be the sole contributor to severe osteophytic lipping at the ankle joint. The applications of this research are 2-fold: forensically and clinically. The degree of lipping can be used by forensics to help identify skeletal remains and classify them into their respective BMI categories. Individuals with BMI >30 show early onset of osteophytes, which signifies

osteoarthritic changes in both the knee and ankle joints. Before developments of these changes occur, obese patients should be counseled on reducing weight to a healthy BMI. These individuals should also be evaluated thoroughly for complications surrounding osteophytic lipping. The BMI of a patient can be used clinically for the assessment of the severity of osteophytic lipping, aiding in the development of specific treatment protocols and management plans for obese individuals. Thus, these findings have important implications for health care providers regarding the care and management of obese patients.

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C33—Pain Management

Don't Forget the Moms! A Survey Study Examining the Efficacy of Osteopathic Manipulative Treatment for Acute Postpartum Pain

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Background: Standard treatments for postpartum pain control include nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, ice packs, and heating pads, and they are often inefficacious. Adequate and timely management of pain is crucial to new mothers while caring for their newborns and transitioning to home life after delivery. Osteopathic manipulative treatment (OMT) is a manual therapy directed at treating musculoskeletal dysfunctions that may contribute to decreased range of motion and increased pain. Extensive research demonstrates that OMT is efficacious for pain management throughout pregnancy, but little is known about its use in the postpartum population. A recent study (Schwerla et al, 2015) showed that OMT performed 4 times over 12 weeks in an outpatient setting decreased intensity of pain and functional disability in postpartum subjects with lower back pain. No additional studies to date have investigated the effectiveness of manual therapies for acute postpartum pain.

Aim/Hypothesis: This pilot study aimed to assess whether OMT is beneficial in reducing postpartum pain within 48 hours of delivery. We examine the efficacy of a single OMT session for pain, regardless of location, and further differentiate the effects of OMT on different types of pain immediately following delivery. We hypothesize that OMT will provide an effective therapeutic relief of discomfort as an adjunct to the standard of care.

Methods: This study was approved by institutional review boards at both the NYITCOM (BHS-1122) and at St. Barnabas Hospital (2015.33). Eligible subjects included those who delivered at St. Barnabas Hospital, Bronx, New York, and were experiencing pain within 48 hours of delivery. All women who agreed to participate were given an initial screening survey and the short form McGill Pain Questionnaire, a validated survey tool. Neuromusculoskeletal medicine/osteopathic manipulative medicine (NMM/OMM) second- and third-year residents treated each subject with OMT for approximately 20 minutes. OMT was tailored to each subject's somatic dysfunction findings and was performed according to osteopathic principles. Subjects then received the McGill Pain Questionnaire again after their treatment. The screening survey accounted for delivery complications, previous OMT exposure, and pain medications. Responses were verified through the subject's medical record.

Statistical Analysis: Analysis was conducted using IBM SPSS Statistics version 22. Paired *t* tests and

McNemar tests were used to analyze changes before and after treatment for continuous and categorical variables, respectively. Differences in visual analogue scale (VAS) pain scores between subjects who had Cesarean section vs vaginal delivery were tested using analysis of variance (ANOVA), while group differences in pain location were tested using χ^2 analysis. Parametric tests were used after verifying the data followed an approximately normal distribution. For each analysis, significance was determined at α=0.05 controlling for type I error per test at 5%. Descriptive statistics are provided as a landscape to examine trends and changes.

Results: Twenty-six subjects received OMT within 48 hours of delivery. The mean reported VAS score for pain before treatment was 5.0, while the mean score for pain after treatment was 3.7. This difference was statistically significant (*P*=.008). Subjects who had Cesarean section (C-section, n=10) reported slightly higher average VAS scores, at 6.2 before treatment and 4.3 after treatment (*P*=.04), compared with subjects with vaginal delivery (n=16) reporting mean VAS scores of 4.3 before OMT and 3.4 after OMT (*P*=.11). The pre-treatment VAS scores significantly differed (*P*=.01) between subjects who had a vaginal delivery and those who had a C-section, and 24.5% of this variability can be explained by delivery type. While 61.5% of subjects reported having back pain before treatment, only 30.8% reported back pain after treatment. This difference was significant (*P*=.008). While 27% of the cohort reported vaginal pain pretreatment, only 15% indicated having vaginal pain after treatment. However, this difference was not significant (*P*=.25). These responses did not differ significantly between subjects who had a C-section vs subjects who had a vaginal delivery (*P*>.05). Subjects most commonly described their pain before OMT as cramping (46.2%), aching (30.8%), throbbing (26.9%), tender (23.1%), or heavy (23.1%). After OMT, frequencies decreased to 34.6% cramping (*P*=.45), 23.1% aching (*P*=.63), and 15.4% throbbing (*P*=.25), but reported tenderness and heaviness remained at 23.1% (*P*=1.0). Overall decreases were seen in both sensory (3.8 pretreatment to 3.1 post treatment) and affective (0.85 pretreatment and 0.5 post treatment) pain scores; however, these differences were also not statistically significant (*P*=.09, *P*=.13, respectively).

Conclusion: Preliminary results demonstrate that OMT is efficacious for pain management after both C-section and vaginal deliveries. The small sample size is likely responsible for the inability to find a wider array of statistically significant results; however, recruitment is currently ongoing, and we anticipate a much larger sample size moving forward to shed light on the significance of our findings. At this time, the lack of a control group or standardized treatment plan precludes the ability to make causal claims. However, these descriptive results provide strong support for additional research to investigate these questions. Future research should attempt randomized controlled clinical trials involving multiple hospitals to solidify treatment efficacy and generalizability.

♦ Abstract that won first or second place in the 2014 SOMA Student Poster Competition.

♦C34—Impact of OMM & OMT

Objective Characteristics of Osteopathic Medical Students Performing Rotational Testing of Lumbar Vertebral Segments

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Research Question: What are objective palpation characteristics of osteopathic medical students evaluating rotation of lumbar vertebral segments?

Introduction: Despite standardized curriculums in osteopathic manipulation courses, students primarily learn diagnostic palpation through subjective feedback. Evidence suggests that most palpation tests have poor reliability, particularly those in-

volving motion testing. The purpose of the current study was to investigate the cause of poor reliability in motion testing by describing objective characteristics of the techniques of osteopathic medical students when performing rotational testing of lumbar vertebral segments.

Methods: The local institutional review board considered this observational study to be exempt. Sixteen students were recruited from the Kirksville College of Osteopathic Medicine class of 2017 to perform lumbar segmental rotational motion testing from L1 to L5 on a prone volunteer. A Novel Pliance-X system was used to collect force data. Skin contact sites overlying the transverse processes were standardized for all lumbar segments using ultrasonography. The objective characteristics analyzed in the current study were chosen for the following reasons: patterns in technique for diagnosis may relate to the consistency of diagnosis by different examiners; force may alter tissue characteristics by inducing reflex contraction, altered tissue textures, and motion at segments above or below the site of restriction potentially skewing examiner findings; and velocity may influence rate-dependent viscoelastic properties of tissue, such as the inability of fluid movement with rapid pressure, while a slower onset of pressure may allow fluids to escape intercellular spaces and cause greater deformation of tissue. Waveform force tracings were processed using a proprietary data analysis tool and included localization of lumbar transverse processes and patterns in technique.

Data Analysis: Force tracings were divided into 2 phases: a pretesting phase, in which student examiners localized hand position over the transverse process landmarks and produced a small, simultaneous force with both hands, and a motion testing phase, in which testing of the rotational motion of the lumbar spine was evaluated. The motion testing phase was further divided into active motion testing where 1 hand was creating peak forces over a transverse process to induce motion and passive motion testing which occurred at the same time as the active motion testing but evaluated the hand that was not inducing motion, creating trough forces. Descriptive analysis of numerical data were done using SAS version 9.4. Mean, standard deviation (SD), and range were calculated for peak force, trough force, change in force (peak force minus previous trough force), velocity of motion testing (peak force minus previous trough force/time of peak force minus time of the previous trough force), number of pushes (peaks in force), and duration of palpation for all student examiners across all lumbar segments. Dominant and nondominant hand data were also analyzed.

Results: In the pretesting phase, 8 student examiners were observed to localize the transverse processes of the lumbar segments by producing a small, simultaneous force with both hands. Five maintained passive force throughout the motion testing phase, while 6 generated a passive force without initial localization. During the motion testing phase, 13 student examiners alternated force between the thumbs to identify resistance, 1 applied force with both thumbs simultaneously, and 2 used a combination method, sometimes applying force in an alternating pattern and sometimes simultaneously. During the active motion testing phase, 10 student examiners were identified as single pushers (applying a solitary anterior force per hand), and 2 were identified as multi-pushers or bouncers (applying multiple small pushes per hand in each active phase). One student examiner applied force with both hands simultaneously rather than in an alternating pattern to diagnose restriction. Three student examiners used a combination of single and multiple pushes during the active phase. The mean peak force was 24.39 N (SD=2.71, range=3.29-52.13) with a mean of 26.20 N (SD=8.20, range=3.29-52.14) for the dominant hand and 22.58 N (SD=6.48, range=7.37-40.47) for the nondominant hand. The mean trough force was 6.23 N (SD=4.70, range=0-35.44) with a mean of 7.80 N (SD=4.82, range=0-35.44) for the dominant hand and 4.66 N

(SD=4.14, range=0-24.67) for the nondominant hand. The mean change in force was 18.16 N (SD=8.36, range=4.39-34.03) with a mean of 18.39 N (SD=9.11, range=4.72-32.55) for the dominant hand and 17.92 N (SD=7.83, range=4.39-34.03) for the nondominant hand. The mean velocity for motion testing was 19.69 N/s (SD=8.47, range=7.69-49.89) with a mean of 20.10 N/s (SD=9.96, range=8.21-49.83) for the dominant hand and 19.29 N/s (SD=6.98, range=7.70-36.75) for the no-dominant hand. The mean number of pushes was 3.90 (SD=1.80, range=1.4-7.8) with a mean of 3.98 (SD=1.82, range=1.4-7.8) for the dominant hand and 3.83 (SD=1.83, range=1.4-7.4) for the nondominant hand. The mean duration of palpation was 4.97 s for L1, 5.67 s for L2, 5.58 s for L3, 5.28 s for L4, and 6.30 s for L5.

Conclusions: The current study suggested that osteopathic medical students with similar training for testing segmental vertebral motion in the lumbar region had significant variability in their techniques. Further, this variability may increase as the time from training increases. These data may also suggest that the current evidence of poor reliability for motion testing results from variable testing procedures. Overall, our study may provide a methodology to evaluate rotational testing of the vertebra in future studies as a means of improving our understanding of the examination process, how the examination process relates to the mechanical properties of the person being examined, how the examination process relates to the examiner's diagnoses, and the reliability and accuracy of this form of testing. The primary limitations of the current study were that only 1 person was examined by all student examiners, the sample size was small, all student examiners were students from a single school of osteopathic medicine, and recruitment was based on the student examiner's interest in osteopathic manipulative medicine.

Acknowledgment/Funding Source: Supported by the Osteopathic Heritage Foundation Endowment for Research in Osteopathic Diagnostic and Therapeutic Palpation.

C35—Chronic Diseases & Conditions

Radiographic Imaging of Infants With Congenital Muscular Torticollis: A Retrospective Study and Clinical Practice Guidelines

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Objective: Despite current literature demonstrating initial x-rays, computerized tomography (CT), or magnetic resonance (MR) imaging of the head or neck is unnecessary for patients suffering solely from congenital muscular torticollis (CMT), physicians continue to order radiographic imaging prior to the patient being evaluated by a specialist. Our objectives are to (1) perform a retrospective study to reaffirm current literature suggesting initial radiographic imaging is unnecessary in most patients with CMT and (2) create guidelines for the ordering of radiographic imaging on patients with the disorder.

Methods: As part of a quality improvement initiative, the New Jersey Pediatric Neuroscience Institute (NJPNI) performed a retrospective analysis utilizing the General Electric Centricity Healthcare Practice Solutions 12 database to identify patients referred to NJPNI for evaluation and management of CMT between August 5, 2005, and July 23, 2015. Information was collected regarding the number of patients with CMT that received an x-ray, CT or MRI, as well as the reason the imaging was ordered. The number of patients whom had a secondary diagnosis or additional significant clinical finding as the reason for initial imaging was compared with the total number of CMT patients whom received imaging. Furthermore, the number of patients who suffered from CMT after 1 year of physical therapy

was obtained and compared with the total CMT population. Guidelines were created based on the results of our study and supporting literature.

Results: Seven hundred fifty-six patients were referred to NJPNI for management of CMT. Sixty-seven patients received initial imaging with 63 identified as having a diagnosis other than CMT or a significant clinical finding as the reason for image request. The remaining 4 patients (0.53% of our total CMT population), received radiographic imaging and in hindsight, should not have as they did not have an additional diagnosis or clinical finding requiring the imaging. No abnormal radiologic findings were found on these patients. Two patients (0.26% of NJPNI's CMT population) who did not receive initial imaging did not achieve resolution of CMT after 1 year of treatment with physical therapy. Imaging was performed and both patients were subsequently diagnosed with abnormalities that were thought to have caused their CMT; 1 patient was diagnosed with a closed dislocation of the second cervical vertebra (ICD9-839.02), and the other patient with an unspecific congenital anomaly of the spine (ICD9-756.10). Of the 693 (n-63) patients diagnosed with CMT that did not have a secondary diagnosis requiring initial imaging, 99.13% had resolution of CMT without undergoing x-ray, computed tomography, or magnetic resonance imaging.

Conclusions: Within the limits of this retrospective study, we find that without the presence of a significant co-existing diagnosis or physical examination findings, initial radiographic imaging is not necessary in infants suffering from CMT. Radiographic imaging is more appropriate after one year of failed physical therapy to ascertain an underlying cause. Current confines in the appropriate use of radiographic imaging for CMT patients may include a lack of inter-professional communication. Best clinical practice requires interpersonal communication of research findings and guidelines between physicians. Our goal is that these guidelines will be communicated to physicians initially evaluating CMT patients and that those physicians will no longer order radiographic imaging on patients with CMT. Our recommendations for radiographic imaging are as follows: (1) clinical examination performed by an experienced clinician is sufficient in the diagnosis of congenital muscular torticollis. Radiographic imaging including x-ray, CT, and MR imaging are not necessary; (2) in cases in which additional significant clinical findings are present, appropriate management and radiographic imaging may be recommended; (3) radiographic imaging must be obtained to ascertain an underlying cause for persisting CMT after 1 year of failed treatment with physical therapy.

Support: These guidelines were funded exclusively by the New Jersey Pediatric Neurological Neuroscience Institute, which received no funding from outside commercial sources to support the development of this document unless otherwise stated in this section.

♦C36—Impact of OMM & OMT

Use of Osteopathic Techniques to Treat Iliotibial Band Dysfunction in CrossFit Athletes

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Research Question(s)/Hypotheses: CrossFit is a competitive fitness regimen that is gaining in popularity across the country. Research has shown that CrossFit may lead to overuse injuries, specifically IT Band Friction Syndrome (ITBFS). However, there is a lack of information regarding prevention and effective, noninvasive treatment options. The objective of this IRB-approved pilot study is to demonstrate the effectiveness of osteopathic manipulative treatment (OMT), specifically a muscle energy technique, to treat iliotibial band dysfunction in CrossFit participants. It is hypothesized that utilization of OMT in

♦ Abstract that won first or second place in the 2014 SOMA Student Poster Competition.

association with at-home stretches will increase the distensibility of CrossFit participants' IT bands, decreasing the prevalence of ITBFS.

Methods: Study participants were required to be active members of CrossFit Spartanburg and were recruited before the beginning of the study through weekly announcements and flyers placed at the gym. After recruitment, each participant was issued a consent form and evaluated based on predetermined inclusion and exclusion criteria. Once enrolled into the study, researchers used an iPhone goniometer and the Ober test to measure the angle of distensibility of each CrossFit athletes' IT band before and after muscle energy was performed. A pre-OMT and post-OMT angle of IT band distensibility was measured weekly for a 6-week period. Participants were also given at-home stretches to perform throughout the week in an effort to maintain and improve the treatment results.

Data Analysis: To analyze the data for this study the program SPSS Version 22.0, 2013 was utilized.

Results: Six male and female patients ranging in age from 27 to 41 years were enrolled into the study. Both legs of each participant were measured over the 6-week period. During week 1, participants had an average pre-OMT angle of distensibility of 11.19 ± 4.28 and a post-OMT angle of 8.19 ± 3.69. At week 6, participants had an average pre-OMT angle of distensibility of 6.21 ± 2.94 and a post-OMT angle of distensibility of 3.36 ± 2.70. Using a paired *t* test the pre- and post-OMT angle for each week was compared and was statistically significant for each week with a = 0.05 .Partial Eta squared revealed a 0.32 decrease in OMT angle each week. When comparing the percentage of time participants completed their stretches with pre-OMT angle and post-OMT angle, there was no statistically significant difference with stretching.

Conclusion: The osteopathic muscle energy technique used was successful in increasing IT band distensibility in CrossFit athletes every week during this 6-week study, thus decreasing participants' risk of developing ITBFS. The statistically significant decrease in pre-OMT angles each week supported that our treatment was effective in maintaining IT band flexibility and could be used as a long-term treatment option. At-home stretches did not show any correlation to a decrease in IT band distensibility, demonstrating that no additional therapies are necessary between successive OMT treatments. The use of muscle energy to treat overuse injuries is a clinically relevant finding that could help reshape the way in which health professionals treat overuse injuries. There is currently a lack of minimally invasive treatment options targeted at truly correcting musculoskeletal dysfunction; therefore, the results of our study are potentially ground breaking. Future studies may be expanded to analyze the use of OMT for other sports-related musculoskeletal overuse injuries.

Acknowledgment/Funding Source: CrossFit Spartanburg; James Moore, OMS IV; Nicole Kitner-Allen, OMS IV; Dalia E. Meisha, DDS, MPH, DScD; Stuart Williams, DO; and Lopa Bhansaly, DO.

C37—Chronic Diseases & Conditions

Program ACTIVE II: Testing Behavioral Interventions for Depression in T2DM

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Objective/Hypothesis: Program ACTIVE II is a multisite, multistate randomized clinical trial designed to assess the comparative effectiveness and cost effectiveness of a combined behavioral ap-

proach to manage major depressive disorder in adults with type 2 diabetes. Specifically, is cognitive based therapy (CBT), CBT + exercise, exercise alone, or usual care the best treatment option for people with these condition?

Design and Methods: This randomized clinical trial utilizes a 2×2 factorial with repeated measures. Participants are randomly assigned to 1 of 4 arms: 10 sessions of CBT, 12 weeks of community-based exercise, a combination of 10 CBT sessions and 12 weeks of exercise and usual care. All participants receive a diabetes education nutrition intervention. Assessments are at baseline, post-intervention, and 6- and 12-month follow-up. Participants are recruited from Indiana University, West Virginia University, and Ohio University. This type 2 behavioral translational study uses a community-engaged research (CEnR) approach by partnering with community fitness centers and mental health practices as the sites for interventions.

Results: Sample to date is 114 participants. Mean (SD) age is 56.3 (10.7) years, with 78% female, 74% Caucasian, and 30% have completed high school or trade school. Half (50%) were married. The modal household income is $21,000-$40,000 supporting an average of 2.3 people. Just over half (52%) work outside the home and 69% own a home. To date there have been statistically significant improvements in depression symptoms, diabetes-specific quality of life, diabetes distress, and food choices.

Conclusions: This is the first study to evaluate the comparative effectiveness of combined CBT and exercise in the treatment of depression using community-based intervention delivery. These preliminary data suggest significant improvement in depression and quality of life for those in the active intervention groups. Further analyses on group differences and HbA1c and cost effectiveness are forthcoming. This treatment approach may serve as a national model of treatment of people with type 2 diabetes and depression.

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C38—Impact of OMM & OMT

Assessing the Influence of Examiner Characteristics on Palpatory Force in Osteopathic Medical Students

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Introduction: Osteopathic medical students are instructed in standardized palpatory technique, with emphasis on the examiner's dominant eye and body position relative to the patient. Motion testing or springing to assess tissue characteristics is fundamental for osteopathic palpatory diagnosis. Limited data exist on whether the examiner's dominant eye or body position during examination influences the performance and interpretation of motion testing.

Hypothesis: For students performing vertebral motion testing using standard procedures, a greater force will be generated by the examiner's dominant hand compared with the nondominant hand. Increasing the examiner's height above the treatment table will reduce variation between the hands. Standing position will create a greater variance between the dominant and nondominant hand when the examiner is positioned on the same side of the treatment table as their dominant hand. Finally, male examiners will show greater variation in force application between their hands.

Methods: The local institutional review board considered the current observational study to be exempt. The palpatory skills of 16 osteopathic medical students were evaluated when testing segmental motion in the horizontal plane on a volunteer participant. Students examined L1 to L5 using a standardized location and assessed the side of greatest restriction. The Novel Pliance-x Expert System was

used to collect baseline and peak pressure data. Prior to data collection for the study, a training laboratory session was completed to teach students how to the use the instrumentation and how to standardize the amount of pressure students were applying with their right and left hands.

Data Analysis: For each student examiner, one baseline trough and several peak forces, corresponding to the number of pushes, were collected for both hands at each lumbar spine level assessed. These data were used to calculate an average force for each examiner's dominant and nondominant hand. The averages were equally weighted among every lumbar spine landmark. A fixed effects linear regression model assessed the difference in force between dominant and nondominant hands and its potential dependence on gender, the height of the examiner above the treatment table, and whether the examiner was standing on the same side as the dominant hand.

Results: Participating students included 9 (56%) males and 7 (43%) females with 42 inches as the mean height of examiners above the treatment table. Fifteen (94%) examiners were right-hand dominant and 1 (6%) was left-hand dominant. Eleven (69%) self-identified as right-eye dominant and 5 (31%) as left-eye dominant. All but 1 examiner stood on the opposite side of the table of eye dominance. Controlling for gender, height, and standing position relative to dominant hand, the mean difference between dominant and nondominant hands was 3.4 N (SE=1.7), but the difference was not significant (P=.07). The height of the examiner above the treatment table had a slight positive relationship with the difference in force (slope 1.4; SE=0.7), but the relationship was not significant (P=.07). Gender and standing position of the examiner relative to the dominant hand did not influence the difference in force (P=.30 and P=.75, respectively). Results did not change after excluding the examiner who stood on the same side of the treatment table as eye dominance.

Conclusion: In the current study, we found no predictor that explained the variability in force difference between dominant and nondominant hands. Although not significant, the dominant hand generated more force. However, 3 of the 16 examiners used more force with their nondominant hand than with their dominant hand. This was not related to their gender, standing position, or height above the treatment table. A positive, non-significant relationship was also found between the force difference and height of the examiner above the treatment table. Gender and standing position of the examiner relative to the dominant hand had no statistically significant effect on the force difference. The limitations of the current study were the small sample size and the single laboratory training session to become familiar with the technology used. In future studies, a larger sample size is needed to explore the possible relationship between force and height and to increase the power to detect any real effects on the force difference because of gender or standing position relative to the dominant hand.

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C39—Osteopathic Philosophy

Evaluation of Household Food Insecurity and Chaos in an Urban Pediatric Patient Population

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Background: Food insecurity and household chaos are 2 aspects of the home environment that have been linked with suboptimal child development. Children in households with limited access to nutritious foods have been shown to be more susceptible

to nutrition-related problems as well as behavioral and cognitive defects. Similarly, chaotic home environments, defined by disorganization and lack of family routines, are associated with increased behavior problems in children. Understanding how the broader family context influences child health and development is critical for providing optimal pediatric patient care consistent with the osteopathic philosophy. This is especially important for low-income households and ethnic minority groups who have been shown to exhibit higher levels of household chaos and food insecurity. The Oklahoma State University (OSU) Pediatric Clinic serves many inner-urban families in the Tulsa area, but the prevalence of pediatric patients facing the potentially detrimental implications of living in a chaotic or food insecure household is currently unknown.

Objectives: The primary aim of this study is to determine the proportion of pediatric patients served by the OSU Pediatric Clinic who are living in food insecure households. Secondary aims include evaluating the level of household chaos and correlating findings with sociodemographic variables. Data obtained from this study will serve as a base from which to develop quality improvement projects related to osteopathic physician training in terms of better identification and assessment of patient needs and optimizing quality of care.

Methods: An anonymous, voluntary, self-report survey was administered to pediatric patient caregivers during routine office visits at the OSU Pediatric Clinic for a total of 10 weeks. The 35-item survey included general demographics, the 6-item Short Form of the United States Department of Agriculture's Household Food Security Scale and a modified 12-item version of the reliable and valid Confusion, Hubbub, and Order Scale. A Spanish version of the survey was also available for Spanish-speaking only caregivers.

Data Analysis: Descriptive statistics were computed for all major study variables. To determine the proportion of pediatric patients living in food insecure households, frequencies were computed to show the number of affirmative responses to each item on the scale. A logistic regression was used to estimate the association between demographic variables and food insecurity. Finally, an independent samples *t* test was computed to determine the association between family chaos and food insecurity.

Results: Preliminary data from 195 surveys were collected. The majority of pediatric patient caregivers visiting the OSU Pediatric Clinic were female with an average age of 30 years. 36% of caregivers reported being single (ie, never married or separated/divorced) and an additional 26% of caregivers reported living with a partner they are not married to. The majority of caregivers completed high school (28.8%) or attended some college or technical school (28.8%) with only 7.9% completing a bachelor's degree. In addition, 55.9% of caregivers identified as a racial/ethnic minority. Although 38% of caregivers reported full-time employment, 29% reported being unemployed and 35% reported annual family income below $10,000. The mean pediatric patient age was 5 years (ranging from <1 month to 17 years), and about half of patient caregivers indicated that they qualified for food stamps and are enrolled in Women, Infants, and Children (WIC) program. With regard to food insecurity, 34.6% of pediatric patients in the current sample are living in a food insecure household with 14.6% of these households experiencing hunger as indicated by 2 or more or 5 or more affirmative responses on the food insecurity scale, respectively. Demographic variables associated with food insecurity included maternal age, minority status, and having qualified for food stamps in the past year. Older maternal age (> 29 years) (OR, 2.07; $P<.049$) and having qualified for food stamps (OR, 3.21; $P=.009$) was associated with an increased risk of food insecurity, whereas identifying as a racial/ethnic minority was associated with a decreased risk of food insecurity (OR, 0.46, $P=.042$). Evaluating the level of family chaos, the mean value was 33.27 (SD=9.75) on a scale

ranging from 15 to 75. As expected, the level of family chaos was significantly associated with food insecurity, (t=-3.60, P=.000) such that food insecure households had significantly higher levels of chaos (M=36.7, SD=10.04) compared with food secure households (M=31.45, SD=8.88).

Conclusion: The prevalence of pediatric patients served by the OSU Pediatric Clinic living in a food insecure household is more than double the state and national averages. Interestingly, the decreased risk of food insecurity observed with racial/ethnic minority groups in our study contradicts findings demonstrated previously in other studies. Further investigation into the association of food insecurity with household geographic location, caregiver employment status, and specific minority groups may provide additional insight into the discrepancies. One limitation of the present study is the smaller than expected sample size, which may be in part, due to a reduced patient volume due to limited staff during a transition to a new electronic medical record system. With a large at-risk population, improving physician assessment of pediatric patient needs to optimize quality and delivery of care for families living in food insecure households is needed.

Acknowledgment: This study was reviewed by the Oklahoma State University Center for Health Sciences Institutional Review Board.

C40—Osteopathic Philosophy

Comparison and Evaluation of Immunofluorescence Assay and Polymerase Chain Reaction Methods in Detecting Respiratory Viruses in Pediatric Patients

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Research Question(s)/Hypotheses: Acute respiratory infections are one of the leading causes of hospitalizations in children. The majority of these infections are of viral etiology. However, patients are likely to be placed on unnecessary antibiotics due to the limitations of not receiving laboratory results in a timely manner. Furthermore, many of the commonly implicated viruses are not included in the routine antigen detection method. Being able to detect a wider range of viruses allows doctors to make a more accurate diagnosis and tailor the patient's course of treatment appropriately. This study will evaluate the discrepancy between detecting Respiratory Syncytial Virus (RSV) by immunofluorescence assay (IFA) and polymerase chain reaction (PCR) by the FilmArray Rapid Respiratory Panel (RRP) method.

Methods: Retrospective chart review of all patients age 0 months to 17 years admitted to the hospital from November 18, 2014, to July 31, 2015, due to respiratory distress and being tested by PCR "FilmArray RRP". The study compared the results from RSV antigen detection test by IFA to those from the polymerase chain reaction by FilmArray RRP. In addition to comparing the 2 detection methods, it also determined if there were any differences in the population and illness caused by RSV vs Rhino/Enterovirus.

Results: Eighty-six patients underwent viral detection testing through FilmArray RRP; 11 patients tested positive for RSV by PCR while simultaneously being tested negative using IFA (Group A). Fourteen patients tested positive for RSV by both IFA and PCR methods (Group B). Twenty-one patients tested positive for Rhino/Enterovirus by PCR method (Group D). Group C includes all patients tested positive for only RSV by PCR. No statistically significant difference between Groups A and B regarding age, gender, race, hospital length of stay (LOS), Pediatric Intensive Care Unit (PICU) LOS, severity of illness and risk of mortality (P>.05). There was a statistically significant difference between Groups C and D regarding age; 4.34 ± 1.44 months for Group C and 10.56 ± 6 months for Group D (P=.02). No statistically significant difference between Groups C and D regarding gender,

Table.
Data Analysis for Abstract C40

Metric	Group A[a] (n=11)	Group B (n=14)	*P* Value	Test Used
RSV Groups A vs B				
Average / median age, mo	20.1 / 1	2.77 / 0.98	.9782	Wilcoxon 2 sided
Gender				
Male	72.7%	50.0%	.4139	Fisher's 2 tail
Female	27.3%	50.0%		
Race[b]				
White	81.8%	85.7%	…	…
Hispanic	18.2%	…		
African American	…	14.3%		
Average / median LOS, h	84.2 / 84.5	104.27 / 78.96	.5654	Wilcoxon 2 sided
Days in PICU	2.9 / 3.4	3.48 / 2.65	.7209	Wilcoxon 2 sided
APR-DRG SOI[b]				
Extreme (4)	9.09%	0%	…	…
Major (3)	36.4%	7.14%		
Moderate (2)	45.5%	50.0%		
Minor (1)	9.09%	42.9%		
APR-DRG ROM				
Extreme (4)	0%	0%	.3500	Fisher's 2 tail
Major (3)	0%	0%		
Moderate (2)	36.4%	14.3%		
Minor (1)	63.6%	85.7%		
Average / median PROM	5.11 / 5 *n=9	6.63 / 5 *n=11	.3290	Wilcoxon 2 sided
Average / median ROM	2.57 / 2.3 *n=9	3.57 / 2.3 *n=11	.3290	Wilcoxon 2 sided

(continued)

race, hospital LOS, PICU LOS, severity of illness, and risk of mortality (P > .05).

Conclusion: PCR is more sensitive in detecting the virus in the nasopharyngeal sample. Those who tested negative by IFA and positive by PCR are comparable to those tested positive by both IFA and PCR; therefore, PCR is needed to accurately detect the etiologic viral agent causing the illness. Viral detection studies are still needed to determine the causative agent. The study reflects that demographics, severity of illness, and risk of mortality alone cannot determine or differentiate the causative agent.

Table (continued).
Data Analysis for Abstract C40

Metric	Group C (n=26)	Group D (n=21)	*P* Value	Test Used
RSV Groups A vs B				
Average / median age, mo	4.34 / 1.44	10.6 / 6	.0202	Wilcoxon 2 sided
Gender				
Male	57.7%	66.7%	.5624	Fisher's 2 tail
Female	42.3%	33.3%		
Race[b]				
White	76.9%	71.4%	…	…
African American	19.2%	28.6%		
Unavailable / Unknown	3.8%	…		
Average / median LOS, h	102.5 / 68.3	92.6 / 51.18	.0850	Wilcoxon 2 sided
Days in PICU	3.28 / 2.6	2.47 / 1.7	.1033	Wilcoxon 2 sided
APR-DRG SOI[b]				
Extreme (4)	3.84%	4.76%	…	…
Major (3)	11.5%	9.52%		
Moderate (2)	38.5%	38.1%		
Minor (1)	46.2%	47.6%		
APR-DRG ROM[b]				
Extreme (4)	0%	0%	…	…
Major (3)	0%	4.76%		
Moderate (2)	15.4%	9.52%		
Minor (1)	84.6%	85.7%		
Average / median PROM	5.77 / 5 *n=22	6.68 / 6 *n=19	.1841	Wilcoxon 2 sided
Average / median ROM	3 / 2.3 *n=22	3.72 / 2.8 *n=19	.1841	Wilcoxon 2 sided

[a] 199-month-old in group A.
[b] Insufficient n for contingency analysis.

C42—Osteopathic Philosophy

Colorectal Cancer Prognosis and Postsurgical Complications Correlated to Genetic Background of KRAS and EGFR

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Introduction: With an aging population and a diet rich in meat and high fat consumption, there has been a growing concern in the rise of colorectal cancer (CRC) worldwide. CRC has been the leading cause of death in Taiwan for the past 31 years, contributing about 28% of deaths each year. For the past 6 years, CRC has remained the most common form of cancer in Taiwan. The progression to CRC is multifactorial and involves genetic modifications of

key regulatory molecules, One of which includes the proto-oncogene KRAS, which is mutated in 30-50% of CRCs. Another key regulator, EGFR, is often overexpressed in CRCs. Past studies have shown KRAS mutations on codons 12 and 13 are poor prognostic markers of CRC due to their poor response to EGFR inhibitors such as cetuximab and panitumumab. Although EGFR is highly expressed in CRC, its role as a prognostic marker of CRC remains unclear. The aim of this retrospective study is to investigate the KRAS status and EGFR expression levels of CRC patients and analyze their relationships in prognosis and postsurgical complications. It is anticipated that a better understanding of the roles of KRAS mutations and EGFR expression in CRC prognosis may help establish favorable treatment decisions and ultimately benefit patients. This study thus underlines the principle of osteopathic practice.

Hypothesis: This study is designed to test the hypothesis that the genetic background of KRAS and expression levels of EGFR impact the cancer stage. Surgery remains the main treatment for early stage CRC, and postsurgical complications remain a serious concern. Thus, we will also investigate the relationship between the genetic background (KRAS and EGFR) and incidence of postsurgical complications of CRC patients.

Methods: Data was collected from 32 patients diagnosed with colorectal cancer who received a KRAS mutation screen and EGFR IHC stain during 2013-2015 at Taipei Hospital, Ministry of Health and Welfare in Taipei, Taiwan. Data were gathered through the review of patient medical records obtained from the Patient Records Office at Taipei Hospital, Ministry of Health and Welfare. The data collected include KRAS status, EGFR IHC expression levels, TNM staging of cancer, cancer site, and postsurgical complications. EGFR IHC expression level was provided as a percentage for positive cells and was scored as 0 (<10%), 1 (11-25%), 2 (26-50%), 3 (51-75%), and 4 (>75%).

Results: Of the 32 confirmed CRC patients who received a KRAS mutation screen and EGFR IHC stain, 59% (n=19) were positive for KRAS mutation. 68% (13/19) were positive for a mutation in codon 12 and 32% (6/19) were positive for a mutation in codon 13. 85% of patients with a KRAS mutation in codon 12 (n=11) were diagnosed with late stage cancer (stage 2 or higher). Interestingly, all patients with a KRAS mutation in codon 13 were diagnosed with late stage cancer. Seventy-four percent (n=14) of patients positive for KRAS mutation showed no postsurgical complications upon tumor resection, whereas 70% (n=9) of patients wild type for KRAS showed postsurgical complications upon tumor resection. The complications include UTI (n=4), intestinal anastomotic leakage (n=4), and pneumonia (n=1). All patients positive for KRAS mutation (n=19) showed positive staining of EGFR (score >2). High expression levels of EGFR with simultaneous KRAS mutation showed more advanced stages of CRC ($R2 = 0.26439$, $P=.00000000111$) while high expression levels of EGFR with wild type KRAS showed more early stages of CRC ($R2 = 0.1235$, $P=.00000000148$).

Conclusion: This study suggests that screening the KRAS status and EGFR expression levels can help assess the prognosis and risk of postsurgical complications in CRC patients. The higher occurrence of KRAS mutation seen in CRC patients at Taipei Hospital (59% compared with 30-50% in other countries) brings awareness in the importance of implementing the KRAS mutation screening during the diagnosis of CRC. The role of KRAS codon mutations in CRC prognosis has been controversial in a few published studies. Our result suggests that KRAS codon 13 mutation in Taiwanese patients is associated with poor clinical outcome. The correlation of high expression levels of EGFR with simultaneous wild type KRAS showing less advanced stages of CRC may provide more possibilities in the decision of treatment op-

tions. Conversely, the correlation of high expression levels of EGFR with simultaneous KRAS mutation showing more advanced stages of CRC poses future studies into looking at the effect of KRAS on EGFR expression levels and their dual effect on cancer prognosis. The higher occurrence of postsurgical complications seen in CRC patients with wild type KRAS is intriguing and should be further investigated in a larger scale study. If proven true, such finding would bring awareness into the possibility of specific preoperative and postoperative care for CRC patients to help minimize these occurrences.

C43—Chronic Diseases & Conditions

Food Insecurity, Numeracy and Literacy Associations With Decreased Glycemic Control in People With Type 2 Diabetes in Solano County

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Research Question/Hypotheses: Our objective was to determine whether patient literacy, numeracy, and food security were independently and additively correlated with poor glycemic control in a clinical population characterized as low-income (Medi-Cal patients) and with type 2 diabetes. We hypothesized that low food security would contribute quantitatively to a higher HbA1c value, indicating poorer glycemic control while patient literacy and numeracy would be found without association to HbA1c values and glycemic control.

Methods: In this cross-sectional study, data was collected during the summer of 2015 at 2 Solano County Primary Care Clinics. Inclusion criteria were as follows: type 2 diabetes mellitus, English-speaking, age 18 years or older, and informed consent. Patients not meeting inclusion criteria were excluded. Trained student investigators recruited participants. Patients were approached at the time of their visit and asked if they would be willing to participate. After informed consent was obtained, student investigators administered a composite of 4 surveys including the USDA Food Security Questionnaire, DNT 15, SKILLD Literacy Survey, and Demographic Questionnaire and Assessment of Education Preferences. Surveys were either read aloud verbatim by trained student investigators or read and answered by patients. Upon completion of the survey, $10 incentive award cards were given. Survey results were then entered into Qualtrics data management software. To evaluate patient management of diabetes, the average blood sugar or HbA_{1c} was used as the primary outcome as established by previous studies to be an effective indicator of diabetes management and progression. Poor glycemic control was defined as $HbA_{1c} >$ 9.0% as according to a Healthy People 2020 goal. IRB approval was granted at Touro University California, College of Osteopathic Medicine in 2015 for Solano County, California.

Data Analysis: Descriptive statistics were performed on demographic and additional variables. Summary statistics were utilized—using mean, median, standard deviation, minimum, maximum, frequency, and percentages calculated as categorical variables. Crude and multivariable logistic regression was used to analyze possible associations between food security and HbA_{1c}, numeracy and HbA_{1c}, and literacy and HbA_{1c}. Statistical significance calculation was based on $P<.05$ on a $\chi 2$ test and student t test. Descriptive and regression analysis was performed using STATA 10.3 as indicated.

Results: At the time of submission, 84 participants have completed the study. Mean age of participants was 57.4 years and duration of diabetes was about 9.7 +/-8.2 years. Just over half had received diabetes education (52%) and only 57% had access to the Internet. Almost half (46.4%) used insulin to treat their diabetes. These participants had low literacy scores (5.2 +/- 2.2, range 0-10), numeracy

scores (5.9 +/- 4.0, range 0-15), and food security (2.9 +/-2.4, range 0-6). Diabetes health literacy scores were lowest with sign and symptoms of hyperglycemia, normal blood sugar range, normal HbA_{1c} value, and recommendations regarding exercise. Scores were highest with treatment for hypoglycemia, how often to check feet, how often to go the eye doctor, and long-term complications. A low total raw score for food security was significantly correlated with worse HbA_{1c}.

Conclusion: Low literacy, numeracy, and food insecurity are common in the Solano County population, and perhaps in most security net communities. Though suspected, no correlate was found between numeracy, and literacy with the current sample size. This study reveals that there are reasonably important areas of patient understanding/education, such as normal values for blood glucose and HbA_{1c}, that can be identified as deficient—thus, these kinds of surveys are easy to distribute and can easily assess the educational needs of a population.

C45—Impact of OMM & OMT

Assessing the Effect of Examiner Fatigue on Palpation Accuracy

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Introduction: Studies suggest that examiners may subjectively experience fatigue from palpation of somatic dysfunctions and performance of manipulative treatment. Few, if any, studies address the impact of examiner fatigue on the accuracy of palpation in an objective manner.

Hypothesis: Examiner fatigue will decrease the accuracy of palpation.

Methods: The current retrospective, longitudinal study was considered exempt by the local institutional review board. Data were collected from 16 Kirksville College of Osteopathic Medicine class of 2017 students. Two identical laboratory assessments, 6 months apart, were conducted to determine the accuracy of palpation in determining positional asymmetry in the coronal plane of calibrated pelvic models. Six landmarks were palpated on adjustable foam-covered pelvic models with an equal number of superior and inferior settings. Anterior pelvic landmarks included the iliac crest (IC-A), anterior superior iliac spine (ASIS), and pubic tubercle (PT). Posterior pelvic landmarks included the iliac crest (IC-P), posterior superior iliac spine (PSIS), and ischial tuberosity (IT). Using blinding methods, students evaluated each landmark 6 times, with the exception of IC-A and IC-P, which were evaluated 12 times. The following asymmetry settings were used for the 6 landmarks: 2-4 mm (PT), 4-6 mm (ASIS, PSIS), 2-6 mm (IT), and 2-7 mm (IC-A, IC-P).

Data Analysis: To assess the influence of fatigue, logistic regression was used to model the probability of correctly identifying the direction of positional asymmetry depending on whether the palpation occurred early (beginning third of the laboratory assessment) or late (last third of the laboratory assessment) and after controlling for the laboratory assessment, landmark, and whether the landmark was evaluated from the anterior or posterior side. A random examiner effect allowed for correlation among diagnoses from the same examiner.

Results: The effect of whether palpation occurred early or late during the laboratory assessment on the probability of correctly identifying the direction of positional asymmetry depended on whether the landmark was evaluated from the anterior or posterior side (P=.02). The probability of correctly identifying the direction of positional asymmetry early in the laboratory assessment was .83 and .81 for posterior- and anterior-evaluated landmarks, respectively. Late in the laboratory assessment, a significant decrease was found for posterior-evaluated landmarks (.73, P=.005), but no significant

change was found for anterior-evaluated landmarks (.83, *P*=.59). Although not significant, the early vs late effect of palpation may have depended on which landmark was being evaluated anteriorly or posteriorly (*P*=.06).

Conclusion: In the current study, a decrease in the accuracy of palpation occurred only with landmarks on the posterior pelvic models in the final third of the laboratory assessment, suggesting that fatigue did not cause this change. If fatigue was the cause, diminished accuracy would be present across all assessments for all asymmetry settings. However, 2 of the posterior landmarks (PSIS and IT) had smaller asymmetry settings in the final third of the laboratory assessments. Therefore, the decrease in accuracy of palpation in posterior pelvic models may be due to the greater difficulty in assessing asymmetry rather than fatigue. Future studies investigating the influence of fatigue on the accuracy of palpation should design assessments that have identical asymmetries in the first and final thirds of the laboratory assessments and that include a fatigue-inducing activity before the second assessment for comparison. Increasing the number of asymmetry settings and number of examiners should also be considered.

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C47—Osteopathic Philosophy

Streptococcal Serotypes in Puno, Peru

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Accounting for 18% of deaths, pneumonia is the leading global infectious cause of death among children younger than 5 years. With 90 different serotypes, streptococcus is the leading cause of pneumonia in this population. In pediatric patients across Peru, streptococcal pneumonia is isolated in high frequency. One of the highest rates of streptococcal pneumonia associated morbidity and mortality can be found in the Puno region of Peru. As a preventive measure, the Peruvian government sponsors a vaccination program, which provides immunity up to 7 of the streptococcal serotypes (Prevnar 7). Despite this program, there is a high prevalence and incidence of infection. The aim of this study was to discover the prevalence of the varying streptococcal serotypes among the pediatric population of Puno, Peru. Additionally, we wanted to see if the government-sponsored vaccination campaign should be transitioned to a more broad vaccination that immunizes against 13 serotypes of streptococcus (Prevnar 13). Over a 6-month period, we collected 286 samples from vaccinated children who presented with symptoms of pneumonia and pharyngitis. These samples were then sent to the CDC for serotyping. Of the 286 samples, 24 (or 8.39%) were seropositive. Of these seropositive samples, there were none that would have been covered by the Prevnar 7. Additionally, only 1 sample would have been fully immunized with Prevnar 13. The remainder of the streptococcal pneumonia serotypes are not covered by either vaccine. This data shows that Prevnar 7 is effective at covering some of the streptococcal pneumonia serotypes found in the Puno region. It

also shows that Prevnar 13 would have only covered one additional patient. Given the high cost of providing vaccination campaigns, the relative ineffectiveness of the Prevnar 13 in the area is cost prohibitive. We believe that sanitation campaigns and patient education on the prevention of infection spreading may be more effective than implementing Prevnar 13 and will allow the government to focus their resources elsewhere.

C52—Impact of OMM & OMT

Influence of Landmark Localization on Palpation Accuracy of Bronze Lumbar Spine Models

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Research Question: What is the influence of providing landmark localization in the overall process of diagnosing vertebral positional asymmetries in bronze lumbar spine models?

Introduction: Accurate diagnosis of vertebral positional asymmetry in the horizontal plane sequentially requires accurate localization of landmarks followed by accurate discrimination of asymmetry by the digits palpating the landmarks. In the current study, we wanted to determine how much accurate localization of landmarks influenced overall accuracy. We hypothesized that student performance would be better when landmark localization was provided compared with when it was not provided.

Methods: The local institutional review board considered the current study to be exempt. Two groups of third-year osteopathic medical students evaluated covered bronze lumbar spine models. They determined whether the model's right transverse process was anterior or posterior to the model's left transverse process. For group A (n=90), the covered models had black dots on the fabric covers over the transverse process landmarks. For Group B (n=70), there were no markings on the fabric covers for the transverse process landmarks. Both groups assessed asymmetry differences for L1 to L5 for 2 models (10 questions) with asymmetries randomized for anterior or posterior sides and ranging from 2 mm to 6 mm in magnitude.

Data Analysis: The number of correct responses was modeled as a binomial random variable in a generalized linear model to compare the effects of marked vs unmarked fabric covers. A logistic regression with random student effects was used to estimate effects of asymmetry while controlling for group. Estimates of the predicted probability of correctly determining the direction of the asymmetry and 95% CIs were calculated.

Results: Group A students scored significantly higher than Group B students for accurately identifying the asymmetry of landmarks ($P<.001$). The estimated probability of correctly identifying the direction of asymmetry was 0.89 (95% CI, 0.87-0.91) for marked models and 0.74 (95% CI, 0.71-0.78) for unmarked models. The direction of the model asymmetry affected the performance of both groups. Although there was a significant interaction of the direction and magnitude of the asymmetry, overall, the performance was better when the right side was anterior relative to the left side (odds ratio=1.9; 95% CI, 1.3-2.7; $P=.001$).

Conclusion: When using the bronze lumbar spine models, student accuracy was 15 percentage points better when landmark localization was provided. Improving palpation accuracy requires developing educational methodologies to improve landmark localization and accurate discrimination of asymmetry by the palpating digits.

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C54—Chronic Diseases & Conditions

Formulating Adjuvant Therapy of rHDL Nanoparticles With Saquinavir to Combat High-Risk Neuroblastoma

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Purpose: Despite major advances in pediatric cancer research, there has been only modest progress in the survival of children with high risk neuroblastoma (HRNB). Current chemotherapy regimens have a serious limitation due to off target toxicity. The purpose of our project is to evaluate the effectiveness of a drug delivery platform with reconstituted/synthetic high density lipoprotein nanoparticles (rHDL) using rHDL-Saquinavir (rHDL-SAQ) formulation for the treatment of HRNB. It is anticipated that upon establishing an improved chemotherapeutic regimen for HRNB, the rHDL technology could be extended to enhance the chemotherapy for other pediatric cancers.

Research Hypothesis: A stable, non-leaking formulation of rHDL-Saquinavir can be prepared and it can have better cytotoxic effect than free drug for high risk neuroblastoma cells.

Aims: (1) To successfully formulate a non-leaking rHDL-Saquinavir particle. (2) Formulate a particle that facilitates the uptake of encapsulated drug by a receptor-mediated mechanism. (3) Develop an rHDL-Saquinavir composition that can kill neuroblastoma cell lines more efficiently than the free drug. (4) Enhance the tolerance of the drug through receptor uptake to diminish systemic side effects.

Methods: The rHDL-Saquinavir nanoparticles were prepared by cholate dialysis method. The entrapment efficiency of Saquinavir was determined by Fluorimetric measurements. The chemical composition of rHDL-Saquinavir particles was estimated by standard kits. The average size of the particles was measured by DeLsa Nano particle size analyzer. The stability of particles was estimated by dialyzing the particles at 37°C, for 48 hours at pH 7.4. The cytotoxic effectiveness of the formulation was tested against 2 HRNB cell lines (SJNKP and IMR-5 obtained from Dr F. Temius, Regina Margherita Children's Hospital, Turin, Italy) as compared with that of the free Saquinavir using CCK-8 kit. The Inhibitory concentration to kill 50% of the cells (IC50) was determined.

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

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

C56—Impact of OMM & OMT

Mechanized Model of Lymphatic Pump Shortens Recovery From Maximal Exercise

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Introduction: During intense exercise, heart rate (HR), oxygen consumption (V02), systolic blood pressure (SBP) and blood lactate (BL) levels all increase. The body's requirement for energy increases causing the aforementioned factors to elevate. Recovery methods that reduce these markers more rapidly help to decrease delayed onset muscle soreness, fatigue, and improve athletic performance. It has been well documented that active recovery methods are more effective for recovery than passive recovery. Passive recovery is when the individual rests (eg, lying down, sitting) while the above markers return to normal levels. Active recovery (eg, walking, biking) is when the body is given time to return to normal levels while the individual continues to move by maintaining a slightly elevated metabolic range, which increases lactate clearance through increased oxidation. The cardiovascular system and lymphatic system operate together to increase oxygen to all cells and remove wastes and carbon dioxide from them. The term *lymphatic pump* was invented by Earl Miller, DO, to describe what was formerly known in osteopathic medicine as the thoracic pump technique. The lymphatic pump is a method of manipulation used by osteopathic physicians to increase the rate of lymph flow. Whole-body periodic acceleration (WBPA) is a mechanical bed that moves cyclically in a head to foot motion, mimicking a thoracic pumping motion. The thoracic pumping back-and-forth oscillating motion in the supine position has been shown to release nitric oxide, allowing for blood vessels to dilate and increased blood flow, thus catalyzing the metabolism of by-products and waste. Thoracic pumping techniques have been used in various diseased populations. It has never been examined whether thoracic pumping at a calculated rate can help improve recovery after intense exercise faster than previously recognized methods. If proven to be effective, this technique may be used as a novel recovery method following intense exercise.

Hypothesis: We hypothesized that using the WBPA bed as a mechanical thoracic pump following maximal exercise will help decrease BL, HR, V02, and SBP more effectively than an active walking recovery.

Methods: This cross-over design study was approved by the NYIT-COM institutional review board (BHS-1129) and registered on clinicaltrials.gov (NCT02482597). Inclusion criteria included individuals between the ages of 18-35 years in good physical condition who exercised regularly. Exclusion criteria included any underlying condition or medications that would affect normal exercise responses. Nine subjects participated in this study. Eight subjects were recruited from the NYITCOM medical school through flyers on campus; 1 subject contacted us through the clinicaltrials.gov website. All subjects read and signed the consent form before participation. Resting BL, V02, HR, and SBP were measured for all subjects before they underwent a graded treadmill exercise test (Bruce Protocol) integrated with a metabolic cart (Medgraphics Ultima) consisting of a maximum of 7 3-minute stages. During the exercise test, SBP, HR, and V02 were measured at the 2-minute mark within each stage. At peak exercise, SBP, HR, V02, and BL were re-measured. Blood lactate was analyzed using the NOVA Lactate Plus lactate analyzer (Nova Biomedical). Subjects were randomly assigned to 1 of 2 recovery methods on 2 separate days. One method of recovery was an active form, in which subjects walked for 20 minutes on the treadmill post-exercise (2.0 mph). The

second method was WBPA, in which subjects were on the WBPA (Exer-Rest) bed supine for 20 minutes. WBPA was set at a frequency of 140 cycles/16 mm distance for 20 minutes. Blood lactate, VO2, HR, and SBP were recorded at minutes 1, 4, 7, 10, and 20 for both recovery methods. Each subject was brought to the same peak level of exercise on both days to keep all outcomes consistent.

Data Analysis: Eight subjects were included in our analysis. A repeated measures *t* test was used to compare all variables (HR, SBP, V02, and BL) from rest to peak exercise. A repeated measures *t* test was also used to compare all variables during recovery at minutes 1, 4, 7, 10, and 20. A value of $P<.05$ was considered statistically significant.

Results: As expected, all participants increased HR, V02, SBP, and BL from rest to peak exercise. There were no significant changes in these peak values from testing day 1 to testing day 2. Post-exercise WBPA showed a significant decrease in V02 at minute 4, 7, and 10 with no change at minute 20. HR showed a significantly more rapid decrease on WBPA at minute 4, 7, 10, and 20 minutes. There was no change in SBP or BL between groups.

Conclusion: In our pilot data, we were able to compile evidence toward showing the efficacy of using thoracic pumping motion on a mechanical model as a recovery method after exercise. This is the first experiment to evaluate the use of a mechanical thoracic pump as a recovery tool for intense exercise. We found no change in BL or SBP between active and thoracic pumping at the intensity we examined. Interestingly, there was a significant difference in the recovery levels of V02 and HR when placed on the WBPA bed as compared with walking post-exercise. This significant difference demonstrates that a mechanical thoracic pump was more effective in recovering the cardiorespiratory system post-exercise than walking active recovery. Thoracic pumping done in the osteopathic profession is a technique that is administered by a physician. There is no way to quantify the intensity or frequency of the pumping motion when studying this technique as being therapeutic. Going further, we will test a larger sample size and we will try to mimic the frequency of the WBPA with providers using a metronome to create the same frequency and displacement that we showed to be effective (140 cycles per minute, 16 mm distance). The results from our pilot data indicate that future studies should explore osteopathic thoracic pumping techniques further as a possible tool for recovery after exercise.

C59—Impact of OMM & OMT

Correlation of Force and Displacement on Diagnostic Accuracy Using Lumbar Segmental Motion Testing

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Introduction: Successful osteopathic manipulative treatment depends on accurate diagnosis of somatic dysfunction. Vertebral dysfunction is often diagnosed based on motion testing, and motion testing assesses the ease or limitation of motion from a manually applied force. However, the correlation between physician clinical diagnoses and force and displacement has yet to be determined.

Hypothesis: During lumbar segmental motion testing evaluating rotational motion, the side of restriction is determined by inducing motion on both sides of the segment with equal force on both sides or greater force on the perceived restricted side and feeling less digit displacement on the restricted side compared with the unrestricted side.

Methods: The local institutional review board considered the current study to be exempt. Sixteen second-year osteopathic medical students performed segmental motion testing in the horizontal plane on 2 volunteer participants. Students assessed vertebral rotational motion from L1 to L5 on each participant and assessed the side of greatest restric-

tion. A Vicon Motion Capture System and a Novel Pliance-x Expert System were used to collect tissue displacement and pressure data, respectively. Ultrasonography was used to localize the lumbar transverse processes and standardize the site for testing for all student examiners. Force and displacement waveforms were collected, identifying points at baseline and at the peaks of displacement of the examiner's palpating digits. The maximum and minimum forces of each examiner for each lumbar segment were also examined. The amount of displacement at the peaks of force was determined.

Data Analysis: Average force and displacement were calculated 2 different ways for each side of the transverse process for each lumbar segment and examiner: using all pushes or using only the last 3 pushes because of a large variability in the number of pushes between examiners. Mixed linear regression models were used to assess differences between restricted and non-restricted diagnosed sides for force and displacement. A random intercept for lumbar segment within examiner allowed for correlation between observations made by the same examiner on the same segment. Lastly, displacement and force were analyzed together. Discordant pairs were either the non-restricted side had greater displacement with less force compared with the restricted side or the non-restricted side had less displacement with more force compared with the restricted side. McNemar's test assessed whether these discordant pairs were equally likely for each lumbar segment.

Results: When using all pushes, there was no significant difference in average force between restricted and non-restricted sides (P=.83). An average force of 24.3 N (SD=1.02) and 24.1 N (SD=1.02) was applied on the restricted and non-restricted sides, respectively. There was no significant difference in average displacement between restricted and non-restricted sides when using all pushes (P=.77). An average displacement of 15.4 mm (SD=0.98) and 15.5 mm (SD=0.98) was observed on restricted and non-restricted sides, respectively. When using only the last 3 pushes, there was no significant difference for force between restricted and non-restricted sides (P=.40), and an average force of 23.9 N (SD=1.74) and 24.4 N (SD=1.74) was applied on the restricted and non-restricted sides, respectively. There was also no significant difference in displacement between restricted and non-restricted sides when using only the last 3 pushes (P=.27). An average displacement of 15.2 mm (SD=1.16) and 15.9 mm (SD=1.17) was observed on the restricted and non-restricted sides, respectively. When assessing discordant pairs, only at L4 were examiners more likely to diagnose the restricted side correctly when a greater amount of force with less displacement was found on the transverse process (P=.05).

Conclusion: In the current study, no significant correlation was found between diagnosis of greatest restriction and the amount of force applied. Similarly, there was no correlation with diagnosis and displacement of the lumbar segment. Although the amount of displacement for the restricted and non-restricted sides was expected, the correlation was not statistically significant. These results suggest that other factors may exist that affect, and possibly better correlate with, determining the side of greatest restriction or that the diagnostic process yields random assessments. Limitations of the current study include the healthy body habitus of the volunteer participants, the likely minor somatic dysfunctions of participants, the variability in rate at which students applied force during motion testing, the differences in palpation techniques, and the varying degree of dependence for tactile and visual sensory information. Further, the effect of consecutive palpation of lumbar tissues may have caused a variation in the dysfunction. Future studies should consider student fatigue during diagnosis, depending on the amount of time spent palpating before assessing participants. Future studies should also consider blindfolding of students to remove

visual input, choosing stricter participant selection criteria, including participants with chronic dysfunctions, and controlling the rate of force applied using an auditory tempo.

Acknowledgment/Funding Source: Supported by the Osteopathic Heritage Foundation Endowment for Research in Osteopathic Diagnostic and Therapeutic Palpation.

♦C60—Impact of OMM & OMT

Relating Accuracy of Asymmetrical Assessment of Osteopathic Medical Students in Directional Diagnosis on Standardized Pelvic Models and Humans

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Introduction: Procedures to evaluate pelvic somatic dysfunction are taught at all osteopathic medical schools. Calibrated, adjustable pelvic models have been used to evaluate the accuracy of palpatory localization and asymmetrical assessment of students, but whether accuracy on models relates to accuracy on humans has not been evaluated. One difference between pelvic models and humans is greater variability among humans because of irregular tissue layers, tissue textures, skeletal structures, and joint mobilities. The current study focuses on relating the accuracy of asymmetrical assessment after landmark localization has occurred on standardized pelvic models to test performance on humans and to assess the significance of this relationship.

Hypothesis: The accuracy of asymmetrical assessment by osteopathic students on standardized pelvic models and human pelvic landmarks will be positively related.

Methods: The current study was considered exempt by the local institutional review board. The digit asymmetry of 16 second-year osteopathic medical students was evaluated using a digital camera measurement system during assessment of positional asymmetry of pelvic bony landmarks in the coronal plane on calibrated, adjustable, foam-covered pelvic models and humans. Students diagnosed the pubic tubercles (PT), anterior superior iliac spine (ASIS), posterior superior iliac spine (PSIS), and iliac crests from the anterior (IC-A) and posterior sides (IC-P). They assessed the IC-A and IC-P 20 times and the PT, ASIS, and PSIS 10 times on the pelvic models at different calibrated asymmetries. They also evaluated each landmark on 6 different humans at least 12 times. The study took place during 4 laboratories on different days. Accuracy was achieved when digit asymmetry agreed with the student's corresponding directional diagnosis.

Data Analysis: The mean percent accuracy was calculated for each examiner by modality type (models or humans) with each laboratory and landmark equally weighted. Spearman's rank correlation coefficient and beta regression were used to assess the association between model and human accuracy.

Results: Model and human accuracy were significantly associated (rs=0.63, P=.01). An increase of 5% accuracy in performance on the models was associated with a 29% increase in the odds of an accurate human diagnosis (P=.001).

Conclusion: Overall, the accuracy of students in asymmetrical assessments of standardized pelvic models was positively related to their accuracy on humans. Although there are many differences between standardized models and humans, our study suggested that a student's performance on standardized models was a reliable indication of their ability to assess asymmetry on human innominates. The primary limitation of the current study is that true accuracy of landmark localization on humans is not possible. The accuracy evaluated in our study was the ability of students to accurately assess their hand asymmetry on the models and humans. Methods for evaluating the accuracy of pelvic landmark localization on humans need to be developed.

♦ Abstract that won first or second place in the 2014 SOMA Student Poster Competition.

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C61—Impact of OMM & OMT

Pilot Study: What is the Best OMM Approach to Affect Autonomic Nervous System Control of Heart Rate Variability

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Introduction: The autonomic nervous system (ANS) regulates all soft tissue structures in the mammalian body in attempt to maintain homeostasis. In a study conducted by Henley et al (2008) it was shown that changes in the autonomic nervous system can be analyzed via heart rate variability (HRV). Recent studies have suggested that osteopathic manipulative medicine (OMM) techniques influence heart rate via the autonomic nervous system (Henley et al 2008, Henderson et al 2010, Shi et al 2011). However, the application of OMM to particular autonomic nervous system anatomy and its influence on the parasympathetic vs sympathetic nervous system control of heart rate is unclear. The aim of this study is to characterize the effect of OMM on autonomic nervous system control of HRV. Our hypothesis is that the OMM techniques chosen will impact autonomic input on HRV spectra corresponding to the parasympathetic and sympathetic influence.

Methods: This study was approved by the NYITCOM institutional review board (BHS-975) and is registered at clinicaltrials.gov (NCT02107638). Our inclusion criteria include individuals aged between 20 and 50 years who do not have a medical history of cardiac or autonomic conditions. Subjects who had a history of cardiac or autonomic conditions or who had caffeine within an hour were excluded. The 48 participants enrolled were randomly assigned to an OMM group and to a sham group. Participants were further subdivided into 1 of 4 OMM techniques: sub-occipital release, rib raising, stellate ganglion release, or a combination of all 3. The trials were split into 2 phases, one excluding OMM which served as each patients control run and one including the assigned OMM technique, which served as the experimental run. In both phases of the trial, the participants were instructed to lie in a supine position for 10 minutes before passively tilted to 50° for a 3-minute cognitive challenge. The cognitive challenges included randomized arithmetic questions and a modified Stroop color test. The assigned OMM technique was performed before the cognitive challenges in the second phase. The HRV of each participant was recorded via electrocardiogram at the initial supine position and then again during the cognitive challenges of each phase. A Biopac Model M150 was used to record the participants' heart rate and the digital recordings were analyzed using an R-wave peak detection algorithm. For analysis, we conducted independent subjects *t* tests comparing the difference in sympathetic tone from cognitive challenge to baseline between the subjects receiving sham or OMM treatment.

Results: Forty-eight subjects participated (28 females and 20 males), with a mean age of 26.9 years. In the sub-occipital release group, looking at change in sympathetic tone during the math or color tests before and after treatment, sympathetic tone (as measured by LFnu) tended to increase more in subjects receiving OMM vs sham, though this difference was not significant (P=.131 for math, P=.462 for color). Parasympathetic tone (as measured by HF) tended to decrease less in this

period in subjects receiving OMM vs sham, though this difference was not significant (P=.451 for math, P=.571 for color). In the stellate ganglion release group, sympathetic tone tended to decrease less during the math test and increase more during the color test in subjects receiving OMM vs sham in this period, though this difference was not significant (P=.527 for math, P=.378 for color). Parasympathetic tone tended to increase more in this period in subjects receiving OMM vs sham, though this difference was not significant (P=.446 for math, P=.953 for color). In the rib raising group, sympathetic tone tended to increase less during the math test and decrease more during the color test in subjects receiving OMM vs sham in this period, though this difference was not significant (P=.832 for math, P=.702 for color). Parasympathetic tone tended to decrease less during the math test and increase more during the color test in this period in subjects receiving OMM vs sham, though this difference was not significant (P=.761 for math, P=.702 for color). In the combined treatment group, sympathetic tone tended to increase more in subjects receiving OMM vs sham in this period, though this difference was not significant (P=.679 for math, P=.222 for color). Parasympathetic tone tended to decrease less during the math test and increase less during the in this period in subjects receiving OMM vs sham, though this difference was not significant (P=.986 for math, P=.922 for color).

Conclusions: In this study, none of the tested techniques, or the combination of techniques, yielded a significant change in autonomic tone. We argue that the protocol for this study was appropriate for inducing an increase in sympathetic tone and that the techniques chosen were adequate to mitigate a sympathetic response. Previous studies have shown that head tilt and cognitive challenges induce a sympathetic shift in autonomic tone (Calister et al 1992, Henley et al 2008). Additionally, sub-occipital release, stellate ganglion release, and rib raising been proven to have an effect on the body's self-regulation mechanisms (Shi et al 2011, Henderson et al 2010, Ettlinger 2013). In this study, bias was accounted for using a single-blinded, randomized trial that utilized exclusion criteria as well as food and sleep diaries to reduce confounding variables. Currently, the limitation of this study is a lack of power, and we argue that as more participants enter into the study, the data will reach significance. For example, the data for the stellate ganglion release is trending in a direction that will likely yield significance as more participants are enrolled. Future studies would benefit by ensuring a larger population of participants thus increasing power. It is important to carry out further studies using HRV to evaluate autonomic tone because there is a significant clinical relevance. In a study published by Hon and Lee (1965) it was demonstrated that in situations of fetal distress, alterations in R-R intervals preceded any noticeable change in heart rate itself. Furthermore, it was later revealed by Dewey et al (2007) that the lack of HRV after exercise was a strong predictor of both cardiovascular and all-cause mortality independent of other clinical factors.

C62—Impact of OMM & OMT

Sympathetic Stimuli: Investigating the Effect of Somatic Dysfunction and Other Factors on Baseline Sympathetic Tone

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Background: Nerves of the automatic nervous system (ANS) supplying the heart from both the vagus nerve and sympathetic chain interact with nearby nerves at their origins in the spine and in the skull, and somatic dysfunction (SD) at these levels

can contribute to an abnormal functioning of the ANS at that level (a somatovisceral reflex). In addition, inherent ANS dysfunction can cause changes in the corresponding musculoskeletal system (a viscerosomatic reflex), diagnosable as SDs. Osteopathic manipulative medicine (OMM) may improve the function of the ANS through treatment of SD, though little is known about the nature of this phenomenon. One way to measure the effect of OMM on the ANS is by using the beat-to-beat heart rate variability (HRV). HRV is currently only used in obstetrics to indicate fetal health in utero, though it also indicates neurological health and cardiac well-being. Control over HRV is multifaceted and can be affected by medical conditions, medications, and diet. In this study we will investigate how SD and lifestyle or personal risk factors for cardiovascular disease impact HRV.

Hypothesis: We hypothesize that subjects will have certain underlying medical or lifestyle stressors that are significantly associated with less parasympathetic tone in the autonomic nervous system control of HRV at baseline and in response to provocation. Specifically, we hypothesize these stressors will include chronic pain, use of hormonal contraceptives, increased tobacco or caffeine use, less physical activity, or more perceived life stressors. We hypothesize age, gender, and family history of cardiovascular disease or mental health disease will not have such an impact. Finally, we hypothesize the presence of SDs at the level of the vagal and sympathetic innervation to the heart will be associated with increased sympathetic tone in the autonomic control of HRV.

Methods: As approved by the Institutional Research Board at NYIT (BHD-1044), subjects aged 20 to 40 years were recruited using a standard flier and email sent to NYIT faculty, staff, and students. Subjects completed a survey asking about the factors investigated in this study, underwent an osteopathic structural examination (OSE), and had their resting heart rate (HR) and blood pressure (BP) measured. Next began HRV measurement. Subjects started lying supine for 10 minutes, with the final 3 minutes recorded (horizontal 1). Subjects were passively raised to a seating position, allowed to sit for 30 seconds, and then subjected to a 90-second math examination with true/false addition, subtraction, multiplication, or division questions, and a 90-second modified Stroop color test, with HRV recorded during the Stroop test (challenge). Subject were passively returned to supine and allowed to rest for 5 minutes, with the final 3 minutes recorded (horizontal 2).

Data Analysis: HRV was computed using spectral analysis in a manner previously described1, but with spline resampling was set at 8.0 Hz. Normalized power in the low frequency band (LF), which roughly corresponds to sympathetic tone, was calculated using the formula: LFnu = (LF)/(VLF+LF+HF), where VLF and HF is the power in the very low frequency and high frequency band respectively. Categorical variables were compared using either a 2×3 or 3×3 repeated measures analysis of variance (ANOVA), with bonferoni *t* test used for post-hoc analysis. Continuous variables were compared with recording periods using a Pearson Correlation. A significance level of $\alpha = 0.05$ was set.

Results: Forty-eight subjects participated (28 females and 20 males), with a mean age of 26.9 years. Subjects with SD on OSE tended to have a higher sympathetic tone as measured by LFnu and parasympathetic tone as measured by HF than subjects without SDs at the OA, and cervical regions, with a higher sympathetic tone and lower parasympathetic tone for SDs at the T1-T4 regions, although this difference was not statistically significant. Specifically, subjects with SD at the OA and T1-T4 tended to have higher resting BP (systolic and diastolic) and lower resting HR than those subjects without SDs, with SDs at T1-T4 subjects having a significant difference in resting HR (P=.015). Such an effect was not present when looking at cervical SDs. The presence of SDs at

any level did not alter the increase in LFnu to sympathetic challenge. Looking at other factors, smoking did have an effect on sympathetic and parasympathetic tone at the horizontal 1 (sympathetic P=.011, parasympathetic P=.048) and sympathetic at the challenge (P=.024) time periods, with smokers having a higher LFnu and lower HF in both periods. Subjects who listed physical activity for stress relief tended to have an increased LFnu, with a significant difference at horizontal 1 (P=.033). Interestingly, subjects reporting a family history of mood or mental health disorders tended to have a higher LFnu than their counterparts, and had an increased response to sympathetic challenge (P=.011). As far as vital signs, the presence of chronic headaches or neck or back pain tended to be associated with higher resting HR and lower resting BP. Subjects reporting significant life stress had a lower resting HR (P=.029), but with similar BP as those not reporting such stress. Other factors were not found to be associated with differences in HRV or vital signs. No correlations were significant with HRV or vital signs.

Conclusion: In this study, we found that the presence of SD in regions containing autonomic nerves innervating the heart was associated with a higher resting sympathetic tone, decreased heart rate, and increased blood pressure. Such a pattern lends support to the concept of viscerosomatic or somatovisceral reflexes. The interaction of a family history of mental health disease is consistent with literature finding HRV changes in patients with mental health disease. This highlights the impact mental health may play in pathophysiologic processes. However, this study is limited by its power, and while several trends can be elucidated, more subjects are needed to reach statistical significance. Additionally, the use of multiple investigators for the OSE, which was necessary due to scheduling conflicts, may have impacted the reliability of SD diagnosis, but was necessary due to scheduling conflicts. Future studies can also investigate whether these factors impact a subject's HRV response to treatment with osteopathic manipulation beyond the baseline measures.

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C63—Osteopathic Philosophy

Wound Healing After Laparoscopic Surgery: A Retrospective Comparison of Suture and Surgical Adhesive Tape in Skin Closure

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Research Question: In patients undergoing laparoscopic abdominal surgery, will surgical adhesive tape or suture provide a lower incidence of infection in wound healing?

Background: Both suture and surgical adhesive tape have been established as standards of care for skin closure following abdominal laparoscopic surgery. However, the majority of present research has compared the combination of suture and surgical adhesive tape to other skin closure techniques. The present study examined the differences in wound healing following closure with either suture or surgical adhesive tape.

Methods: Using a retrospective case-control study, 91 patients (44 men, 47 women) who had undergone outpatient abdominal surgery from 1996-2014 were randomly selected from a pool of various abdominal surgeries based on the type of skin closure that they had received (49 suture, 42 surgical adhesive tape). These patients were further categorized according to BMI (53 with BMI >30, 38 with BMI <30). The primary outcomes measured were infection and direct adverse reaction to the skin closure method (eg, blisters). Infection was defined as the presence of an open wound, hypertrophic granulation, or purulent drainage.

Results: Comparison of skin incisions closed with suture to skin incisions closed with surgical adhesive tape revealed no significant difference in wound healing (OR, 1.9; CI 95%, 0.4-8.7). The data revealed that females with surgical adhesive tape for skin closure had slightly fewer adverse outcomes when compared with males (11.8% and 21.1%, respectively), but these data did not show a significant difference (OR, 0.7; CI 95%, 0.1-5.3). Patients with a high (>30) BMI that received surgical adhesive tape for skin closure showed a slight reduction in adverse outcomes when compared with patients with a low (<30) BMI (15% and 18.8%, respectively), but these data did not reveal a significant difference (OR, 0.98; CI 95%, 0.2-6.1).

Conclusions: Surgical adhesive tape is as effective as suture in wound healing when used as a form of skin closure after abdominal laparoscopic surgery. Because of the similar outcomes, these findings suggest that surgical adhesive tape may be a better alternative to suture to reduce the length of anesthesia and operating times a patient must endure. However, a larger sample size from several institutions is necessary to provide a more comprehensive analysis of the skin closure techniques. Additionally, because this study focused solely on surgical adhesive tape and suture, future research may include all existing options for skin closure to provide a more inclusive comparison of the available techniques.

C64—Chronic Diseases & Conditions

Food Insecurity in the Development of Chronic Diseases

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Background: Over 48 million Americans, including 12 million children and 7 million seniors, live in homes with food insecurity, with limited access to adequate nutritious food. In a suburb of Chicago, Illinois, the nonprofit organization Loaves and Fishes provides hunger relief and emergency assistance to low income families. Approximately 72% of their clients have incomes at or below the Federal Poverty Level. Over 132,000 people are served yearly by Loaves and Fishes. Evidence indicates that food insecure adults are more likely to develop chronic illness, such as diabetes, hypertension, and heart disease. According to a 2014 US study published in *JAMA Internal Medicine*, difficulty in paying for food, drugs, and housing is associated with poor diabetes control. Recently, the CDC stated that over 86 million American have prediabetes, a precursor to type 2 diabetes. Prediabetes is treatable with education and lifestyle change programs. However, when unmet material needs, such as food and housing insecurity are associated with the risk of prediabetes, diabetes, or chronic illnesses, overall outcomes fare much worse. Understanding how food insecurity impacts the overall health of this adult population is the focus of this research study.

Research Question/Objective: To examine the correlation between food insecurity and chronic diseases in low income adults currently receiving food and assistance from Loaves and Fishes.

Methods: Adults currently receiving food assistance from Loaves and Fishes were asked to voluntarily complete a Nutrition and Health Questionnaire before and after voluntarily attending an educational session that focused on diabetes, hypertension, heart disease, and good nutrition. The survey was offered in both English and Spanish, with personal assistance by the principal investigator, if requested. All responses were completely anonymous; a 3-question identifier was used to match pre- and post-survey results. The survey contained both visual analog scale questions as well as free response. Survey questions included forced answer questions, 10-point Likert scale questions, and free response. To date, 203

pre-surveys have been completed; 5 of the surveys were incomplete and will be discarded from the database. After the initial surveys were completed, health care and nutritional information were offered to all participants. Currently, 70 adults have voluntarily attended an educational program to learn about chronic illness prevention, healthy eating, and positive lifestyle changes. Additional information sessions will be conducted to increase the number of clients receiving this important service. Post-surveys will be conducted to determine the potential impact of the educational sessions on food choices and lifestyle habits. This study was approved by Loaves and Fishes and the Midwestern University Institutional Review Board.

Data/Results: Of the 198 adults who fully completed the survey, 20% indicated that they had a chronic respiratory illness such as asthma, chronic bronchitis, emphysema, or COPD. Eighteen percent indicated they had been diagnosed with a chronic metabolic illness, including type 1 or type 2 diabetes. Thirty-six percent said they had a chronic cardiovascular disease, including high blood pressure, congestive heart failure, previous heart attack, arrhythmias, pacemaker, or atherosclerosis. Five percent reported having cancer. Twenty-eight percent indicated they had a musculoskeletal illness, such as arthritis or gout. Thirteen percent had neurological chronic illness such as stroke or seizures. Twenty-seven percent reported suffering from psychological chronic illness, including depression, anxiety, bipolar, or schizophrenia. The descriptive statistics and repeated measure will by analysis of variance (ANOVA) on all data. Type 2 diabetes was initially thought to be prevalent and the initial results have shown that the incidence of type 2 diabetes at 18% is indeed much higher than the CDC reported national average of 7% in the United States.

Conclusions/Clinical Implications: The objective of this study was to demonstrate a link between food insecurity and chronic illness to provide public health recommendations for improving health awareness and education to clients who receive food assistance. The majority of the 70 adults who attended the educational program were seriously concerned with their health and wanted to reduce health risks and their current medication. They had a strong desire to prevent chronic illness through healthier lifestyles and were actively trying to exercise, eat healthier, and make positive lifestyle changes in their homes as a result of their chronic illness. Additional conclusions will be presented after additional data results are complete. The study was limited to the clients who specifically came to Loaves and Fishes in DuPage County, Illinois, and limited in the number of participants by the voluntary nature of the survey. Future research opportunities could focus on the vulnerability of older adults with limited mobility living with chronic illness and food insecurity. In addition, future research could examine the correlation between chronic psychological illnesses and food insecurity. By empowering food pantry clients to make better food choices and lifestyle decisions, it will improve their overall health and reduce the medical burden of low income families. A combination of nutritional education and osteopathic approaches could encourage healthier lifestyles in low income patients living with chronic diseases, and lead to a positive development in patient outcome and patient quality of life.

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C65—Chronic Diseases & Conditions

The tNASP Protein, a Novel Diagnostic Biomarker for Prostate Cancer?

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Introduction: Nuclear auto-antigenic sperm protein (NASP) is a histone chaperone and a facilitator of chromatin assembly (Richardson et al, 2000). NASP is expressed as 2 splice variants: tNASP, specific to the testis and embryonal tissues, and sNASP, expressed in all somatic cells. Interestingly, we and others have shown that tNASP acts as a tumor-associated antigen, present in transformed cell lines and cancer cells in addition to its typical expression in testicular tissue (Ali-Fehmi et al, 2010; Alekseev et al, 2011). Moreover, tNASP is known to be an extremely auto-immunogenic protein. NASP has been reported as a serologic marker for ovarian cancer, which could be suitable for clinical testing in high-risk populations (Chatterjee et al, 2006). We suggest that while in cancer-free patients' tNASP is sequestered in an immunologically privileged compartment behind the blood-testis barrier, aberrant expression of tNASP protein in cancer tissues may induce a robust humoral immune response. With these suggestions in mind and considering the current need for reliable clinical markers of prostate cancer (PC), we have investigated the utility of tNASP as a novel diagnostic marker for PC. We hypothesized that cancer-specific expression of tNASP may serve as a tissue-based marker of PC and that auto-antibodies produced against cancer-expressed tNASP may be detected as a serum-based marker of the disease.

Goals: Goal 1 will validate the detection of anti-tNASP antibodies as serum-based biomarkers of prostate cancer. We will address the hypothesis that tNASP-specific antibodies will be present in the blood of prostate cancer patients but will remain absent in patients with benign prostate hyperplasia (BPH) or otherwise healthy men. Goal 2 will validate the utility of tNASP protein as a tissue-based diagnostic and prognostic biomarker of prostate cancer. We will address the hypothesis that expression of tNASP in prostate tissue samples obtained during needle biopsies can be used to diagnose prostate cancer and differentiate its prognosis from BPH.

Methods: Surgical specimens of prostate tissues and sera were received from Roswell Park Cancer Institute, Fox Chase Cancer Institute, and University of North Carolina at Chapel Hill School of Medicine. Total 10 samples from normal prostate (negative control), 24 samples from BPH, 34 samples from androgen-dependent prostate adenocarcinoma, and 16 castration recurrent prostate adenocarcinoma were obtained. Tissue microarrays and histological sections were immunohistochemically probed with an anti-NASP antibody (specific to both sNASP and tNASP), affinity purified anti-tNASP antibody, and hematoxylin-eosin. Sera from prostate cancer patients and healthy prostate patients (negative control) were tested for the presence of antibodies against tNASP using ELISA with a recombinant tNASP fragment as bait. Spearman rank correlation was used to analyze if levels of anti-tNASP antibody co-vary with the levels of prostate specific antigen (PSA).

Results: Expression of tNASP was detected in 76% of prostate specimens from patients with androgen-dependent prostate cancer (AD PC), 43.8% of castration recurrent prostate cancer (CR PC), 29.2% of benign prostatic hypertrophy (BPH), and 5.3% of normal prostates. Combined detection of sNASP and tNASP was 88.2% for AD PC, 48.7% for CR PC, 46.7% for BPH, and 7.1% for normal prostates. ELISA demonstrated markedly elevated concentrations of anti-tNASP antibodies in the sera of PC patients vs healthy prostate patients. Spearman's ρ was

0.656 (P=.0284) which demonstrates that levels of anti-tNASP antibody co-vary with the levels of PSA.

Conclusion: Detecting high level expression of tNASP in prostate tissue samples obtained during needle biopsies can be used for prostate cancer diagnostic and prognostic purposes. ELISA demonstrated markedly elevated concentrations of anti-tNASP antibodies in the sera of PC patients vs healthy patients. Presence of tNASP specific antibodies detected in the serum of prostate cancer patients together with high levels of PSA could be used as a screening method for early tumor detection in high-risk population groups. This study demonstrated the utility of tNASP as a tissue-based biomarker of PC, and the detection of anti-tNASP antibodies as a serum-based biomarker of PC.

Limitations: We did not have the opportunity to observe the development of patient's disease over time, as well as obtain a full set of clinical information for the patients sampled. These limitations did not allow us to draw any prognostic values from the set of data obtained.

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C67—Osteopathic Philosophy

Low Colorectal Screening Rate Contributes to the Symptomatic Late Stage Colorectal Cancer Incidence in Patients Received in Taipei Hospital

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Background: Colorectal cancer (CRC) is the second most common cause of cancer death in developed countries among men and the third most common among women. Interestingly, for the sixth consecutive year, CRC remains the most prevalent cancer amongst Taiwanese males and the second most prevalent amongst Taiwanese women (after breast cancer). According to the World Health Organization (WHO), prevention is the most cost-effective, long-term control strategy for cancer. Despite the development and promotion of CRC screening programs in Taiwan in the last 20 years, only 38.2% of the eligible population (people aged 50-74 years) have been screened for CRC in Taiwan compared with the 60-70% of the same age group in other countries with similar programs of similar lengths. To date, few studies have been published to address the popularity or acceptance of CRC screening by the Taiwanese people and its impact on the CRC prognosis. Osteopathic philosophy promotes the proper care of the body through health maintenance and pushes preventive screenings that detect and remove early signs of cancer. To help better understand the incidence and improve prognosis of CRC in Taiwan, this retrospective study is aimed at investigating the role of CRC screening in the frequency of CRC incidence and prognosis in patients at the Taipei Hospital, Ministry of Health and Welfare, in Taiwan. It is anticipated that results obtained from this study will help raise the awareness of and strengthen the CRC screening program.

Hypothesis: It is hypothesized that low adherence rate of colorectal cancer screenings contributes to the symptomatic CRC incidence and a higher ratio of late-stage to early-stage colorectal cancers in Taipei Hospital, Ministry of Health and Welfare.

Methods: Data were collected from 76 patients with diagnosed colorectal cancer during the years 2013-2015 at the Taipei Hospital, Ministry of Health and Welfare in Taipei, Taiwan. Data were obtained by reviewing charts and admissions files of patients diagnosed with colorectal cancer acquired from the Patient Records Office at the Taipei Hospital, Ministry of Health and Welfare. The data collected include the tumor/node/metastasis (TNM)

staging of the cancers, cancer location, colorectal screening history, medical history, admission date, diagnosis date, age, gender, chief symptomatic complaint, and duration of cancer symptoms before diagnosis. No other identifying information was taken from these files during this period. Data were analyzed using linear regression analysis.

Results: Out of the 76 cases of confirmed colorectal cancers, 70 patients were above the age cutoff (age ≥50 years) for CRC screening recommendation. Of the 70 patients, only 8.6% of patients (n=6) were diagnosed through regular immunological fecal occult blood test (iFOBT) CRC screenings. The other 64 patients were diagnosed during patient visits due to CRC-related symptoms (n=57), found during work-ups of other non-related problems (n=3), or had no recorded method of diagnosis (n=4). Patients who were symptomatic at the time of diagnosis typically had later stage cancers (Stage 2 or higher) than those who had been screened through the iFOBT test (linear regression analysis, F=14.08, *P*=.0004, R^2=0.18513). Of those who were symptomatic and had TNM and metastasis information available (n=45), 57.8% of patients had CRC that had spread to regional lymph nodes or distant organ metastatic sites at the time of diagnosis.

Conclusion: This study suggests that a majority of colorectal cancer patients do not go through regular CRC screening and that most CRC cases are caught during advanced, symptomatic stages at the Taipei Hospital. The lack of screening could be explained by time, financial, and work constraints that often affect the lower socioeconomic and industrial occupation population that the hospital typically serves. Overall, a focus of Taiwan's CRC screening program is to improve participation in its screening program. The strategy should include evaluating main modality of screenings used (iFOBT in Taiwan vs total colonoscopy of the United States and Europe), frequency of screenings (biennial in Taiwan vs annual of the United States and Europe), cultural sensitivities (fear of cancer diagnoses and "contagiousness" of cancer in Taiwan), and educational barriers (lack of knowledge about typical CRC symptoms) that may affect a person's choice to participate in a CRC screening in Taiwan.

C68—Chronic Diseases & Conditions

Effects of Lifestyle Factors on the Prevalence of Diabetes Mellitus and Hypertension in Southwestern Virginia Coal Counties

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Introduction: Diabetes mellitus and heart diseases are ranked number 7 and number 1 respectively in the top 10 causes of death in the United States. The prevalence of both diabetes mellitus and hypertension, a selected heart disease, are higher in southwestern Virginia than in other regions in Virginia. Others have reported that living in coal producing environments contributes to higher rates of chronic diseases. Buchanan and Tazewell counties are coal producing counties in southwest Virginia. Evaluation of chronic disease prevalence rates and risk factors are necessary to reduce the prevalence of these deadly chronic diseases in these counties.

Objective: This study was done to establish the prevalence of diabetes mellitus and hypertension in Buchanan and Tazewell County, Virginia, and to evaluate the lifestyle factors of those with and without the diseases. A secondary outcome was also to determine the prevalence of diabetes mellitus and hypertension in the coal working community of these 2 counties. A retrospective cohort study was used to complete the study objectives because the study was looking back at a patient's past medical

history or lifestyle. These counties in Southwestern Virginia were chosen because of their coal production and because they were the counties that we were able to obtain data from.

Methods: An IRB protocol was approved from a larger, longitudinal VCOM study, allowing for the use of de-identified electronic medical records (EMR) from selected hospitals. EMR's were selected using systematic randomization from hospital admissions in 2011/2012, recorded in the survey software Qualtrics, LLC (2014), and cleaned and analyzed using SPSS, V.22.0. Records (n=1339) were obtained; after cleaning, 819 records were available for statistical analysis. Records that were eliminated were records that had either missing data or records that had answered the questions with "no data available."

Data Analysis: χ^2 analysis was performed on various lifestyle factors, such as physical activity frequency, tobacco use, and alcohol use on diabetes mellitus and hypertension. Light physical activity was defined as walking on a level surface at 2.5 to 3 mph, garage work, electrical trades, carpentry, restaurant trades, house cleaning, child care, golf, sailing, and table tennis. Moderate physical activity frequency was walking 3.5 to 4 mph, weeding and hoeing, carrying a load, cycling, skiing, tennis, and dancing. Heavy physical activity frequency was walking with a load uphill, tree felling, heavy manual digging, basketball, climbing, football, soccer, and running. Tobacco use and alcohol use were divided into current use, former use, and never used.

Results: The prevalence of diabetes mellitus and hypertension in our study population was 26.5% and 41.5%, respectively. After χ^2 analysis, there was a significant difference between tobacco use in individuals with and without hypertension, with a P value of .012. There was no significant difference between tobacco use in diabetics and non-diabetics, alcohol use in diabetics and non-diabetics, physical activity frequency in diabetics and non-diabetics, alcohol use in individuals with or without hypertension, and physical activity frequency in individuals with or without hypertension, with *P* values of .255, .061, .543, .735, and .430, respectively.

Conclusion: The study reported that the association between tobacco use and hypertension was significant, which was consistent with previous research and expectations. For the other diabetes and hypertension associations that were reported, there were no significant associations, which contradicted previous literature and expectations. Various study limitations may have influenced the findings. These limitations were a small sample size, self-reported data, and additional confounding lifestyle factors (diet, access to care, etc). Future studies should expand the research to explore additional lifestyle factors, such as gender, age, etc. Also, future studies should increase the study sample size by adding more EMR data and/or more hospitals to the study. Our results provide preliminary data in an ongoing study to reduce the prevalence of chronic diseases in Southwest Virginia by investigating the effects of various lifestyle factors. This information may also help these populations reach some of the goals set by Healthy People 2020, such as increasing the proportion of physician office visits that include counseling or education related to physical activity and increasing the proportion of adults who engage in aerobic physical activity of at least moderate intensity for at least 150 minutes per week, or 75 minutes per week.

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C69—Chronic Diseases & Conditions

Cancer Death Rates in Coal Production Counties in Southwest Virginia Evaluated on County and Individual Levels

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Background: The health disparities in Central Appalachian have persisted over time at elevated rates compared with other regions. Since 1990, rates of cancer deaths have improved, with declines better in men than in women and better in Southside and comparison counties than in counties in southwest Virginia (VA). Previous reports have implicated coal production as the primary causal factor in elevated chronic health conditions. Counties in southwestern VA that produce coal have not met Healthy People 2020 lifestyle goals associated with improvements in cancers like other counties in VA. However, the majority of individuals with the most direct environmental contact with coal production are miners, mostly men.

Question: The primary objective of this study was to provide descriptive data on cancer and lung cancer death trends in coal production counties in VA from 2 data sources: (1) longitudinal data aggregated by county over 50 years and (2) from individual medical record diagnoses from hospital admissions in 2012.

Methods: VA Department of Health (VDH) mortality records (n=755,414) were obtained for years 1960-2012 (n=5213). Data extracted for each county in 2 health districts in southwest VA were reported for years 2000-2010 and descriptive statistics provided for age, gender, education, place of residence, and place of death. Data extracted from individual electronic medical records (EMR) were obtained from participating hospital admissions for the year 2012. Coal production was obtained from the US Energy Information Agency for 2000-2010.

Results: Preliminary findings (n=878) were reported in coal miners and those with other occupations, confirming cancer diagnosis by International Classification of Diseases (ICD) codes, clinical and laboratory tests, and physician's notes. For EMR preliminary data by occupation were used to categorize highest coal exposure individuals, 155 were coal miners, 351 had other occupations, and for 372 information was not reported or missing, thus, excluded from further analysis. Family histories were recorded indicating that family members in their first and second generations also had chronic health conditions.

Analysis: From VDH information lung cancer was the most prevalent diagnosis (34%) of all cancers, 4 times greater than breast cancer. Most records (56%) indicated place of death was the residence, with the counties of Tazewell and Wise most frequently cited. The major of reported deaths from 1999-2012 were among seniors with low levels of education. Cancer diagnosis did not differ by occupation (data shown in previous reports). EMR data to confirm diagnosis by codes, laboratory tests results, clinical examinations, and physician's impressions were consistent for both occupation groups. From VDH data the percentage of all chronic diseases reported due to all types of cancers were distributed throughout the 2 health districts. The most prevalent diagnoses in the 7 counties reporting rates of cancers of 3-6% were identified graphically in 15 zip code areas as the place of residence on mortality records.

Conclusion: Cancers, particularly lung cancers, remain a health concern in coal dependent communities. However, the higher rates in women

(VDH data) and no differences detected by occupation between coal miners and other occupations (EMR data) contradict popular beliefs and previous reports associating coal mining with higher rates of cancers. Thus, further study with a more robust sample size is warranted. Virginia County Health Rankings for targeted counties in 2010 and 2013 were ranked 116 and 123 out of 132 counties, respectively. This information coincides with prior reports that personal behavior factors should be studied further. Likewise, the regions lag behind other counties achieving Healthy People 2020 goals for cancer prevention and treatment. Additional inquiry into individual level data will help identify hospital admission patients at risk for cancers in SW VA and study findings will be available from EMR to support VDH data to guide health education programs to improve healthful behaviors associated with cancer.

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Health Services

HS2—Musculoskeletal Injuries and Prevention

Primary vs Conversion Total Hip Arthroplasty: Differences That Affect Clinical Performance Measurements and Reimbursement

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Introduction: The demand and cost of joint replacement surgery continues to grow at a rate that will soon overwhelm hospitals, insurers, and patients. Therefore, total hip arthroplasty (THA) is a prototype for cost control plans that utilize clinical performance measurements to reimburse defined episodes of care. Regulatory and reimbursement agencies use universal codes that often fail to convey essential clinical discrepancies that can lead to inaccurate performance measurements and greater cost burden on the health care system. Although conversion THA is a more complex procedure than primary THA, current ICD-9 and ICD-10 codes classify both primary THA and conversion THA under ICD-CM 81.51. The purpose of this study is to confirm clinical differences between primary and conversion THA and to compare the costs among the inpatient episode of care for each procedure.

Methods: In this retrospective cohort, we identified a total of 1574 primary THA and 41 conversion THA cases from 2009 to 2013. Data collected from medical records included: demographics, comorbidities, transfusion data, operative data, and cost data for the inpatient episode of care for each case. An episode of care was defined as starting on the day of the procedure and ending on the day of discharge. Cost data included direct costs, indirect costs, and total charges associated with the orthopedic procedure and perioperative treatment within the episode of care.

Results: The results confirmed that conversion THA is a more complex, labor intensive, and costly procedure than primary THA. Intraoperative blood transfusion was required in 51.22% (21/41) of conversion THA cases compared with only 7.56% (119/1574) of primary THA cases ($P<.001$). The average operative time for conversion THA was 210.5 ±29.4 minutes compared with 128.8 ±18.9 minutes for primary THA ($P<.001$). Patients who underwent conversion THA experienced a greater median length of stay in the hospital than patients who underwent primary THA (5 days [3, 5.5] vs 3 days [3, 4], $P<.001$). The average direct cost of a conversion THA was $18,409.50 ±6,730.04, and the average direct cost of a primary THA was $12,913.40 ±4,829.29 ($P<.001$). Indirect costs associated with the episode of care also averaged $9,679.34 ±3,096.41 for conversion THA and $6,542.15 ±2,672.45 for primary THA ($P<.001$). The combined total charges accrued during the episode of care for each conversion THA averaged $98,895.46 ±31,506.30 and $69,004.55 ±20,205.50 for each primary THA.

Conclusions: The clinical and cost disparities for each procedure confirm that conversion THA and primary THA need separate and unique coding classifications, performance measurement criteria, and reimbursement rates. Procedures like joint replacement undergoing experimentation with payment and quality of care models require further research to ensure accurate evaluations and maximal cost effectiveness.

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HS3—Osteopathic Philosophy

Characteristics of Comorbidities in Taiwanese Patients Who Are Infected With Multi-Drug Resistant Tuberculosis

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Introduction: According to the World Health Organization (WHO), tuberculosis (TB) is still one of the world's deadliest communicable diseases. The spread of drug-resistant TB is a major public health problem with potential global threats. Drug resistance is largely associated with improper use of antibiotics, such as administration of improper treatment regimens and failure to ensure that patients complete the whole course of treatment. Multi-drug resistant tuberculosis (MDRTB), defined by resistance to 2 of the most commonly used drugs (isoniazid and rifampin) used in the first line treatment regimen, counts 3.5% of new TB cases globally. Treatment of MDRTB is complex, requiring the use of second-line agents for 2 years or longer and involving daily injections for 6 months. Moreover, many second-line drugs have severe side effects. Patients with comorbidities such as hypertension, diabetes mellitus, and cancer further complicate the management of MDRTB as physicians need to evaluate drug interactions and other toxicities for the patient. Indeed, studies have shown that MDRTB patients with comorbidity have poorer treatment outcomes. There is thus a need to raise awareness for the development of favorable treatment regimens and patient outcomes among comorbid patients infected with MDRTB. TB is the most serious communicable disease in Taiwan. To help establish effective treatment regimens for MDRTB with comorbidities, this study is aimed at evaluating clinical characteristics in MDRTB patients received at Taipei Hospital, Ministry of Health and Welfare, Taiwan.

Methods: As a retrospective study, data for 26 patients with MDRTB from the years 2009 to 2014 were gathered from the TIHTC Taipei Hospital. The independent variables in the data included age, drug treatment regimen, drug sensitivities, and type as well as number of comorbidities. The drug sensitivity report helped confirm MDRTB status as well as provide reasoning for the varying drug regimen given to the patients. Statistical analysis was performed on the variables of age and the various comorbidities with the MDRTB patients.

Results: The sample (N=26) consisted of 16 males (61.5%) and 10 females (38.5%) and the mean age (±SD) of the patients with MDRTB was 58.3 ± 19.4 years. Patients with at least 1 comorbidity was 38.5% (N=10) and at least 2 comorbidities was 25.9% (N=7). 68.8% (N=11) of the males and 20.0% (N=2) of the females had at least 1 comorbidity in addition to the MDRTB infection. There were higher percentages of MDRTB patients presenting with hypertension, 23.1% (N=6), and cancer, 15.4% (N=4). Other comorbidities included diabetes mellitus, 11.5% (N=3), hepatitis B, 7.7% (N=2), anemia, 7.7% (N=2), and miscellaneous-grouped diseases, 38.5% (N=10). Out of the 10 patients with comorbidities, hypertension counts 60% (N=6).

Conclusion: The WHO reports that in 2013, there were 97,000 patients beginning treatment for MDRTB, a 3-fold increase compared with 2009. This illustrates the importance of treating MDRTB and improving patient outcomes for the overall progress of quality of care. To our best knowledge, there has been no published study addressing comorbidities in MDRTB patients in Taiwan. This study suggests that patients infected with MDRTB and were treated in Taipei Hospital tend to have a higher probability of having comorbidities (38.5%), especially in males (68.8%) over females (20.0%). With the average age of MDRTB-infected patients at 58.3, it is reasonable to assume that old age and the natural deterioration of the body's immune system causes more comorbidities. Among the MDRTB patients with comorbidities, hypertension counts 60% (6 out of 10), suggesting that hypertension is likely to be the comorbidity in MDRTB patients received at Taipei Hospital. Hypertension is a worldwide epidemic with a rising prevalence, and some studies have examined pulmonary hypertension in active TB infection and also in posttreatment symptoms. Many anti-hypertension drugs are associated with serious toxicities, which can complicate the management of MDRTB. It is thus necessary to establish favorable treatment regimens for MDRTB patients with hypertension.

♦ Abstract that won first or second place in the 2014 SOMA Student Poster Competition.

♦HS4—Chronic Diseases & Conditions

Association Between Method of Delivery and Exclusively Breastfeeding at Hospital Discharge

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Context: Studies have shown that exclusively breastfeeding at hospital discharge is strongly associated with successfully breastfeeding long-term. It is recommended that mothers exclusively breastfeed for the first 6 months of life. Method of delivery (MOD) has been identified as one of the barriers that may hinder breastfeeding practices. However, research examining the association between MOD and exclusive breastfeeding at hospital discharge is lacking.

Methods: We conducted a cross-sectional analysis including 1494 women who participated in the population-based Infant Feeding Practices Study II conducted by the CDC between May 2005 and June 2007. The main outcome of interest was exclusive breastfeeding at hospital discharge. Logistic regressions were utilized to estimate the OR and the 95%

CI of the association between MOD and exclusive breastfeeding at hospital discharge, after adjusting for potential confounding variables.

Results: The crude prevalence of vaginal delivery and cesarean section was 74.8% and 25.2%, respectively. The prevalence of exclusive breastfeeding at hospital discharge was 70.6% among women who gave birth by cesarean section compared with 80.0% of women who gave birth vaginally (P=.001). After adjusting for sociodemographic, behavioral, and anthropometric factors, the odds of exclusive breastfeeding at hospital discharge were lower among women who gave birth by cesarean section compared with women who gave birth vaginally (OR,, 0.41; 95% CI, 0.24-0.71).

Conclusion: Women who give birth by cesarean may require additional attention and training during their stay in the hospital to improve rates of exclusively breastfeeding at discharge. It is important that health care providers address MOD when educating patients on exclusively breastfeeding to maximize the potential for longer-term breastfeeding success.

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HS5—Osteopathic Philosophy

Association Between WIC Enrollment and Exclusive Breastfeeding at 3 Months Postpartum Among Low-Income Mothers

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Research Question(s)/Hypotheses: Existing literature suggests participation in the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) in the prenatal and postnatal periods is associated with lower rates of breastfeeding among WIC-eligible mothers. However, minimal research has been published on how the degree of exposure to the WIC program influences exclusive breastfeeding. The purpose of this study was to examine the association between WIC exposure and exclusive breastfeeding at 3 months postpartum.

Methods: We conducted a secondary data analysis using 784 low-income women who participated in the longitudinal population-based Infant Feeding Practices Study II (IFPS II) between May 2005 and June 2007. The main outcome of interest was exclusive breastfeeding at 3 months postpartum.

Data Analysis: Logistic regression analysis was used to estimate ORs and 95% CIs for exclusive breastfeeding relative to WIC enrollment status, controlling for the confounding effects of other maternal characteristics. We further conducted a sub-group analysis among those exposed to WIC prenatally to examine the association between receipt of information about infant feeding from WIC and exclusive breastfeeding at 3 months postpartum.

Results: The crude prevalence of exclusive breastfeeding at 3 months postpartum was 18.1% of women enrolled in WIC and 41.1% of WIC-eligible non-participants (<0.0001). After adjusting for sociodemographic, behavioral, and anthropometric factors, the odds of exclusive breastfeeding at 3 months were lower for women enrolled in WIC (OR, 0.57; 95% CI, 0.37-0.88) when compared with women not in the program. In the subgroup analysis, receipt of information about feeding infants from WIC during the prenatal period was not significantly associated exclusive breastfeeding at 3 months.

Conclusion: Additional improvements in educational promotion of exclusive breastfeeding for at least 3 months are necessary among WIC participants. Furthermore, osteopathic physicians and other health care providers caring for low income WIC enrolled women should encourage and educate women about the importance of exclusive breastfeeding in at least the first 3 months.

HS7—Chronic Diseases & Conditions

Mini-Doc Program: Community-Oriented Asthma Education at Kamaile Academy in Waianae, Hawaii

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Purpose: There is an increased incidence of asthma in the Native Hawaiian population on the Waianae coast of Oahu. The objective of this interventional program evaluation was to determine whether providing asthma education to elementary students in the classroom setting would effectively improve health literacy regarding asthma within the Waianae community.

Methods: The "Mini-Doc" program is a multi-disciplinary educational intervention that provides information on healthy living to elementary students in an underprivileged community. Asthma lessons were given as part of the "Mini-Doc" program at Kamaile Academy. To assess students' the baseline knowledge of asthma, third and fourth graders (218 students) were given a multiple choice pre-assessment survey. Guidelines from the American Lung Association and Centers for Disease Control were used to create assessment surveys and lesson plans. Following the lessons, teachers administered post-test surveys with the same pre-test survey questions and 2 additional qualitative questions. Results were compiled to evaluate the efficacy of the program.

Project outcome analysis: The pre-test survey response rate was 82.6% (n=180) and post-test response rate was 43.6% (n=95). There was an average increase of 9.5% (SD=0.03) in correct responses from pre-test to post-test surveys. According to the postsurvey, 96% of subjects enjoyed learning about asthma and 4% did not. 66% of the students indicated that they shared what they learned about asthma with their friends or family.

Conclusion: Our results indicate that there was increase in asthma knowledge and that the overwhelming majority of students enjoyed learning about asthma. Additionally, most students shared their knowledge with family or friends. We predict that increased knowledge and awareness of asthma in the community can decrease asthma-related visits to the Waianae Coast Comprehensive Health Center. Future research will need to address the long-term effect of health education in elementary schools. This model can be replicated at other community health centers by partnering with local schools and offering to provide health-related lessons to students.

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HS9—Chronic Diseases & Conditions

Preparation for Medical Review of Hospital Admission Records to Obtain Individual Level Data to Determine Chronic Disease Prevalence Rates in Rural Areas of Virginia

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Background: Medical literature on diagnosis generally reports on sensitivity, specificity, predictive values and likelihood ratios addressing the validity of a test and not often on the interpretation agreement. "Nosologists," trained medical record reviewers, are available in Virginia but only at the state department of health.

Questions: The objective was to monitor data reporting consistency, preventing "drift," and assuring the highest quality data outcomes in a multi-facility, multi-rater pilot study comparison of medical record reporting of diagnoses chronic conditions and patient information. A secondary objective was to pretest functionality and effectiveness of a new and novel form for electronic submission of medical record data for analysis.

Methods: Sample medical records (n=20) were received from a privately owned clinic. A team of reviewers (n=10) with varying levels of experience and expertise completed reviews anonymously. Data were used internally only to evaluate inter-rater reliability, to highlight specific data extraction items needed/not needed, form functionality, and submission completeness.

Data Analysis: The process was evaluated using the Kappa statistic (a computed score from 0-1), a widely used tool for evaluating subjective observations. A kappa of 1 reflected almost perfect agreement and a kappa of 0 reflected agreement equivalent to chance.

Results: The pilot project outcomes were invaluable and allowed for refinement of all aspects of the process and secondary benefits. The initial survey form created was honed through numerous renditions as a result of the pilot testing. The process also allowed for estimating time to complete reviews per patient record to assist with estimates of how many records could be done per day and estimate budget expenses to meet the desired number of records to achieve statistical power (n=1600). Kappa statistics with 95% CIs were computed and paired to a medical professional review. The findings showed collectors' interpretations varied and were not always predictable among levels of experience or areas of expertise. By virtue of a pilot project inconsistencies provided great insight into the direction and specificity of needed training prior to beginning an actual hospital medical record review. Miscalculations, entry errors, omissions, duplicate entries, and other typical technical errors were encountered. Revealed were issues related to ICD code versions and conditions not initially of direct interest but possibly of influence in future interventions. Also noted was a tendency for reviewers to complete sections of particular interest to their expertise in greater detail. Opportunities to confirm the importance of patient medical record confidentiality were maximized. The pilot project allowed for staged inconsistencies for training purposes to express the subjective, variable, and error-prone process.

Conclusion: The benefits of a pilot project allowed for troubleshooting the process and training before initiating a funded, peer-reviewed study of chronic disease prevalence from de-identified and protected individual medical records.

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