2014 SOMA 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. Student poster competition participants submitted their abstracts through either the AOA's Council on Research or the Student Osteopathic Medical Association (SOMA). Abstracts submitted through the AOA's Council on Research were published in the August 2014 issue of *The Journal of the American Osteopathic Association* and are available online at http://www.jaoa.org/content/114/8/e84.full. Abstracts submitted through SOMA appear on the following pages.

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

This year's AOA Research Conference took place in Seattle, Washington, from Saturday, October 25, to Monday, October 27, during the AOA's 2014 Osteopathic Medical Conference & Exposition. On October 26, 2014, judges met with the student presenters to discuss and review their research. Judges identified 3 first-place winners, who received $500 each, and 6 second-place winners, who received $250 each. The 9 winners are as follows:

First Prize

- Lyudmila Burina, OMS II, from the New York Institute of Technology College of Osteopathic Medicine for abstract S29, "Effects of Resveratrol on Mitochondrial Mitophagy in Doxorubicin Treated Cardiomyocytes" (see page e147)
- Theresa Apoznanski, OMS IV, from the New York Institute of Technology College of Osteopathic Medicine for abstract S34, "Comparison of Multiple Balance Measures as Predictors of Falls in Parkinson Disease: A Pilot Study" (see page e137)
- Shirley Kim, OMS II, from the Midwestern University/Arizona College of Osteopathic Medicine for abstract S21, "A Novel Lipid-Based Nanoemulsion Formulation to Overcome Paclitaxel Resistance in Ovarian Carcinoma Cells" (see page e143)

Second Prize

- Sarah VanDine, OMS IV, from the New York Institute of Technology College of Osteopathic Medicine for abstract S17, "Thyroid Hormone Disruption Effects Lamination of the Neocortex but Not the Cerebellum in a Model of Developmental Hypothyroidism and Hypothyroxinemia" (see page e141)
- Samantha Seitter, OMS IV, from the New York Institute of Technology College of Osteopathic Medicine for abstract S27, "Effect of Triiodo-L-Thyronine Treatment and Reperfusion on Postmyocardial Infarction Recovery" (see page e146)
- Alyssa Imperatore, OMS II, from the Kansas City University of Medicine and Biosciences College of Osteopathic Medicine for abstract S23, "TGFβ Pathway Inhibition Enhances Vascular Network Formation by Human Endothelial Cells Pretreated With Doxorubicin" (see page e143)
- Casey Sigerson, OMS II, from the Midwestern University/Chicago College of Osteopathic Medicine for abstract S54, "Submicron Topographical Patterns Enhance Peripheral Nerve Regrowth Ex Vivo" (see page e159)

- Alex Wertheimer, OMS II, from the Western University of Health Sciences College of Osteopathic Medicine of the Pacific for abstract ME5, "Central Column Knee Classification: A Novel Approach to Augment Specific Knee Structures of Clinical Relevance" (*J Am Osteopath Assoc*. 2014;114[8]:e114-e115)
- Timothy Bikman, OMS III, from the West Virginia School of Osteopathic Medicine for abstract S3, "Experiential Learning: An Irreplaceable Tool in Osteopathic Student Education" (see page e161)

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. Neither the AOA Research Council nor the *JAOA* assume responsibility for the abstracts' content. The winning abstracts are noted with "♦". (doi:10.7556/jaoa.2014.181)

AOA Research Fellowship

F1

Investigating the Role of *Lactobacillus reuteri* in Bone Health

Darin Quach, DO; Fraser Collins, PhD; Regina Irwin, MS; Laura Schaefer, PhD; Nara Parameswaran, PhD; Laura McCabe, PhD; Robert Britton, PhD

Michigan State University College of Osteopathic Medicine, East Lansing

Introduction: Osteoporosis and osteopenia are estimated to affect more than 200 million people worldwide. All individuals can be affected, but the largest population affected is postmenopausal women. Current therapies that prevent bone loss have adverse effects, so the development of novel treatments is crucial. It is observed in human and animal studies that increased inflammatory cytokines contribute to the development of osteoporosis caused by estrogen deficiency. Inflammatory cytokines increase bone resorption by increasing osteoclast (OC) formation and differentiation, ultimately leading to net bone loss. We previously showed that the probiotic *Lactobacillus reuteri* prevented osteoporosis in estrogen-deficient mice, and this finding correlated with decreased osteoclasts.

Hypothesis: *Lactobacillus reuteri* affects genes related to OC differentiation and function; gut microbial communities play a role in bone health; and *L reuteri* affects these communities after estrogen deficiency prior to bone loss.

Objective: To investigate host mechanisms targeted by *L reuteri* to inhibit OC formation.

Methods: Estrogen-deficient mice, generated by surgically removing their ovaries (OVX), were treated with *L reuteri* for 30 days. *Lactobacillus reuteri* was cultured in MRS broth at 37°C for 16 hours and was given to mice orally or with drinking water. At the end of treatment, parameters of bone health, osteoclast function, and fecal microbial communities were measured to assess *L reuteri* treatment effects. Bone density was measured by computed tomography (CT). In vitro assays were performed by differentiating a cell line into OCs and treating them with *L reuteri*. RNA was collected from all experiments, and quantitative polymerase chain reaction was used for gene expression analysis. 16s RNA analysis was performed to characterize microbial communities from intestinal and fecal samples.

Results: *Lactobacillus reuteri* downregulates genes related to OC differentiation and function. Estrogen deficiency alters gut microbial communities, and *L reuteri* treatment alters them again. Treatment with *L reuteri* inhibits bone resorption.

Conclusion: Results demonstrated that *L reuteri* is effective in preventing osteoporosis in OVX mice, potentially owing to a decrease in osteoclastogenesis. Current studies focus on how this phenomenon is mediated and may ultimately lead to the development of a novel, safe, and cost-effective therapeutic for patients with osteoporosis.

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Osteopathic Manipulative Medicine/Osteopathic Principles and Practice

S14

Electrophysiological Assessment of Tender Zones in Upper Trapezius—Determining the Optimal Electrode Position and Rate of Contraction

Raksha Hemanth, OMS I[1]; Erica Errigo[1]; Maizie Faber, BS[2]; Annette Pantall, PhD[3]

[1]Michigan State University College of Osteopathic Medicine (MSUCOM); [2]Michigan State University; [3]Department of Osteopathic Manipulative Medicine, MSUCOM, East Lansing

Introduction: Many patients attend osteopathic clinics for neck-pain. Tender zones (TZs) and tissue changes in neck and shoulder muscles are frequently associated with neck pain. Two types of palpatory TZs associated with pain in the upper trapezius (UT) are Dr Jones' tender point and Dr Travell's myofascial trigger point. The diagnosis of TZs involves subjective tissue palpation and provoking a pain response.

Objective: To investigate objective diagnostic methods for TZs and assess their relationship to chronic pain by spectral and amplitude analysis by electromyography (EMG) of the UT during a range of shoulder movements.

Methods: The EMG parameters depend on many factors, including electrode placement and force and speed of muscle contraction, which were investigated before commencing the main study. Six EMG surface electrodes were placed across the UT in 5 participants: P1 at C3 spinal level, P2 at C5 spinal level, P3-6 supraclavicularly from medial to lateral. Shoulder elevation was recorded with an electrogoniometer. Participants initially performed maximum voluntary contractions of the UT through shoulder elevation against resistance, with a load cell recording force. Isometric ramp contractions of the UT were performed with 20% increments of maximum voluntary contractions. Participants then elevated and depressed their shoulders bilaterally for a period of 1 minute at 0.5, 0.25, 0.167, and 0.125 Hz.

Results: The EMG data were normalized to maximum voluntary contractions, and mean frequency was determined through wavelet analysis. For ramp contractions, there were significant differences between force bins for intensity and frequency. In most participants, frequency was significantly different between force bins 1 to 2 and 3 to 10, whereas for intensity there were significant differences between all force bins. Correlation between intensity and force was high (r^2=0.79) across all ramp data and low between force and frequency (r^2=0.34). Position had a significant effect on frequency. For isokinetic contractions, the highest correlation for frequency/angular elevation was for P4 (r^2=0.45) and P6 (r^2=0.42) and intensity/angular elevation for P4 (r^2=0.60) and P6 (r^2=0.61) at a rate of 0.125 Hz. P3-6 had the highest EMG signal to noise ratio.

Conclusion: These data have identified the optimal positions for electrodes on the UT and the optimal rate of cyclic movement necessary for a study of participants with neck-pain, which will enhance the understanding of the neurophysiologic mechanisms responsible for the development of TZs in the UT.

Clinical Studies

S1

Is Negative Pressure Wound Therapy a Prudent "Bridge to Reconstruction" for Poststernotomy Mediastinitis?

Bradley White, OMS III; Cassandra J. Beck, BS, OMS III; David B. Johnson, BS, OMS III; Stephanie A. Luster, MS, OMS III; Stephen L. Harlin, MD

Lake Erie College of Osteopathic Medicine–Bradenton, Florida

Introduction: Poststernotomy mediastinitis (PSM) is a life-threatening complication after open-heart surgery, and its treatment is multistaged. Conventional treatment involves mediastinal debridement,

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open drainage, and reconstruction with vascularized soft tissue flaps such as omentum or pectoral muscle. Recently, the application of a negative-pressure wound therapy (NPWT) device to the postdebridement mediastinum has been proposed as a "bridge to reconstruction."

Hypothesis: Negative pressure wound therapy is efficacious in preparing sternal wounds for flap reconstruction.

Methods: Of 434 reports, 14 studies met strict inclusion criteria and described patients with a diagnosis of PSM who underwent NPWT followed by omental and/or myocutaneous flap reconstruction. Eligible studies were assessed for length of stay, mortality, manufacturer involvement, and methodologic rigor.

Results: Among a total of 429 patients, median length of stay was 29 days (±16). There were 41 deaths in this inpatient group, a mortality rate of 10%. Seventy-one percent of the reports were nonrandomized. Five studies (36%) accurately accounted for baseline differences between severity, and 14% failed to report diagnostic criteria. In all but 1 study, outcomes, including length of stay and mortality, were reported. Only 1 study reported follow-up results. Five studies (36%) declared no conflict of interest, and the remainder failed to make a statement regarding manufacturer involvement. In this analysis of quality, 8 (48%) of the studies were of very low to low quality. In 5 studies (36%), the evidence was of moderate quality. One study was of high quality.

Conclusion: Ample support for the routine use of NPWT as a "bridge to reconstruction" was not found. Serious complications related to the use of NPWT, including right ventricular rupture, atrial fibrillation, respiratory arrest, recurrent infection when used for greater than 21 days, and retained sponge were reported in this group of studies. Rigorous evaluative studies that assess the true effectiveness of NPWT as a "bridge to reconstruction" must precede its adoption.

S2

A Noninvasive Study of the Correlation Between Digit Length Ratios and the Risk Factors Associated With Metabolic Syndrome

Matthew J. White, OMS IV[1]; Carolyn Komar, PhD[2]; Lance Ridpath, MS, OMS IV[3]

[1]West Virginia School of Osteopathic Medicine (WVSOM), Bridgeport; [2]Department of Biomedical Sciences, WVSOM, Lewisburg; [3]WVSOM, Lewisburg

Introduction: Metabolic syndrome refers to a group of risk factors that increase a person's chance of developing cardiovascular disease and/or type 2 diabetes mellitus. The Adult Treatment Panel III states that 33 or more of the following risk factors are required to diagnose metabolic syndrome: waist circumference (male, ≥40 in; female, ≥35 in), triglycerides (≥150 mg/dL), high density lipoprotein (HDL) cholesterol (male, <40 mg/dL; female, <50 mg/dL), blood pressure (>130/85 mm Hg), and fasting glucose (>100 mg/dL). Hypertension and insulin resistance, 2 factors associated with metabolic syndrome, are associated with high levels of prenatal testosterone exposure. Testosterone exposure in utero is also related to the length ratio of the second and fourth digits of the hand (2D:4D). Significant correlations between the 2D:4D and the risk factors for metabolic syndrome would promote digit measurement as a noninvasive tool for assessing a patient's metabolic risk factors.

Hypothesis: The 2D:4D correlates with known risk factors for developing metabolic syndrome, and it may be a noninvasive screening tool for such risk factors.

Methods: Forty-four adult patients were recruited from a community clinic. The lengths of the second and fourth digits on both hands were measured with a vernier caliper. The 2D:4D for each hand was calculated and correlated with each individual's body mass index (BMI), waist circumference, blood pressure, triglycerides, HDL, and fasting glucose levels.

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The data were analyzed by logistic regression to predict the probability of the 2D:4D correlating with a patient's risk for metabolic syndrome. Log transformation of the continuous variable (2D:4D) was conducted before the analysis to normalize the distribution of measurements.

Results: Significant correlations were found between the 2D:4D of the right hand, triglyceride levels, and BMI. With a 95% CI, a high right hand 2D:4D indicated that triglycerides were in the risk range for metabolic syndrome. A 2D:4D of 1 or greater suggested a triglyceride level of ≥150 mg/dL. The Spearman rank correlation coefficients also showed a positive relationship between the right hand 2D:4D and BMI.

Conclusion: The direct relationship between the 2D:4D of the right hand, triglyceride levels, and BMI supports the use of this digit ratio as a noninvasive screening tool for metabolic syndrome. This tool may increase the number of patients willing to be screened, enabling earlier detection and initiation of lifestyle modifications for those at risk.

S4

Effects of General Anesthesia on the Blood-Brain Barrier: A Primary Role in Postsurgical Delirium

Eric Goldwaser, OMS III[1]; Nimish Acharya, PhD, OMS IV[2]; George Godsey, BS, OMS IV[2]; Martin Forsberg, MD, OMS IV[2]; Robert Nagele, PhD, OMS IV[2]

[1]New Jersey Institute for Successful Aging, Rowan University, Clementon; [2]New Jersey Institute for Successful Aging, Rowan University, Stratford

Background: Delirium is a neurobehavioral syndrome comprising altered attention, awareness, and cognition. General anesthesia (GA) has been linked to delirium and accelerated cognitive decline in elderly patients after surgery.

Hypothesis: Postsurgical delirium is caused by a transient, GA-induced breakdown of the blood-brain barrier (BBB). This breakdown results in disruption of brain homeostasis and altered neuron function that plays a key role in the phenomenology of delirium.

Objectives: To determine whether sevoflurane and isoflurane, 2 commonly used surgical GAs, increase BBB permeability, and whether older age increases the frequency and/or severity of this effect in mouse and rat models.

Methods: The effects of sevoflurane and isoflurane on BBB permeability were investigated using young (3-6 months), middle-aged (9-12 months), and older (18 months) animals subjected to surgical-plane GA for 3 hours with or without 24 hours of recovery. Animals were perfusion-fixed and their brains were removed and processed for scanning electron microscopy and immunohistochemistry. Scanning electron microscopy allows direct visualization of the integrity of tight junctions of brain vascular endothelial cells (BVECs) that form the BBB. Immunohistochemistry was used to detect plasma-derived biomarkers of a BBB leak in the brain tissue.

Results: Both GAs caused marked flattening of the luminal surfaces of BVECs and disruption of BBB tight junctions. This change led to holes in the BVEC lining and increased BBB permeability as shown by enhanced immunoglobulin (Ig) G–positive immunostaining of brain interstitial spaces and local neurons. In middle-aged and especially older animals, BBB breakdown, extravasation of plasma components into the brain interstitium, and binding of IgGs to neurons was increased compared with younger animals. Furthermore, semiquantitative differences were noted between sevoflurane and isoflurane in terms of their effects on the parameters measured, with sevoflurane causing greater disruption of cell ultrastructure.

Conclusion: Commonly used surgical GAs such as sevoflurane and isoflurane cause immediate structural changes in BVECs, which transiently increase the permeability of the BBB and facilitate plasma

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influx into the brain interstitium. The frequency and magnitude of this effect increases with age. This influx disrupts brain homeostasis, alters the pattern of neuronal activity, plays a role in the manifestation of postsurgical delirium, can trigger subsequent cognitive decline, and may be linked to early onset of Alzheimer disease.

S5

Salivary Uric Acid Levels Correlate to Blood Levels Independently of Salivary Flow Rate

Meghan Pauley, OMS II[1]; Bethany Boggess, BA[1]; Maria Soukup, BS[2]; Edward Bridges, PhD[2]; Jill Cochran, PhD, FNP[3]; Andrea Nazar, DO[3]; Kristie Bridges, PhD[2]

[1]West Virginia School of Osteopathic Medicine (WVSOM), Lewisburg; [2]Department of Biomedical Sciences, WVSOM, Lewisburg; [3]Department of Clinical Sciences, WVSOM, Lewisburg

Introduction: Salivary uric acid has been identified as a potential noninvasive biomarker of disease risk, but the relationship between uric acid concentration in blood and saliva has not been well characterized.

Objective: To determine whether there is a correlation between salivary and plasma uric acid levels and how this relationship is affected by salivary flow rate.

Hypothesis: It was hypothesized that there would be a positive correlation between salivary and plasma uric acid levels, which would not be affected by flow rate.

Methods: This study was approved by the West Virginia School of Osteopathic Medicine Institutional Review Board. Healthy adult volunteers (n=51) fasted for at least 1 hour before blood and saliva collection. Unstimulated whole saliva was collected using the passive drool method, and flow rates were determined. Blood samples were collected by venipuncture, centrifuged, and then transferred to cryotubes. All samples were immediately stored at –20°C. Mucins and peroxidase enzymes were removed from saliva via centrifugation and spin column, respectively. Salivary uric acid concentration was determined using the Pointe Scientific enzymatic assay and corrected for flow rate to calculate its rate of secretion. Statistical analyses were completed using IBM SPSS Statistics 21. After confirming normal distribution using Shapiro-Wilk testing, linear regression modeling was performed using both uric acid concentration and uric acid secretion as the independent variable.

Results: There was a significant correlation between salivary and plasma uric concentration (r=0.415; P=.002) but not between salivary uric acid secretion and plasma uric acid concentration (r =0.01; P=.942).

Conclusion: Several studies have proposed the use of salivary uric acid as a noninvasive biomarker of disease status. The results indicate that uric acid levels in whole saliva collected using the passive drool method reflect blood levels without requiring correction for salivary flow rate. This information is relevant for the design of future studies investigating the clinical usefulness of salivary uric acid measurement.

S6

Insulin Is Present in the Saliva of Children at Levels Detectable by a Commercially Available Clinical Assay

Bethany Boggess, OMS II[1]; Meghan Pauley, BS[1]; Maria Soukup, BS[2]; Jill Cochran, PhD, FNP[3]; Kristie Grove Bridges, PhD[2]

[1]West Virginia School of Osteopathic Medicine (WVSOM), Lewisburg; [2]Department of Biomedical Sciences, WVSOM, Lewisburg; [3]Department of Clinical Sciences, WVSOM, Lewisburg

Introduction: The prevalence of childhood obesity has raised concern over a potential increase in metabolic diseases such as type 2 diabetes mellitus in the pediatric population. Screening children for cardiometabolic risk factors such as hyperinsulinemia could prove beneficial for preventing or delaying the onset of these diseases. However, screening ve-

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nipuncture compliance in children is low. Salivary insulin is a potential noninvasive biomarker for assessing disease risk in children, but a reliable assay for measuring salivary insulin levels has not been established. The goal of this study was to examine the potential of standard immunoassay techniques for measuring salivary insulin concentration in children.

Hypothesis: Insulin will be present in the saliva of children at levels detectable by a commercially available clinical diagnostic assay.

Methods: This study was approved by the West Virginia School of Osteopathic Medicine institutional review board. Initial assay characterization was done using pooled saliva from deidentified donors. Diluted saliva was spiked with known amounts of insulin, and concentrations were measured using the Ultrasensitive Insulin ELISA kit from ALPCO. Subsequent analysis of salivary insulin levels in children was done using the same methods. Children participating in CARDIAC Boot Camp, a program for patients who are overweight, obese, or have other cardiometabolic risk factors, were recruited for the study. After obtaining parental consent and assent from the child, saliva samples were collected using the passive drool method and kept in freezer storage until assays were performed.

Results: The intra-assay variability of this method was less than 15%. The average recovery of insulin from the spiked saliva was 86% and 94% for high and low concentrations, respectively. Interassay variability ranged from 4% to 18% (mean, 11%). Insulin could be detected in all of the pediatric saliva samples. Salivary insulin levels in this population ranged from 1.35 to 112.67 µIU/mL (mean [SD], 19.48 [2.27]).

Conclusion: Salivary insulin is present in the saliva of children at levels detectable by a commercially available clinical assay. However, interassay variability was slightly higher than desired for a diagnostic method. Additional studies aimed at increasing the reliability of salivary insulin measurement are needed before its use as a diagnostic tool can be accurately tested.

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S7

Motorized Walker Reduces Variance of Gait in People With Parkinson Disease

Lauren Cooke, OMS IV; Corinne Fischer, BS; Jocelyn Young, BS; Sara Hyatt, BS; Ely Rabin, PhD

Department of Biomedical Sciences, New York Institute of Technology College of Osteopathic Medicine, Old Westbury

Introduction: The effects of Parkinson disease (PD) on gait include increased cadence, decreased stride length and gait velocity, and freezing and delays in initiation, all of which can lead to increased falls and decreased independence. Manual contact with a stable surface stabilizes balance by adding mechanical support and providing sensory feedback. Although banisters decrease stride length and slow gait, touching a moving handrail increases gait speed and stride length. This finding suggests that walking with a self-powered walker could also increase speed and stride length and decrease gait-cycle variance during turning, all of which are associated with freezing of gait and falling in individuals with PD. The goal of this study was to determine whether using a motorized walker as a speed cue would improve the gait of people with PD.

Hypothesis: Using the motorized walker as a speed cue will increase gait speed, increase stride length, and decrease gait speed variability and stride length variability while walking and turning.

Methods: Participants were recruited from NYITCOM's clinic and were instructed to walk and turn under 3 conditions: (1) unassisted, (2) conventional walker, and (3) automatic motorized walker. Velocity was determined from movement of sensors placed on the shoulders. Stride length was determined from movement of sensors placed on the feet. VICON cameras were placed around the room to

pick up the movements of the sensors. Each sensor was identified as the appropriate body part with VICON software. Stride length and walking speed were determined using MATLAB software. The data were analyzed using planned pairwise comparisons (2-tailed *t* test, α=.05).

Results: Stride length was decreased during both walking and turning conditions when using the motorized walker in comparison with both conventional walker and walking unassisted (*P*=.01). Stride length variability was lower during walking and turning using the motorized walker vs the conventional walker (*P*=.01). Stride length variability during turning was decreased when comparing the motorized walker with walking unassisted (*P*=.05). Gait speed decreased when using the motorized walker when compared with walking unassisted (*P*=.02). Gait speed variability was decreased when using both the conventional walker and motorized walker vs walking unassisted (*P*=.0, *P*=.04, respectively).

Conclusion: In general, conventional walkers help persons with PD walk with larger strides than when walking with no assistive device. Persons with PD walk with less stride length variability when using a motorized walker. The authors will further develop this walker to increase the speed to accommodate the potential increase in gait speed experienced while using the automated vs the conventional walker.

S8

Remote Assessment of Rehabilitation in Patients With Parkinson Disease

Corinne Fischer, OMS IV; Lauren Cooke, BS; Zain Memon, BS; Ely Rabin, PhD

Department of Biomedical Sciences, New York Institute of Technology College of Osteopathic Medicine, Old Westbury

Introduction: Parkinson disease (PD) is a progressive neurologic condition characterized by motor symptoms such as impaired gait, resting tremor, initiation delays, and reduced movement amplitudes. Assessment of symptoms is often difficult to measure objectively because of variation in patient performance. A study by Morris et al documented that when PD patients were being monitored, walking stride length was less symptomatic than when covertly monitored. It is possible that patients with PD may perform much differently during activities of daily living at home—which rehabilitation is meant to serve—from what is observed in the clinic.

Hypothesis: Gait and chair-rising kinematics differ during clinical assessment compared with at-home assessment throughout the course of physical therapy.

Objective: To determine the extent to which clinical assessment fairly represents general spontaneous function during activities of daily living.

Methods: Participants include patients with a diagnosis of PD (Hoehn and Yahr scale 2-3) participating in a 3-month rehabilitation program at NYIT-COM. Movement of the trunk and feet were integrated from accelerations measured by 3 accelerometer sensors (CC2541DK-Sensor, Texas Instruments) attached to the participants trunk and each ankle, transmitted to a smart phone (Nexus5, Google). Two common types of movement were the focus: (1) gait and (2) chair rise. Gait was assessed in terms of (1) stride length (distance between successive points of initial contact of the same foot), (2) stride duration (interval between successive heel-strikes), and (3) double supportive duration (both feet on the ground). Chair rise was assessed in terms of (1) vertical, lateral, and anterior trunk speed; (2) movement duration; and (3) sway amplitude on standing (to assess stability).

Results: Twenty patients participated. A 2-way repeated measures analysis of variance tested the effects of location (home, clinic) and intervention duration (each weekly visit) on these outcome measures. Speed of gait and chair rise were higher during clinic observations compared with spontaneous conditions (*P*<.05).

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Conclusion: Patient kinematics differ in and out of direct clinical observation. Monitoring patients outside the clinic can give insight for clinicians about patient performance during activities of daily living to enhance clinical assessment.

S10

Abnormal Vital Signs Fail as a Predictor of Patients Returning to the Emergency Department

Tomasz Przednowek, OMS II; John Graneto, DO

Midwestern University/Chicago College of Osteopathic Medicine, Downers Grove, Illinois,

Background: One quality measure in emergency medicine is to review records of patients returning within 48 hours to screen for possible missed pathology.

Research Question: Can abnormal vital signs serve as a predictor of patients returning to the emergency department within 48 hours?

Methods: Retrospective review of medical records from patients seen in the emergency department at Swedish Covenant Hospital (Chicago, Illinois) between January 2014 and June 2014. All patients who returned to the emergency department and who registered for a second visit within 48 hours were identified. Adult patients who did not return within 48-hours were identified to serve as controls. Vital signs at initial visit discharge and the discharge diagnosis were collected.

Results: Of the 48-hour-return patients, 46 (14%) were found to have at least 1 abnormal vital sign at discharge in the general 48-hour-return population, whereas in the control population, 21 of 100 patients (21%) met the criteria for at least 1 abnormal vital sign at discharge. One abnormal temperature was recorded in the control population (1%), and 2 abnormal temperatures were recorded in the 48-hour-return population (0.6%); 13 abnormal heart rates were recorded at discharge in the control population (13%), and 29 were recorded in the 48-hour-return group (9%); no abnormal respiratory rates were found in either population at discharge; 7 abnormal systolic blood pressure readings were found in the control group (7%), and 10 were found in the 48-hour-return population (3.1%); 1 abnormal diastolic blood pressure was found in the control group (1%), and 6 were found in the regular 48-hour-return group (2%); and 1 abnormal pulse oximetry reading was recorded in the 48-hour-return population (0.3%), and no abnormal recordings were found in the control group.

Conclusion: When compared with the control group, there was no significant association between the presence of an abnormal vital sign and the likelihood of the patient returning within 48 hours.

S11

Exercise and Quality of Life in Parkinson Disease Patients

John Paul Govindavari, OMS IV; David Tegay, DO; Kathleen Pergament, DO; Thomas Chan, DO; Christina Ciraco, BS; Bhuma Krishnamachari, PhD

New York Institute of Technology College of Osteopathic Medicine, Old Westbury

Introduction: Parkinson disease (PD) is the second most common neurodegenerative movement disorder in the United States. Medication is the standard mode of treatment but loses efficacy over time, has side effects, and is not effective in treating all PD symptoms. Adjunctive therapies, including exercise, are available to treat PD patients. Although these therapies may not slow the progression of PD, they can alleviate rigidity and pain in the shoulder, hip, and back, and may improve function in some motor tasks. The effect of these therapies on quality of life (QoL) and depression is not well established.

Hypothesis: Exercise will be associated with better QoL, and depression will be associated with decreased QoL.

Methods: Sixty patients with PD were surveyed using the validated Parkinson's Disease Questionnaire (PDQ)–39 tool to assess QoL and the validated

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Geriatric Depression Scale–30 tool to assess depression. Patients were asked about exercise habits in childhood, exercise habits in adulthood before PD diagnosis, and exercise habits/knowledge after PD diagnosis. The associations between those who knew and did not know that exercise does not stop PD progression and depression as well as the mean PDQ-39 score difference between groups were calculated.

Results: There was no significant difference between those who do and do not participate in prescribed exercise after PD diagnosis in terms of QoL scores. However, exercising in adulthood before PD resulted in a mean 35.65% decrease in PDQ score ($P<.01$), indicating that QoL was significantly better in those who exercised before PD diagnosis than those who did not. Similarly, exercising in childhood before PD resulted in a mean 32.94% decrease in PDQ score ($P=.03$). Depression resulted in a mean 24.06% increase in PDQ score ($P<.001$), indicating that QoL is decreased in those who are depressed. Knowledge about whether or not exercise stops the progression of PD was not associated with PDQ scores.

Conclusion: Exercise before PD diagnosis may be beneficial for optimal QoL, perhaps as a result of better physical health before diagnosis and decreased symptoms after diagnosis. Additional research should examine types of exercises done before diagnosis as well as the types of exercise prescribed after diagnosis. A weakness in this study was lack of H and Y severity scores; thus, results could not be controlled for disease severity. Additionally, there was a small sample size of those who did not exercise in this study. Further studies should be conducted with a larger sample size.

S16

Primary Care Practitioners Do Not Discuss Environmental Factors When Counseling Patients About Physical Activity

Kesha Baxi, OMS II; Alison Scharber, MPH, RDN; Jake Martinez, BS; Emily Freeman, MS; Tiffany Toomey, BA; James Yoon, MPH, MS; Kanwar Singh; Richard Suminski, MPH, PhD

Kansas City University of Medicine and Biosciences College of Osteopathic Medicine, Missouri

Introduction: The evidence is "inconclusive" regarding the efficacy of physical activity counseling by primary care practitioners (PCPs). The effects on patients' physical activity are variable, with a substantial proportion not responding. One reason could be a lack of discussion about environmental factors (eg, places for exercise, safety), which can facilitate or deter physical activity. To date, information about PCPs considering environmental factors when counseling patients about physical activity has not been published.

Hypothesis: Characteristics of PCPs, their practices, and patient visits determine whether PCPs discuss environmental factors when counseling patients about physical activity.

Objective: To determine whether PCPs discuss environmental factors when counseling their patients about physical activity.

Methods: In this cross-sectional study, 84 PCPs from 20 safety net clinics providing primary care medicine to low-income adults were asked to complete a survey about whether they discussed environmental factors when counseling patients about physical activity. In addition, they were queried about personal characteristics (eg, male or female), practice characteristics (eg, number of patients), and patient visits (eg, average length). The questionnaire was developed using a 2-stage, expert panel review process. Its internal consistency was acceptable for an exploratory study (Chronbach α, .67). The uni-

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versity's institutional review board approved the study protocol.

Results: A total of 24 completed surveys were returned (29% response rate). A mean (SD) of 2.1 (1.7) environmental factors were discussed. Only 1 PCP covered all 6 environmental factors asked about, 66.7% discussed 2 or fewer factors, and 25% did not discuss any factors. The sex of the PCP was significantly related to discussing environmental factors. Female PCPs discussed a mean (SD) of 2.7 (1.9) factors vs 1.1 (0.9) for male PCPs ($P<.05$). Safety was mentioned by 53.0% of female PCPs but not mentioned by any of the male PCPs. More time was identified by 79.3% of PCPs as a resource that would help them more effectively discuss environmental factors.

Conclusion: Primary care practitioners are not likely to discuss environmental factors that could influence their patients' physical activity. How this omission affects patient behavior should be determined.

S20

Relationship Between Worry and Metabolic Syndrome in the Mexican American Population

Anita Chaphekar, OMS II; James Hall, PhD

University of North Texas Health Science Center Texas College of Osteopathic Medicine, Fort Worth

Introduction: Mexican Americans in the United States have a high prevalence of metabolic syndrome. Metabolic syndrome is defined as risk factors that increase an individual's risk for cardiovascular disease and diabetes. Risk factors include abdominal obesity, hypertension, dyslipidemia, and elevated blood glucose levels. Research has suggested that worry, independent of anxiety, can contribute to poor health effects, such as those seen with metabolic syndrome. Mexican Americans have a high prevalence of worry and metabolic syndrome; however, a relationship between these variables has yet to be investigated for this population.

Objective: To analyze the relationship between metabolic syndrome and worry in the Mexican American population.

Hypothesis: Individuals with high levels of worry will be more likely to have metabolic syndrome and show elevated risk factors.

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

Results: Odds ratio calculation was not significant for the presence of metabolic syndrome (95% CI, 0.443-1.163; $P=.18$) between individuals of differing levels of worry. Participants with high and low worry showed a significant difference in abdominal circumference ($P=.025$) and blood glucose level ($P=.038$). Participants in the high worry category had a significantly greater abdominal circumference (mean [SD], 41.95 [6.46]) when compared with individuals in the low worry category (40.72 [5.41]). Individuals in the high worry category also had a higher serum glucose level (128.23 [60.26]) when compared with those in the low worry category (118.11 [46.78]). There was no significant difference found for the blood pressure, serum triglycerides, or high-density lipoprotein cholesterol levels.

Conclusion: Individuals with a high level of worry did not have an increased likelihood of metabolic syndrome compared with individuals with a low level of worry. However, when analyzing each risk factor alone, participants in a high worry group had a greater abdominal circumference and higher fasting glucose levels compared with those in a low worry group. The results of this study suggest the association of waist size and blood glucose with elevated levels of worry in the Mexican American population.

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S24

Defining Fever in Critically Injured Patients: Test Characteristics of 3 Different Thresholds

Omeed Sizar, OMS II[1]; Abid Farooq; Fahim Habib[2]

[1]Nova Southeastern University College of Osteopathic Medicine, Fort Lauderdale, Florida; [2]Broward General Hospital, Fort Lauderdale, Florida

Introduction: Fever remains the most common sign that prompts the workup for a possible infectious origin in critically injured trauma patients admitted to the intensive care unit. Yet, the definition of fever is highly variable, and the test characteristics of the various cutoff temperatures used have not been clearly defined. An accurate cutoff would allow for more precise and cost-effective management of the febrile trauma patient.

Hypothesis: The commonly accepted standards for fever do not accurately predict an infectious origin in febrile patients.

Methods: Medical records for 621 trauma patients at an urban level-I trauma center were retrospectively evaluated for fever and culture results. The maximum oral temperature during the 24-hour period before obtaining culture samples was used. Temperatures were correlated with positive or negative culture results to determine sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios, and area under the curve.

Results: Sensitivity and specificity were calculated using using cutoff values of 100.4F°, 101F°, and 101.5°F. Receiver operator curve cutoffs identified 99.75°F as the temperature with the best test characteristics. Sensitivity showed an inverse relationship with temperature. 99.75°F exhibited a maximum value of 75.30% (CI, 70.27-79.88), with 101.5°F exhibiting the minimum value of 25% (CI, 20.87-29.50). Specificity had a direct relationship to temperature, with 99.75°F having a minimum specificity of 59.46% (CI, 51.00-61.00) and 101.5°F having a maximum specificity of 92.96% (CI, 88.65-96.00). Positive likelihood ratio had a lowest value of 1.86 (CI, 1.51-2.28) at the lowest temperature of 99.75°F, and the highest value of 3.35 (CI, 2.12-5.95) at a temperature of 101.5°F. Negative likelihood ratio was also lowest at 99.75°F with a value of 0.42 (CI, 0.33-0.52), and highest at 101.5°F with a value of 0.81 (CI, 0.75-0.86). Positive predictive value was lowest at a temperature of 99.75°F at 80.46% (CI, 75.57-84.74) and highest at a temperature of 101.5°F at 39.29% (CI, 35.00-43.70). Negative predictive value was highest at 99.75°F with a value of 52.07% (CI, 44.27-59.80) and lowest at 101.5°F with a value of 39.29% (CI, 35.00-43.70). Area under the curve was inversely related to temperature with a maximum value of 0.32 (CI, 0.690-0.774) at 99.75°F and a minimum value of 0.498 (CI, 0.450-0.546) for 101.5°F.

Conclusion: These results suggest that none of the current cutoffs used to define fever accurately predict an infectious origin in febrile patients. Although a temperature of 99.75°F demonstrated the best test characteristics, none of the commonly accepted standards of fever showed a strong correlation to culture results. Further research is warranted to identify biomarkers that accurately identify the presence of infectious processes in trauma patients.

S31

National Trends in Elderly Trauma Patients

Abid Farooq, OMS II[1]; Omeed Sizar, OMS II[1]; Fahim Habib, OMS II[2]

[1]Nova Southeastern University College of Osteopathic Medicine, Fort Lauderdale, Florida; [2]Broward General Hospital, Fort Lauderdale, Florida

Introduction: Trends in the incidence and outcomes of traumatic injury among the patients aged 65 through 84 years and patients aged 85 years or older are unknown. This information has the potential to offer insight into informed trauma system

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planning and improve outcomes in this highly vulnerable population.

Hypothesis: There is a significant rise in elderly patients having poorer outcomes in geriatric trauma.

Methods: The Healthcare Cost and Utilization Project Nationwide Inpatient Sample (HCUP-NIS) database was queried to identify patients with ICD codes for a traumatic injury. Data, stratified by age group was then abstracted for incidence, lengths of stay, charges, mortality and discharge status for patients for the period 1997-2012. The study period was divided into 4 periods of 4-years each. Statistical analysis was performed using the ANOVA, *t* test, and χ^2 test as appropriate. A *P* value of <.05 was used to determine significance.

Results: Duriing the 16-year study period, traumatic events in elderly patients aged 65 through 84 years have increased by 6.8% (*P*=.0005) and by 29% in those aged 85 years or older (*P*<.001). In contrast, admissions for injury decreased in both adults and children (6%, and 29.5%, respectively; *P*=.0005). A decrease in length of stay was seen with decrease from 6.0 to 5.2 days in patients aged 65 through 84 years (*P*<.0001) and 6.2 to 5.0 days in those aged 85 years or older (*P*<.0001). Length of stay for adults on the other hand has increased from 4.83 to 5.1 (*P*=.06). Pediatric patient in-hospital mortality has decreased significantly (*P*=.001), with concurrent increases in discharge to home (*P*=.003). Adult in-hospital mortality rates and discharges home have remained stable (*P*=.83 and *P*=.24, respectively). Elderly patients aged 65 through 84 years have shown stable in-hospital mortality rates (*P*=.149) with decreased discharges home (*P*=.0003). Elderly patients aged 85 years or older have shown the worst trend in outcomes, with significant increases in in-hospital mortality (*P*=.0003) and significantly fewer patients being discharged home (*P*=.0004). Costs have risen for patients in all age groups during the study period (*P*<.0001).

Conclusion: Geriatric trauma is incresing at an exponential rate, with elderly patients forming an increasing proportion of the trauma population. These patients have been shown to have poorer outcomes as demonstrated by in-hospital mortality and discharge status. Geriatric-specific trauma programs are urgently needed to address this evolving problem.

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S33

Diagnostic Sacroiliac Joint Block via L4-5 Dorsal Rami and S1-3 Lateral Sacral Nerves

Catherine Monigan, OMS II[1]; Terence.Gray, DO[2]; Frank Willard, PhD[3]

[1]University of New England College of Osteopathic Medicine (UNECOM), Biddeford, Maine;
[2]Mercy Hospital Pain Center, Portland, Maine;
[3]Department ofAnatomy, UNECOM, Biddeford, Maine

Introduction: Sacroiliac (SI) joint pain is a relatively common ailment, with these patients comprising 7% to 35% of all low back pain sufferers. The commonly accepted standard of SI pain diagnosis is an intra-articular injection of local anesthetic; however, this diagnostic technique does not account for pain caused by the extra-articular soft tissue and ligamentous structures of the joint, which may make a significant contribution to pain in this patient population.

Hypothesis: Anesthetic block of L4-5 dorsal rami and S1-3 lateral sacral nerves will confirm a diagnosis of intra-articular or extra-articular SI pain by temporarily relieving pain patterns by greater than 50% in a majority of patients.

Methods: We completed an uncontrolled retrospective study of 25 consecutive patients with a diagnosis of SI joint pain. The diagnosis was made with tenderness to palpation of the SI joint sacral sulcus and one or more positive provocative maneuvers of the SI joint including Gaenslen's test, FABERE test, pelvic compression/pelvic rocking and straight leg raise, all positive with radiation to the SI joint on the respective side. Patients received fluoroscopy-guided injections using a combined mixture of bupi-

vacaine (1 cc; 0.25%) and triamcinolone (6-8 mg; 40 mg/cc) to each location. Locations included the dorsal rami of L4 and L5, as well as the lateral sacral branches of S1-S3. A subset of patients (19 of 25) who had tenderness along the belly of the piriformis muscle also received an intramuscular injection of bupivacaine 0.25% (4 cc) and triamcinolone (20 mg) to the piriformis muscle belly under fluoroscopic guidance using a medial approach just lateral to the sacrum.

Results: Twenty-two of 25 patients (88%) had a greater than 50% reduction in their pain patterns immediately following injections. Seventeen patients (68%) achieved 100% relief following the procedure. In 7 patients (28%), relief lasted at a 3- to 4-week follow-up.

Conclusion: These results provide preliminary evidence that a diagnostic block of the dorsal branches of L4-5 and the lateral sacral branches of S1-3 may be of clinical use when diagnosing SI pain of extra-articular or intra-articular etiology. Further studies are needed to determine if successful block (>50% relief) of these nerves could serve as an improved predictor of success for radiofrequency ablation of the same nerves for denervation of the SI joint, an emerging and promising technique for management of SI pain.

♦S34

Comparison of Multiple Balance Measures as Predictors of Falls in Parkinson Disease: A Pilot Study

Theresa Apoznanski, OMS IV[1]; Joanne Donoghue, PhD[1]; Morcos Hanna, OMS II[1]; Priscilla Chow, OMS II[2]; Jayme D. Mancini, DO[2]; Sheldon Yao, DO

[1]New York Institute of Technology College of Osteopathic Medicine (NYIT-COM), Nesconset; [2]Department of Osteopathic Manipulative Medicine, NYIT-COM, Old Westbury

Introduction: Falls are common in patients with Parkinson disease (PD), with up to 50% of patients falling in a 3-month period. Individuals with PD are at an increased risk for falls, owing to a decline in balance systems and postural control, as well as hypokinesia. There are several clinical tests to evaluate balance, including the Mini-Balance Evaluation Systems Test (Mini-BESTest), Sensory Organization Test (SOT), and Limits of Stability (LOS). The Mini-BESTest is currently the most reliable test for identifying patients with PD at risk for recurrent falls. It has yet to be determined whether the LOS and SOT correlate with the Mini-BESTest in their ability to predict falls.

Hypothesis: Scores on SOT and LOS will be reliable indicators of PD fallers compared with the Mini-BESTest.

Methods: Twenty participants with PD were identified as fallers (n=9) or nonfallers (n=11) based on a history of 2 or more falls in the past 6 months. The participants participated in all 33 balance tests over 1 to 2 visits. The severity of PD was established using the Unified Parkinson's Disease Rating Scale Part III (UPDRS-III). Statistical analysis was performed using independent *t* tests and bivariate correlations.

Results: There was a significant difference in mean scores between fallers and nonfallers for the Mini-BESTest (P=.000), but no significant difference in the UPDRS-III (P=.145) or SOT scores (P=.677) was observed. Furthermore, the UPDRS-III inversely correlated with the Mini-BESTest (r=−0.713, P=.001) and SOT (r=−0.435, P=.071). The SOT positively correlated with the Mini-BESTest (r=−0.451, P=.060). Analysis of the 40 outcome measures for LOS showed no relationship with the other balance tests or UPDRS-III.

Conclusion: These pilot data do not support the hypothesis that SOT and LOS are reliable predictors of falls in patients with PD. The data do support previous research that the Mini-BESTest is a reliable predictor of falls in patients with PD. The correlations between each pair of balance tests suggest that trends exist between those who fall and those who do not. However, a larger sample size needs to

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be examined, which may also enable physicians to differentiate the relationships among different types of falls and the most appropriate test to administer. Understanding each test and its role in predicting falls in patients with PD can help create more effective treatment plans and establish more accurate assessment tools.

S44

Reported Prenatal Substance Use Among Women in the New River Valley of Southwest Virginia During 2013

Annemarie Anglim, OMS II

Edward Via College of Osteopathic Medicine, Christiansburg, Virginia

Introduction: Despite the best efforts of many dedicated private and public health care practitioners, drug use during pregnancy remains a problem in the New River Valley (NRV) of rural southwest Virginia. A recent study with the Montgomery County Health Department looked at the primary source of prenatal care for women reporting prenatal substance use during 2013 and the corresponding number of prenatal visits.

Hypothesis: Owing to patient population demographics, health department patients who attended few prenatal visits will report the highest rate of prenatal substance use.

Methods: Using the NRV birth records from 2013, the source of prenatal care and the number of prenatal visits attended was compared between pregnant women who reported substance use and those who did not.

Results: In 2013, there were 1621 births on record in NRV, and 13.42% of those mothers were patients who received care from a private physician and reported substance use during pregnancy (including tobacco, alcohol, heroin, methadone, marijuana, cocaine, amphetamines, or other drugs). Among patients who received care at the health department, 7.81% reported substance use. Of patients who attended prenatal visits at both the health department and a private physician's office, 33.33% reported substance use. There was a negative correlation between the number of women who reported substance use and the number of prenatal visits. After 12 visits, however, the trend stabilized below 8.4%. Among women who attended 0 to 5 prenatal visits, 36.84% reported substance use, whereas those who went to 6 to 8 visits reported 26.44% substance use. Women who attended 9 to 11 visits reported 17.75% substance use.

Conclusion: Patients who attended few prenatal visits and used both the health department and a private physician for prenatal care had the highest rate of prenatal substance use, indicating that continuity of care is vital in reducing the rate of substance use. These results reinforce the fact that education and substance abuse counseling are important parts of every prenatal visit. Patients are best served when health care professionals treat the whole person. In the case of prenatal care, judgment-free communication can serve to educate the patient about potential outcomes for the unborn child, while focusing on continuity and regularity of care.

S52

Comparing Risk Factors for Cancer in Virginia Coal and Non–Coal Production Counties Currently Meeting Healthy People 2020 Cancer Objectives

Katie Kennedy, OMS II; Susan Meacham, PhD, RD; Cody Goessl, MS, LAT, PhD Candidate; Dalia Meisha, DDS, MPH, DScD

Edward Via College of Osteopathic Medicine–Virginia Campus, Blacksburg

Introduction: In Virginia, cancer mortality is markedly higher in southwestern counties engaged in coal production. Previous research has been directed at establishing a cause-effect relationship between coal and cancer; however, this study exam-

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ines other factors that are known health determents associated with a higher incidence of cancer. Data focusing on health determinants that are modifiable and known to have a negative impact on cancer can direct future health intervention programs. Several Virginia counties have achieved the Healthy People 2020 (HP2020) nationwide goals to improve cancer mortality.

Hypothesis: Measures of multiple known modifiable risk factors for all cancers will be better in Virginia counties with lower cancer mortality rates that are currently meeting HP2020 objectives for reducing all cancers than in counties with higher cancer mortality rates.

Methods: This retrospective descriptive study obtained coal production from the Environmental Information Agency and used cancer mortality rates from the National Cancer Institute. Prevalence rates for modifiable risk factors were obtained from the County Health Rankings (2014) report. Leading causes of cancer mortality per county were determined from Virginia Department of Health mortality records (2006-2012).

Results: Compared with the state mean, cancer mortality in the top 6 counties in Virginia currently producing coal (CC) was 13% higher. The mean cancer mortality rate for 11 counties meeting Virginia HP2020 goals (HP) was 19% lower than the state mean. For most health outcomes and measures, the data confirmed that environmental factors were discriminating with poorer ranking and measures associated with higher rates of cancer. Adult smoking in CC was twice that in HP (mean [SD], 27.7 [4.3%] vs 14.1 [6.0%], respectively). Physical inactivity was worse in CC than in HP (33.0 [4.6%] vs 22.1 [3.7%], respectively). Obesity was more prevalent in CC than in HP (31.1 [2%] vs 25.7 [3.2%], respectively). The availability of physicians was 60% better in HP vs CC (46,900 vs 79,170, respectively, residents per physician). Mammography screening had greater use in HP than in CC (66.6 [6%] vs 55.7 [3.8%], respectively). Statistical significance was achieved with 2-tailed *t* tests; $P \leq .00$ for each measure.

Conclusion: Improvements in environmental factors, other than coal production, impacting physical activity, access to physicians, and adverse health behaviors were associated with improvements in cancer mortality rates in selected Virginia counties.

Basic Science

S9

Juvenile Diffuse Brain Injury Results in Alteration of the Neurovascular Unit

Timothy Ellis, OMS I[1]; Rachel K. Rowe, PhD[2]; Jordan L. Harrison, BA[3]; Jenna M. Ziebell, PhD[2]; P. David Adelson, MD[4]; Jonathan Lifshitz, PhD[4]

[1]Midwestern University/Arizona College of Osteopathic Medicine, Phoenix; [2]Department of Child Health, University of Arizona College of Medicine Phoenix; [3]Neuroscience, Arizona State University, Tempe; [4]Barrow Neurological Institute, Phoenix Children's Hospital, Arizona

Introduction: Juvenile traumatic brain injury (TBI) has the potential to leave patients with a lifetime of consequences that may manifest as cognitive, somatic, and emotional symptoms. Most juvenile TBI is diffuse in nature, and effective treatments remain sparse. The neurovascular unit (NVU) is composed of neurons, glia, and vasculature. These elements are principal biomarkers of injury as well as targets for treatment.

Hypothesis: Midline fluid percussion injury (mFPI) results in a diffuse brain injury that alters the NVU of the juvenile rat (postnatal day 17) up to 1 month after injury.

Methods: Diffuse brain injury was induced using a mFPI with a force of 1.4 atm. Verification of injury severity was determined by clinical end points such as righting reflex inhibition, seizure, and apnea. Tissue was collected at 2 hours, 1 day, 7 days, and 28 days after injury, and components of the NVU were examined via histologic and immunohistochemical studies.

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Results: Contrary to what is seen in mFPI in adult rats, righting reflex was inconclusive in juveniles. However, 87% of juveniles experienced seizures lasting a mean (SD) of 72 (8.5) seconds, and 77% of the animals experienced apnea lasting a mean (SD) of 31 (6.7) seconds. Further, all injured animals had epidural and subdural hematomas and herniation through and around the craniotomy. Physiologically, animals experienced reduced weight gain in comparison with sham animals. Similar to magnetic resonance imaging after clinical injury, hematoxylin and eosin staining confirmed a diffuse juvenile TBI without cavitation. Immunoglobulin (Ig)G extravasation revealed vasculature damage in the cingulate and motor cortices, indicating permeability of the blood brain barrier (BBB) at 2 hours and 1 day, with resolution by 7 days after injury. Astrocyte (glial fibrillary acidic protein) and microglia (ionized calcium binding adaptor molecule 1) activation were observed after injury in the same region as IgG before returning to sham-levels by 28 days after injury. Pan-neuronal staining identified neuronal damage consistent with the presence of BBB permeability and glial activation.

Conclusion: Midline fluid percussion injury is a clinically relevant model of diffuse juvenile TBI, and it can be used to investigate possible neurologic deficits associated with injury. The acute timeline associated with BBB permeability and the inflammatory cascade can be used to screen possible time-dependent therapeutic treatments.

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S15

Mechanobiology of Cyst Formation in Polycystic Kidney Disease

Sarah Raza, OMS IV[1]; Fatima Kutty, OMS II[2]; Aleksandr Vasilyev, MD, PhD[3]

[1]Department of Basic Sciences, New York Institute of Technology College of Osteopathic Medicine (NYIT-COM), Glen Cove; [2]Department of Biomedical Sciences, NYIT-COM, Old Westbury; [3]NYIT-COM, Old Westbury

Introduction: Autosomal dominant polycystic kidney disease (ADPKD) is a major cause of chronic renal failure. Mutations in the *PKD1* and *PKD2* genes result in renal cysts along with numerous extrarenal manifestations. The exact mechanism of cyst formation in PKD remains largely unknown. It has recently been shown that in some mouse models of ADPKD, cysts only form after epithelial injury. This study extends this result into the hypothesis that cyst formation occurs as a result of postinjury luminal obstruction.

Hypothesis: It is commonly assumed that cyst formation in ADPKD is driven by increased tubule cell proliferation. The authors propose that ADPKD is fundamentally a defect in handling obstructive hydrodynamic load on the kidney, resulting in renal cyst formation; which is independent of cell proliferation. The hypothesis was tested using a zebrafish model of ADPKD. On inducing renal injury via kidney photoablation, causing localized obstruction of the tubules from cell debris and a resultant formation of transient cysts proximal to the site of injury, it was predicted that cyst initiation would precede any significant increase in cell proliferation and that after injury, PKD mutants would progress to permanent cysts, owing to an aberrant ability to clear the luminal obstruction.

Methods: In this experimental study, *PKD2* mutant and control kidney GFP transgenic zebrafish embryos were photoablated using confocal microscope. The time course of cyst formation was determined using time-lapse microscopy and com-

pared with a time course of kidney tubule bromodeoxyuridine incorporation. The PKD2 mutant and control zebrafish were analyzed at 36 hours postinjury using immunofluorescence. The kidney epithelial morphometry and luminal diameter were measured using ImageJ (National Institutes of Health), and analyzed in Excel (Microsoft Corp).

Results: Cyst initiation occurred as early as 3.5 hours postinjury ($P<.05$) and cyst formation preceded bromodeoxyuridine incorporation by greater than 24 hours. Our preliminary results show that PKD mutants have a decreased ability to resolve transient cysts after injury.

Conclusion: Cyst formation due to luminal obstruction occurs independently of cellular proliferation, which is a secondary phenomenon. In *PKD2* mutants, there was a decreased ability to resolve transient cysts after obstruction. These results significantly change the understanding of the mechanisms involved in cyst formation in PKD.

♦S17

Thyroid Hormone Disruption Effects Lamination of the Neocortex but Not the Cerebellum in a Model of Developmental Hypothyroidism and Hypothyroxinemia

Sarah VanDine, OMS IV[1]; Mary E. Gilbert, PhD[2]; Raddy L. Ramos, PhD[3]

[1]New York Institute of Technology College of Osteopathic Medicine (NYIT-COM), Huntington; [2]Toxicity Assessment Division, Neurotoxicology, US Environmental Protection Agency, Research Triangle Park, North Carolina; [3]Department of Biomedical Sciences, NYIT-COM, Old Westbury

Introduction: Research on neurodevelopmental changes resulting from thyroid hormone (TH) disruption has important basic and clinical implications. The authors previously demonstrated, in a rodent model, that developmental hypothyroidism or hypothyroxinemia can cause the formation of subcortical band heterotopia (SBH; Gilbert et al 2014), indicating that TH plays a role in neuronal migration during corticogenesis. However, the effects of TH disruption on cerebellar development and lamination have not been evaluated in this model.

Hypothesis: Hypothyroidism and hypothyroxinemia result in neuronal migration defects and altered lamination of the cerebellum by affecting the migration of granule cells. In light of the authors' recent findings that about 30% of control rats exhibit spontaneous molecular layer heterotopia (MLH) of the cerebellar vermis (Van Dine et al 2013), it was hypothesized that TH disruption would increase the prevalence and size of MLH.

Methods: Pregnant Long-Evans rats were administered propylthiouracil (PTU) via the drinking water from gestational day 6 until postnatal day 21. Brains from adult offspring from 0% (n=15), 0.0001% (n=13), and 0.001% (n=15) PTU dose groups were harvested for Nissl staining and immunocytochemical analysis to visualize cell types and lamination defect in the cerebellum and neocortex. Digital photomicrographs of cerebellar and neocortical sections were used for analysis. χ^2 analyses were used to compare effects across groups (α set at $P \leq .05$).

Results: All doses of PTU tested produced an SBH in the cortex, which increased in size with increasing dose level and were correlated with reduced serum levels of T4. In contrast, no cerebellar lamination defects were observed at any dose, although the presence of MLH was observed in all groups. χ^2 analyses indicated no significant dose-dependent increase in prevalence or size of cerebellar MLH.

Conclusion: Although hypothyroidism and hypothyroxinemia produce robust and permanent neocortical malformations, cerebellar lamination and foliation appear intact when assessed in adult tissue. However, examination of neonatal and juvenile cerebellar tissue from treated rats may reveal migration delays as has been previously reported. Together with the previous findings, these data indicate

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that mild TH disruption can affect brain development, but these effects are both timing- and region-specific.

S18

Quantitative Analysis of Chronic Inflammatory Infiltrates Between Sun-Exposed and Sun-Protected Skin With a Correlational Analysis of Vessel Quantity to Chronic Inflammation Between Sun-Exposed and Sun-Protected Skin: A Cadaveric Study

Karan Lal, OMS IV[1]; Maria Plummer, MD[1]; Mariya Milko, DO[2]; Mariya Belyayeva, BS[1]; Dirk Elston, MD[3]; Min-Kyung Jung, PhD[1]

[1]Department of Biomedical Sciences, New York Institute of Technology College of Osteopathic Medicine, Old Westbury; [2]Department of Internal Medicine, Largo Medical Center, Largo, Florida; [3]Ackerman Academy of Dermatopathology, New York City, New York

Introduction: Chronic sun damage is an area of great concern. The mechanism of photoaging has been debated but previous studies identified increased chronic inflammation in sun-exposed sites compared with sun-protected sites. This finding has led to conclusions that mediators from these inflammatory cells cause collagen breakdown. Ultraviolet radiation has also been found to promote angiogenesis by a cascade-inducing vessel endothelial growth factor. In this study, inflammatory infiltrates and dermal vessels from sun-exposed vs sun-protected skin were quantified and compared.

Hypothesis: Increased chronic inflammation and vessel number is predicted in sun-exposed skin.

Methods: Two elliptical excisional biopsies from the face (sun-exposed skin) and inner thigh (sun-protected skin) were taken from 15 white cadavers (8 male and 5 female; mean age, 75.7 years). Dermal vessels and inflammatory cells were counted in hematoxylin and eosin stained slides per 10 consecutive high-power fields (×400).

Results: Data from 13 cadavers were analyzed, owing to poor tissue preservation in 2 blocks. Face biopsy specimens showed a statistically significant increase in mean (SD) number of both chronic inflammatory cells and vessels compared with thigh specimens (19.17 [8.08] vs 6.98 [5.43] per 10 hpf; $P<.001$ and 5.69 [1.71] vs 4.15 [1.52] per 10 hpf; $P=.019$, respectively). Comparison of the mean number of inflammatory cells between the face and thigh specimens, adjusted for age and sex, was not statistically significant ($P=.33$). No statistically significant correlation was found between mean number of vessels vs mean number of chronic inflammatory cells in both face and thigh specimens ($r=-0.37$, $P=.21$, and $r=0.24$, $P=.43$, respectively).

Conclusion: Sun-exposed skin has increased chronic inflammatory cells compared with sun-protected skin, which supports the findings of previous studies showing an inflammatory component to photoaging. There was an increase in the vessel number in the superficial dermis in sun-exposed specimens compared with sun-protected specimens, which may indicate that angiogenesis occurs in sun-exposed skin. This finding may also relate to the vascular changes that occur in UV radiation–induced malignancies, but it does not seem to support the findings in studies that found a decrease in vessel density in sun-exposed skin. No relationship between the number of chronic inflammatory cells and the number of dermal vessels in sun-exposed vs sun-protected skin could be ascertained.

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♦S21

A Novel Lipid-Based Nanoemulsion Formulation to Overcome Paclitaxel Resistance in Ovarian Carcinoma Cells

Shirley Kim, OMS II; Jiten Mehta, BS; Akshara Malla; Bernardo Chavira, BS; Ritambhara Wadhwa, BS; Tamer Elbayoumi, PhD; Vinay J. Nagaraj, PhD

Midwestern University/Arizona College of Osteopathic Medicine, Glendale

Introduction: Drug resistance is a major factor in the failure of chemotherapy for many cancers. The upregulation of P-glycoprotein (P-gp)—a cell surface drug efflux pump—is a key molecular mechanism that confers drug resistance to cancer cells. Strategies that involve effective drug delivery to cancer cells while inhibiting the action of P-gp offer an opportunity to overcome drug resistance and effectively treat cancer. In this study, formulations of a novel lipid-based nanoemulsion consisting of paclitaxel (Px, a commonly used chemotherapeutic drug) along with genistein (Gn, a soy-derived P-gp inhibitor) were tested for their drug delivery abilities and antidrug resistance properties.

Hypothesis: Drug resistance in ovarian cancer cells can be overcome by the use of lipid-based nanoemulsions to effectively deliver a combination of chemotherapeutic agents and inhibitors of the multidrug resistance protein P-gp.

Methods: Lipid nanoemulsions were prepared using a combination of vitamin E, argan oil, solutol, water, and either Px or Gn in an ethanol solution. The alcohol was removed by evaporation, and the resulting particles were reconstituted and characterized. Cultured ovarian cancer OVCAR-8 (Px-sensitive) and NCI-ADRr (Px-resistant) cells lines were exposed to various doses of Px and nanoemulsion formulations consisting of Px and/or Gn alone or in varying ratios. Cell viability was assessed, and the IC_{50} was determined in each case.

Results: Delivery of Px via lipid nanoemulsions resulted in a significant reduction in the IC_{50} compared with treatment without the nanoemulsion in both OVCAR-8 and NCI-ADRr cell lines. When these cells were exposed to nanoemulsions consisting of Px mixed with nanoemulsions consisting of Gn, they demonstrated a further reduction in IC_{50} or increased cell death. The calculated combination indices show a strong synergistic effect of Px- and Gn-containing nanoemulsions when mixed in 1:1 and 1:2 ratios. Nanoemulsions by themselves or with Gn alone did not show significant toxicity toward either cell line.

Conclusion: Lipid-based nanoemulsions offer superior drug delivery and can be used for drug-synergism to overcome drug resistance in cancer cells. While the precise molecular mechanisms for enhanced drug delivery and observed synergistic effect of Px and Gn need further investigation, this study offers great promise for the development of novel treatments to overcome chemotherapy resistance in patients with cancer.

♦S23

TGFβ Pathway Inhibition Enhances Vascular Network Formation by Human Endothelial Cells Pretreated With Doxorubicin

Alyssa Imperatore, OMS II[1]; Jill Schriewer, BS[1]; Eugene Konorev, PhD[2]

[1]Kansas City University of Medicine and Biosciences College of Osteopathic Medicine (KCUMB-COM), Missouri; [2]Department of Pharmacology, KCUMB-COM, Missouri

Introduction: Multiple anticancer treatment modalities cause severe cardiovascular complications. Cardiovascular disease is a primary cause of morbidity and mortality in cancer survivors. Specifically, doxorubicin (DOX) causes development of cardiomyopathy that responds poorly to therapy and often progresses in treated patients to fatal heart failure. The authors' laboratory previously detected decreased capillary density in cardiac tissues of treated mice and described suppression of vascular

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network formation in vitro by DOX-treated human endothelial cells.

Hypothesis: Transforming growth factor β (TGFβ) pathway inhibition enhances the formation of vascular network in human endothelial cells pretreated with DOX via increased migration. In addition, vascular endothelial cadherin protein (encoded by *CDH5* gene) is known to inhibit migration and vascular sprouting.

Objective: To create a *CDH5* short hairpin RNA (shRNA) knockdown human endothelial cell line to test the role of *CDH5* expression in DOX-induced suppression of angiogenesis.

Methods: ALK4/5/7 receptor kinase inhibitor SB431542 (SB) was used to inhibit TGFβ pathway activity. Human umbilical vein endothelial cells (HUVEC) were used in migration studies and to produce a *CDH5* short hairpin RNA knockdown cell line. Vascular network formation was examined using a co-culture of HUVEC and human cardiac fibroblasts.

Results: Doxorubicin inhibited migration of HUVEC and suppressed the formation of vascular networks by these cells in co-culture with human cardiac fibroblasts. The removal of DOX treatment from co-cultures did not restore the ability of endothelial cells to form vessel-like structures. SB increased migration of DOX-treated HUVEC and enhanced formation of vessel-like structures when added to endothelial cells pretreated with DOX for 4 days in co-culture. Doxorubicin increased *CDH5* messenger RNA (mRNA) in HUVEC, and SB significantly reduced *CDH5* mRNA abundance in DOX-treated cells. *CDH5* knockdown moderately increased the migration of DOX-treated endothelial cells.

Conclusion: Increased expression of *CDH5* in endothelial cells contributes to the suppression of migration and vascular network formation in DOX-treated cells. SB decreases *CDH5* expression, increases migration, and enhances the formation of vessel-like structures by endothelial cells pretreated with DOX.

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S25

Heat Shock Protein 70 Expression Reduces *Chlamydia muridarum*–Induced Oviduct Pathology

Jennifer Do, OMS II[1]; Weidang Li, PhD[2]; Ashlesh Murthy, MD, PhD[2]; Mae Ciancio, PhD[3]

[1]Midwestern University/Chicago College of Osteopathic Medicine (MWU/CCOM), Carol Stream, Illinois; [2]Department of Pathology, MWU/CCOM, Downers Grove, Illinois; [3]Department of Biomedical Sciences, MWU/CCOM, Downers Grove, Illinois

Introduction: *Chlamydia trachomatis* genital infections lead to severe pathological consequences, including pelvic inflammatory disease and infertility. The host's immune response has an important role in causing bystander damage to target tissues. Heat shock protein 70 (HSP70) is an evolutionarily conserved stress-induced protein with significant cytoprotective and immunoregulatory activities. However, the role of HSP70 in genital chlamydial pathologic conditions has not been studied.

Hypothesis: Epithelial cell-specific HSP70 expression protects against *Chlamydia*-induced oviduct pathology.

Objective: To evaluate whether HSP70 expression in the female urogenital tract would protect against *Chlamydia muridarum* infection using a mouse model of genital infection with *C muridarum*, which mimics human genital chlamydial infection.

Methods: Heat shock protein70 transgenic (HSP70 Tg) mice were created by injecting a villin promoter-driven HSP70 targeting vector into C57Bl/6 oocytes. Female mice, 6 to 8 weeks old, HSP70 Tg and nontransgenic (NTg) littermates were infected intravaginally with 5×10^4 infectious units of *C muridarum*. Vaginal chlamydial shedding (NTg, n=8; HSP70 Tg, n=8) and bacterial burden (NTg, n=2; HSP70 Tg, n=3) were studied over the initial 30 days of infection. Immunological parameters and genital tract pathology were studied at 80 days post-primary infection (NTg, n=5; HSP70

Tg, n=5) and 9 days postsecondary infection (NTg, n=3-5; HSP70 Tg, n=3-5). A 2-tailed *t* test and χ^2 analysis were used on data, with significance set at $P<.05$.

Results: Vaginal chlamydial shedding, bacterial burden in the upper genital tract, tumor necrosis factor α levels, and serum antibody levels were comparable between NTg and HSP70 Tg mice. However, oviduct dilation at 80 days after primary infection and 9 days after secondary infection was significantly reduced in incidence but not severity in HSP70 Tg mice (10% incidence with mean diameter, 0.6 mm, at day 80 after primary infection; 30% incidence with mean diameter 1.5 mm at day 9 after secondary infection) compared with NTg mice (80% incidence with mean diameter of 2.1 mm at day 80 after primary infection; 80% incidence with mean diameter of 2.2 mm at day 9 after secondary infection).

Conclusion: Epithelial cell-specific HSP70 expression in the urogenital tract serves a protective function against oviduct pathology after chlamydial infection. Understanding HSP70's host defense mechanism against *Chlamydia*-induced pathology may provide another avenue for therapeutic intervention.

S26

Mechanisms of Fenofibrate-Induced miR3189-3p Expression in Glioblastoma

Don Parish, OMS II[1]; Mariacristina DeLuca, BS[2]; Duane Jeansonne, PhD[2]; Francesca Peruzzi, PhD[2]

[1]William Carey University College of Osteopathic Medicine, Hattiesburg, Mississippi; [2]Louisiana State University Health Sciences Center, Stanley S. Scott Cancer Center, New Orleans

Introduction: Glioblastoma is the most aggressive type of brain tumor. Current treatment methods, including surgical resection, radiation, and chemotherapy, are largely ineffective, rendering glioblastoma essentially untreatable. Expression levels of growth differentiation factor 15 (GDF15) and its co-encoded microRNA, miR-3189-3p, were increased in LN-229 glioblastoma cells by treatment with fenofibrate, a lipid-lowering drug with multiple anticancer activities. Expression of this microRNA is low in clinical samples of astrocytomas and glioblastomas, suggesting that a forced expression of miR-3189-3p in these tumors has the potential to inhibit their growth and migration. Fenofibrate is a peroxisome-proliferator–activated receptor α (PPAR-α) agonist that is commonly used for the treatment of cardiovascular disease and various metabolic disorders. Although identified as a PPAR-α agonist, fenofibrate can also activate PPAR-α independent pathways.

Research Question: Does fenofibrate upregulate miR3198-3p through a PPAR-α dependent or independent pathway in glial tumors?

Methods: LN-229 cells were treated with 10 mmol of an PPAR-α antagonist or transfected with 10 μmol small interfering PPAR-α for 24 hours before stimulation with 50 μmol of fenofibrate. Cells were lysed 48 hours after incubation with fenofibrate. Total RNA was isolated using the miRVana miRNA extraction kit. Quantitative real-time polymerase chain reaction (RT-PCR) was performed in duplicate using a Roche LightCycler 480 Real-Time PCR System and normalized using GAPDH or RNU6B control. Relative quantification of gene expression was calculated using the comparative Ct ($2^{-\Delta\Delta Ct}$) method.

Results: Quantitative RT-PCR analysis revealed increased expression of both GDF15 and miR-3189-3p in all samples treated with fenofibrate and the addition of the PPAR-α inhibitor. The silencing of this receptor through small interfering RNA did not significantly change the levels of expression. The effectiveness of small interfering PPAR-α in downregulating PPAR-α messenger RNA was also evaluated by quantitative RT-PCR, and results showed this downregulation.

Conclusion: Increased expression of GDF15 and miR-3189-3p by fenofibrate treatment is PPAR-α independent, and increased expression of

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miR-3189-3p results in increased levels of phosphorylated STAT3. Since miR-3189-3p inhibits cell proliferation, the role of phospho-STAT3 in miR-3189-3p-mediated effects remains to be determined.

♦ S27

Effect of Triiodo-L-Thyronine Treatment and Reperfusion on Postmyocardial Infarction Recovery

Samantha Seitter, OMS IV; C. Pol, PhD; V. Rajagopalan, PhD; Y. Zhang, PhD; Y. Chen, MD, PhD; A. M. Gerdes, PhD

New York Institute of Technology College of Osteopathic Medicine, Old Westbury

Introduction: Despite advances in the management of myocardial infarctions (MI), many patients develop debilitating chronic conditions such as heart failure; a more adequate treatment is needed. MIs trigger low thyroid function in cardiac tissue and it is known that hypothyroidism alone can lead to dilated heart failure while promoting a maladaptive change in myocyte shape and impaired coronary blood flow. Therefore, restoration of thyroid function may beneficially improve remodeling and outcome in MI patients.

Hypothesis: Thyroid hormone management of MI with reperfusion of the culprit artery leads to improvements in infarct remodeling due to reduced apoptosis, stimulation of angiogenesis, and increased survival of myocytes in the infarcted and border zones.

Methods: Adult female Sprague-Dawley rats underwent surgery to occlude the left anterior descending coronary artery for 1 hour creating an infarction. After 1 hour, the ligation suture was released and the chest closed. Shams were treated similarly without applying a constriction. Oral T3 (8µg/kg/d) or placebo treatment was started right after surgery. LV function and remodeling were assessed by echocardiography and hemodynamics (Millar catheter) after 2 months. The hearts were then removed, weighed, and sliced for fixation in formalin for paraffin embedding or frozen in liquid nitrogen. Serum was collected 1 week after surgery and 2 months after surgery. Western blots are used to assess the changes in fetal genes responsive to thyroid hormones.

Results: Infarct/Reperfusion (IR) resulted in an infarcted area of 20%±5% in the untreated group and 17%±6% in the T3 treated group. T3 treatment resulted in an estimated increase of non-infarcted LV/septum tissue of 15%. IR rats showed impaired contractility as indicted by reductions of fractional shortening and maximal rate LV pressure development (dP/dt_{max}). T3 treated IR rats showed normalized dP/dt_{max}. Diastolic function was impaired as shown by increased maximal rate of pressure decline (dP/dt_{min}) and tau, with some improvement in the T3-treated group.

Conclusion: These results suggest that treatment with T3 after post-MI reperfusion improves contractility/relaxation while also increasing viable myocardium.

S28

Inhibition of Doxorubicin-Induced Mitochondrial Fragmentation Alleviates Cardiac Myoblast Injury

Michael Catanzaro, OMS IV[1]; Satoru Kobayashi, PhD[2]; Qiangrong Liang, MD/PhD[2]

[1]New York Institute of Technology College of Osteopathic Medicine (NYIT-COM), Brooklyn; [2]Department of Biomedical Sciences, NYIT-COM, Old Westbury

Background: Doxorubicin (DOX) is a widely used and highly effective chemotherapeutic antineoplastic agent that is associated with severe cardiotoxicity. New strategies are needed to reduce DOX cardiotoxicity. Recent studies have implicated excessive mitochondrial (MT) fragmentation in DOX-induced cardiomyocyte death. However, it is unclear whether the mitochondrial fragmentation mediates the DOX-induced cell damage in cardiomyocytes (CMs) or is a compensatory response.

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Objective: To determine whether inhibiting mitochondrial fragmentation can reduce the cardiotoxicity associated with DOX.

Methods: An H9c2 cardiac myoblast cell line was pretreated with siRNA targeting dynamin-related protein 1 (DRP-1), a protein required for MT fission, before DOX administration. After infection with an adenovirus-encoded mitochondria-targeting protein, DsRed, changes in MT morphology were monitored with confocal microscopy. Morphologic descriptors (particle size, form factor [FF], aspect ratio [AR]) were measured using ImageJ analysis software (National Institutes of Health) to quantify changes in the degree of MT fragmentation. Propidium iodide (PI), which enters dead cells through disrupted membranes, was used to quantify the extent of DOX-induced cardiomyocyte injury. The protein expression levels of apoptotic markers, cleaved caspase-3 and cleaved PARP, were measured with Western blotting.

Results: Morphometric analysis demonstrated that pretreatment of cells with DRP-1 small interfering RNA (siRNA) markedly diminished mitochondrial fragmentation as shown by decreased FF ($P<.01$), AR ($P<.01$), and mean mitochondrial size ($P<.01$) in DOX-treated cells (n=26) compared with control (n=22) and siRNA-treated cells (n=28). Pretreatment of cells with DRP-1 siRNA markedly diminished DOX-induced CM death as shown by percentage of PI-positive cells (mean [SD] control, 18.0 [10.3] vs DOX, 64.9 [15.1], $P<.01$; DOX, 64.9 [15.1] vs DOX + siRNA, 26.2 [18.6], $P<.01$; n=3), cleaved caspase-3, and cleaved PARP. Additionally, siRNA reduced baseline CM death as demonstrated by PI staining ($P<.05$).

Conclusion: Downregulation of DRP-1 prevents DOX-induced mitochondrial fragmentation and protects cells against DOX-induced cardiotoxicity.

♦ S29

Effects of Resveratrol on Mitochondrial Mitophagy in Doxorubicin-Treated Cardiomyocytes

Lyudmila Burina, OMS II; Satoru Kobayashi, PhD; Qiangrong Liang, MD, PhD

Department of Biomedical Sciences, New York Institute of Technology College of Osteopathic Medicine, Forest Hills

Introduction: Doxorubicin (DOX) is a widely used chemotherapeutic agent with limited therapeutic utility owing to its dose-dependent cardiotoxic effects. It is critical to identify an adjunctive cytoprotective agent that will attenuate DOX cardiotoxicity without affecting its chemotherapeutic potential. Resveratrol (RSV) is a plant-derived polyphenol shown to exert cardioprotective effects in DOX-treated cardiomyocytes, but its mechanisms of cardioprotection remain unknown. Preliminary studies have demonstrated excessive mitochondrial degradation in DOX-treated cells.

Hypothesis: Resveratrol protects against DOX-induced cardiomyocyte injury by inhibiting excessive degradation of mitochondria through the autophagy-lysosome pathway (mitophagy).

Methods: H9C2 cardiac myoblasts were infected with an adenovirus encoding a mitophagy reporter (Mt-Rosella) and cultured under 44 conditions: 0.5 uM DOX, 5 uM RSV, 5 uM RSV + 0.5 uM DOX, and ethanol (control). Necrotic cell death was quantified by propidium iodide staining, and apoptotic cell death was determined by the cleavage of caspase 3 and PARP using Western Blotting. Mt-Rosella is composed of a mitochondrial targeting sequence and a RFP-GFP fusion protein. Red puncta in merged confocal microscopy images indicate mitochondrial fragments that are being degraded in lysosomes, where the pH sensitive GFP is quenched. The numbers of red puncta were counted to quantify the level of mitophagy.

Results: Compared with ethanol control, DOX significantly increased the number of propidium io-

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dide–positive cells (8.37 vs 0.5; $P<.05$), which was attenuated by RSV pretreatment (8.37 vs 3.63, $P<.5$). Resveratrol also inhibited DOX-induced apoptosis as shown by the extent of PARP cleavage. Finally, DOX triggered mitophagy in H9C2 cells as indicated by the red puncta, which was reduced by RSV.

Conclusion: Resveratrol protects against DOX-induced cell death in H9C2 cardiac myoblasts, which are associated with reduced mitochondrial degradation. Further studies are needed to determine whether the cardioprotective effect of RSV is mediated by its ability to inhibit mitophagy.

S30

Dioxin Exposure Causes Pseudarthrosis in a Rat Spine Fusion Model

Christian Park, OMS II[1]; Sharath Bellary, MD[2]; Kevin Sonn, MD[2]; Chawon Yun, PhD[2]; Joseph Nicolas[2]; Sohaib ZHashmi, MD[2]; John Nelson, MD[2]; Amruta Ashtekar, MS[2]; Marco Mendoza, MD[2]; Michael Nickoli, MD[2]; Jason Ghodasra, MD[2]; Anjan Ghosh[2]; Stuart Stock, PhD[3]; Wellington KHsu, MD[2]; Erin L. Hsu, PhD[2]

[1]Alabama College of Osteopathic Medicine, Dothan; [2]Department of Orthopaedic Surgery, Northwestern University, Chicago, Illinois; [3]Department of Cellular and Molecular Biology, Northwestern University, Chicago, Illinois

Introduction: Cigarette smoking inhibits bone healing and leads to increased rates of pseudoarthrosis, but the mechanisms behind these effects are controversial. 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (dioxin) negatively affects bone quality and is suggested to affect osteoblast differentiation.

Hypothesis: Dioxin exposure inhibits spinal fusion in a rat posterolateral arthrodesis model, and its effects on osteoblast precursors are mediated by the aryl-hydrocarbon receptor (AHR).

Methods: In vitro studies were performed to elucidate the involvement of the AHR by co-treatment with receptor blockers α-naphthoflavone (ANF) and resveratrol. Rat bone marrow stromal cells (BMSC) were grown under standard or osteogenic conditions and treated with vehicle, dioxin, ANF, resveratrol, nicotine, or combined treatments. The effects of dioxin and co-treatment with AHR antagonists on alkaline phosphatase (ALP) activity, cell migration, and mineralization were determined. In vivo, female Long-Evans rats were pretreated with dioxin or vehicle for 6 weeks and then underwent a bilateral posterior lumbar fusion (PLF) across the L4-L5 transverse processes. Treatments continued until the rats were killed at 4 weeks after the operation. A third group was treated with dioxin for 6 weeks, followed by treatment cessation for 4 elimination half-lives to allow for recovery from dioxin exposure (dioxin-recovery), before PLF. Bone formation and spine fusion were evaluated using radiographs, micro computed tomography , manual palpation scoring, and histologic analysis.

Results: Dioxin inhibited osteoblast progenitor cell migration, ALP activity, and mineralization capacity. Resveratrol and ANF co-treatment rescued this effect. Radiographs showed decreased bridging bone formation in dioxin-treated rats. Fusion scores in dioxin-treated and dioxin-recovery rats were significantly lower than control animals, suggesting that the effects of dioxin exposure on the capacity for new bone formation are prolonged. On the other hand, although fusion rates were significantly reduced in dioxin-treated animals relative to controls (50% vs 100%, respectively; $P<.01$), the reduced fusion rate in dioxin-recovery animals was not statistically significant (80% vs 100%), indicating that spinal fusion capacity could potentially be recovered after a prolonged removal from dioxin exposure. Four successfully fused spines per group underwent micro computed tomography analysis, and although new bone volumes trended downward for both dioxin-treated groups, the differences were not significantly different from successfully fused controls.

Conclusion: Dioxin and dioxinlike compounds may be at least partially responsible for the effects

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of smoking on bone healing, and AHR antagonists such as resveratrol—a nutraceutical found in red wine and available as an over-the-counter supplement—may have therapeutic potential for improving bone regenerative capacity and spine fusion rates in the cigarette-smoking population.

S32

Regulation of COX-2 Expression by Flavonoids in Colorectal Cancer Cells

Joshua Ziehm, OMS II; Dan Dixon, PhD

Kansas City University of Medicine and Biosciences College of Osteopathic Medicine, Missouri

Introduction: Colorectal cancer (CRC) is the third most common cancer among American adults and a leading cause of mortality. Commonly observed in CRC tumors is elevated expression of the prostaglandin synthase cyclooxygenase-2 (COX-2), which is the main chemoprevention target of aspirin and COX-2-selective inhibitors (eg, Celebrex) in both human and animal models of CRC. COX-2 expression is normally tightly controlled and reserved for times of tissue damage and inflammation where it functions as the rate-limiting step in prostaglandin formation. In normal intestinal epithelium, the COX-2 mRNA is targeted for rapid decay through its 3'-untranslated region (3'UTR), whereas loss of rapid mRNA decay leads to COX-2 over expression in tumors.

Hypothesis: Flavonoid compounds will inhibit COX-2 expression in CRC cells by promoting rapid COX-2 mRNA decay.

Methods: As a means to identify small molecule compounds that can promote COX-2 mRNA decay in CRC cells, a "suicide gene" method was developed in CRC cells where 3'UTR-dependent RNA decay was necessary for cell survival. High-throughput screening of >1000 compounds had identified the structurally-related flavonoid compounds: chrysin, apigenin, kaempferol, and hesperetin. Validation of these flavonoids to selectively promote cell viability was assayed using MTT growth assay and cell staining. COX-2 protein and mRNA expression after flavonoid treatment of CRC cells were assessed using western blot and quantitative real-time polymerase chain reaction (RT-PCR) analysis, respectively.

Results: Flavonoid treatment permitted the COX-2 3'UTR to function in attenuating suicide gene expression allowing for cell survival. All flavonoids promoted at least a 2-fold reduction in endogenous COX-2 expression with most efficient inhibition occurring with kaempferol > hesperetin > chrysin ≥ apigenin.

Conclusion: We conclude from these in vitro studies that COX-2 expression is significantly reduced with treatment of flavonoid compounds. These results provide mechanistic insights into the established chemopreventive effects of flavonoid compounds (found abundantly in fruits and vegetables) in CRC.

S36

Effects of Enforced Exercise on *Caenorhabditis elegans* Longevity

James Akers, OMS II; James Lakers, BS; Christopher Carls, BS; Bethany Hampton, BS; Predrag Krajacic, MD

West Virginia School of Osteopathic Medicine, Lewisburg

Introduction: The benefits of exercise in humans and other mammals are well known. Methods of inducing exercise in higher-model organisms (eg, mouse using treadmill) are well established. However, the efforts of inducing exercise in *Caenorhabditis elegans* have been limited to a liquid environment. *C elegans* exhibits electrotaxis—a behavior specific to nematodes that allows the use of the electric field as a powerful stimulus to control the worms' movement. We used this behavior to initiate and maintain locomotion to induce enforced exercise. Although this behavior is obligatory, expo-

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sure to the electric field has no adverse effect on the ability of worms to survive or reproduce. The aim of this study was to determine the effects of enforced excessive exercise on the lifespan of *C elegans*.

Hypothesis: Moderate exercise will have a beneficial effect, whereas repeated excessive exercise will have a detrimental effect on the lifespan of *C elegans*.

Methods: To make the worm treadmill, a specially formulated gel and buffer were placed in a classic DNA-electrophoresis box. The treadmill also included a power source, a microscope camera, a small fan, and a thermometer. Wild type worms were divided into excessive exercise, moderate exercise, and no exercise groups. One hundred fifty hypochlorite synchronized worms for each group were transferred to the gel, and a voltage of 4 v/cm or greater was applied. The poles of the electric field were alternated as the nematodes reached the end of the gel. The excessive exercise group was run once a day on the treadmill until greater than 75% of the worms were no longer engaging in forward movement toward the anode (about 60 minutes). The moderate exercise group was on the treadmill for 30 minutes daily. The no exercise group served as the control and was not submitted to the treadmill.

Results: The excessive exercise group with a median survival of 9 days had a statistically significant decrease in longevity compared with wild type (13 days). The moderate exercise group had a statistically significant increase in longevity with median survival of 14 days.

Conclusion: Exercise was induced in crawling *C elegans*. This study provides the foundation for potential pharmacologic and physiologic evaluations in exercised nematodes.

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S37

Exercise, but Not Overexpression of HSP70, Decreases Gut Transit Time in a Mouse Model of Diet-Induced Obesity

Daniel Linden, OMS II[1]; Aneesh Chawla, MS[2]; Mae Ciancio, PhD[1]; Christian Evans, PT, PhD[3]

[1]Midwestern University/Chicago College of Osteopathic Medicine (MWU/CCOM); [2]Biomedical Sciences Program, MWU/CCOM; [3]Physical Therapy Department, MWU/CCOM, Downers Grove, Illinois

Introduction: A high-fat (HF) diet is known to cause weight gain and increased adiposity. Voluntary exercise (Ex) prevents diet-induced obesity through a multifactorial process. We recently showed that continuous transgenic (Tg) heat shock protein 70 (HSP70) expression can prevent diet-induced obesity. This study explored the possibility that Ex and HSP70 expression prevent diet-induced obesityby decreasing gut transit (GT) time and limiting nutrient absorption.

Hypothesis: Exercise and Tg HSP70 overexpression will alter GT in vivo.

Methods: Nontransgenic (NTg), male, C57Bl/6 littermates (5 weeks) were separated into 44 groups: low-fat diet (LF; 10 kcal % fat)/sedentary (Sed) (n=6); LF/Ex (n=5); HF (60 kcal % fat)/Sed (n=5); and HF/Ex (n=6). Male, HSP70 Tg littermates (5 weeks) were placed on the HF/Sed protocol (n=7). HSP70 Tg mice were created by injecting a villin promoter driven HSP70 targeting vector into C57Bl/6 oocytes. Weekly body weights were recorded, but GT and 24-hour food intake were assessed at week 13. For GT determination, mice were individually housed in specially designed metabolic cages and gavaged with 0.1 mL of 0.5 mM 70 kDa fluorescein isothiocyanate (FITC)-dextran. Hourly fecal FITC-dextran content was measured by reading the fluorescence intensity (excitation = 492 nm, emission = 518 nm) and used to determine GT. All procedures were approved by MWU's An-

imal Care and Use Committee, and IACUC on June 2, 2014. Data are expressed as mean (SEM), with significance determined at $P<.05$. A *t* test was used to compare NTg HF/Sed and Tg HF/Sed groups, and a 2-way ANOVA was used to compare NTg LF/Sed, LF/Ex, HF/Sed, and HF/Ex groups with a Sidak posthoc test.

Results: An HF diet resulted in diet-induced obesityin NTg mice ($P<.01$), but Ex was able to normalize body weight ($P<.01$). Tg HSP70 expression also prevented HF diet-induced obesity($P<.01$), normalizing body weight. The 24-hour food intake was increased by Ex ($P<.01$), but not by Tg HSP70 expression compared with NTg. Ex significantly increased GT rate (Hill Slope): LF/Sed=0.14 (0.02); LF/Ex=0.21 (0.01); HF/Sed=0.13 (0.03); HF/Ex=0.19 (0.04) (Ex effect $F[1,18] = 4.97$, $P<.05$). There was no significant effect of diet or overexpression of HSP70 on GT ($P>.05$).

Conclusion: Ex, but not HSP70 expression, shortened GT in a mouse model of diet-induced obesity. These findings demonstrated that Ex may exert an effect on body weight through GT, but that Tg HSP70 protection from diet-induced obesity is not due to shortened nutrient absorption time.

S38

Mechanism of Dorsal Axis Curvature Formation in Polycystic Kidney Disease

Sarah Raza, OMS IV[1];
Aleksandr.Vasilyev, MD, PhD[2]

[1]Department of Basic Sciences, New York Institute of Technology College of Osteopathic Medicine (NYIT-COM), Glen Cove; [2]Department of Biomedical Sciences, NYIT-COM, Old Westbusy

Introduction: Autosomal dominant polycystic kidney disease (ADPKD) is due to mutations in the genes, *PKD1* and *PKD2*; it is one of the most common debilitating genetic disorders, affecting many organ systems. The exact mechanism by which mutations in the PKD genes cause these various defects remains unknown. Zebrafish are a widely used model of PKD. They develop prominent renal cysts, along with dorsal axis curvature (DAC). Our study aims to identify tissue-level interactions underlying DAC.

Hypothesis: The DAC is due to a decreased rate of elongation and nuclear proliferation in the dorsal myotomes of *PKD2* morphant zebrafishes.

Methods: In this experimental study, zebrafish embryos at a 1- to 2-cell stage were microinjected with polycystin-2 morpholino, inducing renal cysts and DAC. The embryos were imaged at 1, 2, and 8 days postfertilization to record their myotome morphology, which was analyzed with ImageJ (National Institutes of Health) and Excel (Microsoft Corp). Immunofluorescence staining (green fluorescent protein, 4',6-diamidino-2-phenylindole) and confocal imaging were performed on *PKD2* morphants and controls at 2 days postfertilization to determine the quantity of nuclei in the ventral and dorsal myotome segments and to correlate it with myotome length.

Results: The morphology of individual myotome segments was examined in control and *PKD2* morphant embryos; in the morphants, the dorsal myotome had a significantly decreased rate of elongation as early as 1 day postfertilization ($P<.05$). In addition, the *PKD2* morphants had significantly taller myotomes ($P<.05$) and significantly shorter total trunk length when compared with controls ($P<.05$). Contrary to the hypothesis, *PKD2* morphants did not have a significant difference between the quantity of nuclei per muscle fiber in the ventral and dorsal segments, as compared with controls. However, aberrant segmentation, consisting of boundary defects, was exclusively present in the dorsal myotome.

Conclusion: Dorsal curvature in *PKD2* morphants is driven by a decreased rate of elongation of the dorsal myotome. Contrary to the initial hypothesis, there was no evidence that DAC is due to decreased nuclear proliferation in the dorsal myotome seg-

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ments. Instead, the results suggest that the underlying mechanism of DAC is due to a defect in convergence extension because shortening of the myotomes is accompanied by a relative increase in the height of individual segments. Further studies should reveal the molecular mechanisms underlying convergence extension defects and somite dysgenesis.

S39

Acquired Factors in the Plasma of Burn Patients Are Inhibitory to Erythrocyte Lineage Commitments Leading to Anemia

Harris Shaikh, OMS II[1]; Shirin Hasan, PhD[2]; Richard L. Gamelli, MD[3]; Kuzhali Muthumaiappan, PhD[2]

[1]West Virginia School of Osteopathic Medicine, Lewisburg; [2]Burn and Shock Trauma Research Institute, Loyola Stritch School of Medicine, Maywood, Illinois; [3]Trauma, Surgical Critical Care and Burns, Loyola Stritch School of Medicine

Introduction: Each year, 450,000 patients are treated for burns in United States. Patients with major burns develop critical anemia not responsive to erythropoietin (Epo). Blood transfusions remain the only viable treatment option but are often associated with severe immune consequences. Understanding the cellular mechanisms causing anemia in burn patients is critical for pursuing alternate treatments. A previous report from this laboratory revealed a significant reduction in late-stage erythroblast development owing to limited generation of colony-forming units erythroid in patients with a 20% or greater total body surface area (TBSA) burn. The previous study used ex vivo expansion and differentiation of circulating hematopoietic stem cells, which reside within peripheral blood mononuclear cells (PBMCs). Erythroblasts begin to express Epo receptors only from the colony-forming units erythroid stage onward, and burn patients are resistant to Epo. Therefore, it is likely that the developmental defects in burn patients start at an earlier stage in hematopoiesis and are influenced by the burn-mediated microenvironment.

Hypothesis: Acquired factors in the plasma of burn patients will inhibit erythropoiesis at the stage of megakaryocyte erythrocyte progenitor (MEP) generation.

Methods: Informed consent and institutional review board approval were obtained to collect blood from study participants. Plasma and PBMCs were isolated after ficoll-gradient centrifugation from 5 adult volunteers and 1 burn patient (29% TBSA burn). Peripheral blood mononuclear cells (2×10^6) were incubated with either burn plasma or autologous control plasma for 1 hour before being placed in liquid culture with myeloid growth factor cocktail (stem cell factor, interleukin 3, and granulocyte-macrophage colony-stimulating factor) for 5 days. A combination of magnetic bead and flow cytometry methods were used to isolate MEPs ($CD34^+$, $CD38^+$, $CD45RA^-$, $CD123^-$) from the lineage negative fraction of nonadherent cells from phase I culture.

Results: Viable, nonadherent cells, retrieved from burn plasma– or control plasma–treated PBMCs were comparable. Nonetheless, the percentage of MEPs in the lineage-negative fraction was significantly decreased in burn plasma vs control plasma (35% decrease; P=.004).

Conclusion: The erythroid potential of hematopoietic stem cells residing in control PBMCs was impeded by the addition of plasma from a burn patient, indicating that the burn-induced microenvironment is inhibitory to erythroid lineage commitment, leading to anemia.

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S40

Alterations in Brain Energy Metabolism Pathways in Young-Adult Carriers of the Alzheimer Risk Factor APOE4

Daniel Shonebarger, OMS III; Patrick Pangle, MBs; Michelle Perkins, MSc, Lauren Ballina, BA, Johana Vallejo, PhD; Garilyn Jentarra, PhD; Jonathan Valla, PhD

Midwestern University/Arizona College of Osteopathic Medicine, Phoenix

Introduction: The ε-4 allele of apolipoprotein E (*APOE4*) provides the strongest established genetic risk for developing late-onset, sporadic Alzheimer disease (AD). While a definitive, mechanistic link between AD and *APOE4* has not yet been established, there exists significant overlap in brain energy metabolism functional deficits between these populations. 18-Fluoro-deoxyglucose positron emission tomography studies on young adult *APOE4* carriers show reductions in cortical glucose metabolism similar to reductions observed in the brains of persons with AD. The authors previously showed that postmortem posterior cingulate cortex (PCC) samples from a young adults with *APOE4*(+) exhibited reduced electron transport chain complex IV activity. In an effort to elucidate the foundation of these functional declines, the expression of various proteins involved in brain energy metabolism was examined.

Hypothesis: Expression levels in the energy metabolism pathways will be significantly altered.

Methods: Frozen postmortem PCC samples from persons aged 18 through 40 years from the previous study were prepared for sodium dodecyl sulphate-polyacrylamide gel electrophoresis and Western blotting as well as quantitative polymerase chain reaction.

Results: Samples from 12 individuals with *APOE4* and 12 without *APOE4* were analyzed. Carriers of the *APOE4* allele demonstrated significantly ($P<.05$) increased expression of proteins and RNA involved in glucose transport (glucose transporter 3, 107% increase over noncarriers) and metabolism (hexokinase-1, 69%). Increased protein expression was also found for neuronal ketone body and lactate transport (monocarboxylate transporter [MCT]2, 117%), ketone metabolism (succinyl-CoA:3-keto-acid CoA transferase, 50%), and oxidative phosphorylation (complex I, 148%; complex II, 115%; complex IV, 165%). Conversely, MCT1, the principal blood-brain barrier and astrocyte ketone body and lactate transporter, showed a substantial but not statistically significant (35%, $P=.059$) reduction in protein expression in participants with *APOE4*.

Conclusion: These striking and widespread increases in PCC metabolic protein expression in *APOE4*(+) samples, in the face of the previously-reported decrease in oxidative metabolic function in the same participants, suggest substantial dysregulation of brain energy metabolism in *APOE4* carriers. The solitary decrease in expression apparent in MCT1 points to possible involvement of blood-brain barrier ketone or lactate transport, and/or a potential differential response between astroglia and neurons. Determination of the foundation for these disparate responses may provide a mechanism of *APOE4*-associated AD risk and clues to AD cause.

S41

Exercise Induces Rapid Exhaustion in *Caenorhabditis elegans* Duchenne Muscular Dystrophy Mutants

Christopher Carls, OMS II; James AkersAkers, BS; Bethany Hampton, BS; Predrag Krajacic, MD

West Virginia School of Osteopathic Medicine, Lewisburg

Introduction: The nematode, *Caenorhabditis elegans*, displays a specific locomotion response to various stimuli, including food, chemicals, and electricity. *C elegans*' response to electricity has been previously well described and termed *electrotaxis*—the repeatable behavior of crawling toward

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the negative pole when subjected to an electric field. This behavior has been used in various capacities, primarily in worm sorting platforms. For the first time, we used this behavior to initiate and maintain locomotion to perform exhaustion tests.

Objective: To examine the response of the Duchenne muscular dystrophy (*dys-1*) mutant to excessive exercise, compared with wild type as well as other neuromuscular mutants.

Hypothesis: Endurance will be decreased in dys-1 mutants, when compared with the wild type worms. Also, the dys-1 mutant's muscles will display structural damage.

Methods: The worm treadmill consists of a specially formulated gel and buffer placed in a classic DNA-electrophoresis box, a power source, a microscope camera, and an infrared thermometer to monitor gel temperature. 50-150 hypochlorite synchronized worms were transferred to the gel, and a voltage of 4 V/cm or greater was applied. The poles of the electric field were alternated as the nematodes 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. To examine muscle structure, after reaching the point of exhaustion, the worms were stained with rhodamine-phalloidin (which stains myosin filaments) and imaged using fluorescence microscopy.

Results: Time to exhaustion when compared with wild type was statistically significantly decreased for *dys-1* worms. Additionally, distance ran showed a statistically significant difference in *dys-1* worms. Postexhaustion *dys-1* staining revealed shortened muscle cells.

Conclusion: Our platform provides a unique phenotype for dys-1 mutants comparable to the DMD mouse model that was previously lacking. It offers a cost-effective and simple way for initial screening of novel pharmacologic compounds to find a cure for this currently incurable disease.

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S43

Inhibitory Effect of Caffeic Acid Phenethyl Ester on Human Multiple Myeloma Cell Growth: Induction of Apoptosis and Oxidative Stress Pathways

Nam Pham, OMS III[1]; Hana Paek, BA[2]; Marie Bozman, AS[2]; Xinyu Wang, PhD[2]

[1]Georgia Campus-Philadelphia College of Osteopathic Medicine (GA-PCOM), Suwanee; [2]School of Pharmacy, GA-PCOM, Suwanee

Introduction: Caffeic acid phenethyl ester (CAPE), a naturally occurring compound found in bee propolis, has shown inhibitory effects on multiple myeloma (MM) cell proliferation. To better understand the mechanism of this effect, MM cell apoptosis, pathway-focused gene expression, and protein studies were conducted.

Hypothesis: An inhibitory effect on MM cells is exerted by CAPE through apoptosis and oxidative stress pathways.

Methods: Cell growth inhibition: Cultured MM 8226 cells were treated with 1, 5, 10, and 20 μM of CAPE for 6 hours, 24 hours, or 48 hours, respectively. Cell viability was measured using the Presto Blue assay. Apoptosis assay: Cultured MM 8226 cells were treated with 1, 5, 10, 25, and 50 μM of CAPE for 24 hours. A FITC Annexin V Apoptosis Detection Kit (BD Biosciences) was used to detect apoptosis of MM 8226 cells treated with CAPE. Stress/toxicity pathway analysis: Cultured MM 8226 cells were treated with 20 μM of CAPE or 0.1% dimethyl sulfoxide(vehicle control) for 6 hours. Total RNA was prepared from treated cells, and gene expression was analyzed using specific PCR arrays (Stress & Toxicity PathwayFinder, RT2Profiler PCR Array; SABiosciences, Qiagen). A cutoff of 2-fold in terms of fold changes between CAPE treated and control groups was selected. A *P* value less than .05 was used to identify statistically significant up- and downregulated genes. Protein studies: Cultured MM 8226 cells were

treated with 20 µM of CAPE and a vehicle control of 0.1% dimethyl sulfoxide for 24 hours. A Western blot analysis was performed using the Li-cor reagent kit and mouse antibodies against upregulated genes found in the gene expression study.

Results: Growth of MM 8226 cells in both dose and time-dependent manner is inhibited by CAPE. Apoptosis of MM 8226 cells was detected after 24-hour CAPE treatment and found to be dose dependent. A number of genes of MM 8226 cells were identified with expressions significantly altered by 20 µM of CAPE at 6 hours. Those genes, heme oxygenase-1, ferritin heavy polypeptide-1, thioredoxin reductase-1, and NADPH:Quinone oxidoreductase (NQO-1) were related to oxidative stress. Protein products of the NQO-1 gene were confirmed with the protein analysis.

Conclusion: The inhibition of growth of MM cells by CAPE may be due to an induction of MM cell apoptosis. The expression of genes involved in oxidative stress pathways was significantly altered. This finding may provide an insight into the mechanism of CAPE's inhibitory effects on MM cell proliferation.

S45

Determination of Antibiotic Resistance Patterns of the Enteric Pathogen *Plesiomonas shigelloides*

Samantha Garbo, OMS II[1]; John-Matthew Swords, BS[1]; Jerry Marlin, MS[1]; Tracey Taylor, PhD[2]; John Taylor, PhD[1]

[1]Kansas City University of Medicine and Biosciences College of Osteopathic Medicine, Missouri, [2]Oakland University, Rochester, Michigan

Introduction: *Plesiomonas shigelloides* are gram-negative, motile, rod-shaped bacteria that can cause gastroenteritis and, more rarely, extraintestinal infections. The diarrheal symptoms are usually self-limiting, although in some cases, symptoms may become more serious. Immunocompromised individuals, infants, children, and elderly persons are especially susceptible to serious, life-threatening extraintestinal infections such as septicemia, meningitis, septic arthritis, osteomyelitis, and pneumonia. Determination of the antibiotic resistant properties of *P shigelloides* is important to efficiently and properly treat infected individuals. Although there have been some research studies of antibiotic resistance of *P shigelloides* strains, the resistance mechanisms and genes involved remain largely unknown to date.

Objective: To identify the antibiotics that *P shigelloides* are resistant and sensitive to, and determine the genes involved in the resistance mechanism(s).

Methods: We have previously created a bank of over 1000 *P shigelloides* ATCC strain 14029 chromosomal transposon mutants with the transposome EZ-Tn5 Tnp (Epicentre). These mutants were tested for susceptibility to chloramphenicol, gentamicin, tetracycline, and doxycycline at a low concentration that the wild type strain is resistant to, to test for loss of resistance, and also at a high concentration that the wild type strain is sensitive to, to test for a gain of resistance.

Results: Four of these mutants showed a gain of resistance to doxycycline, and 1 showed a gain of resistance to gentamicin.

Conclusion: It is known that the number of *P shigelloides* that invade human epithelial cells and become internalized increases with infection time; therefore, it is crucial to administer the correct antibiotics to patients in a timely manner. The authors plan to perform sequence analysis to identify the chromosomal location of the transposon insertion of the resistant bacterial mutant(s), and then investigate the resistance mechanisms further.

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S46

Brain Ketone and Cholesterol Metabolism Is Altered in Young Adult *APOEe4* Carriers

Jon-Peter Meckel, OMS II; Michelle Perkins, MS; Daniel Shonebarger, BS; Patrick Pangle, MS; Lauren Ballina, BS; Jon Valla, PhD

Midwestern University/Arizona College of Osteopathic Medicine, Phoenix

Introduction: Alzheimer disease (AD) is a progressive dementia that affects approximately 5 million Americans. The greatest risk factors for the development of AD are increasing age and apolipoprotein E (APOE) genetic status. The *APOE* gene encodes the ApoE protein and is found in 3 different isoforms in humans: ε2, ε3, and ε4. ApoE ε4 has been linked to an increased level of risk for AD development. ApoE is used for lipid and cholesterol transport, and since very little cholesterol or fatty acids are able to pass through the blood-brain barrier, these vital components must be synthesized de novo and transported between cells. Ketone bodies (acetoacetate and β-hydroxybutyrate) are important substrates for the synthesis of these lipids during brain development and throughout life.

Hypothesis: The transport and anabolic processing of ketone bodies for cholesterol synthesis will be altered in the brains of young-adult *APOEε4* carriers.

Methods: The sample comprised postmortem specimens of posterior cingulate cortex from human young adult (mean age, 29 years) carriers (n=12) and noncarriers (n=12) of the *APOEε4* allele. Previously frozen cortical blocks were mechanically homogenized and lysed with a radioimmunoprecipitation assay buffer, then analyzed via Western blot to examine the relative expression levels of the ketone body transporters (monocarboxylate transporter [MCT]1 and MCT2), and acetoacetyl-CoA transferase (AACS), the cytosolic enzyme responsible for the initial conversion of acetoacetate to acetoacetyl-CoA, the first step in the synthesis of cholesterol and other lipids from ketone bodies.

Results: Expression of the primary blood-brain barrier and astroglial ketone body transporter MCT1 was decreased in *APOEε4* carriers 35% ($P<.06$) from noncarrier levels. In contrast, carrier expression of the neuronal transporter MCT2 showed an increase of 117% over noncarriers, and AACS expression increased 56% ($P<.05$, 2-tailed *t* tests).

Conclusion: The altered expression of MCT1, MCT2, and AACS suggests that *APOEε4* carriers manifest a chronic alteration in ketone body use for cholesterol synthesis. The decrease in MCT1 expression suggests potential dysregulation in the import of ketone bodies into the brain. Given the known role of ApoE as a lipid transporter and the critical need for de novo synthesis of brain lipids, altered ketone body processing and cholesterol handling in the brain is suggested as a mechanism for the significant association of *APOEε4* and AD.

S47

Loss of Neuronal Plasma Membrane Calcium Adenosinetriphosphatase in Parkinson Disease: Are Microglia the Culprit?

Patricia Riggs, OMS II; Paul T. Ramlow, MS; Asma Zaidi, PhD

Kansas City University of Medicine and Biosciences College of Osteopathic Medicine, Missouri

Introduction: Calcium (Ca^{2+})overload and toxicity is implicated in the progressive death of dopaminergic (DA) neurons in Parkinson disease (PD). Dopaminergic neurons must be especially efficient at removing Ca^{2+} because of the additional Ca^{2+} influx from autonomous pace-making activity. The plasma membrane Ca^{2+}-ATPase (PMCA) is the major mechanism for extruding Ca^{2+} out of neurons. The PMCA activity and protein levels undergo a progressive decline in PD. The PMCA is sensitive to oxidative stress, which causes loss of activity and proteolytic degradation. Increased oxidative

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stress is a component of the pathogenesis of PD, but the source of the reactive oxygen species is not entirely clear. The goal of this study was to determine whether the inflammatory molecules and reactive oxygen species generated by activated microglia influence neuronal PMCA activity and protein levels.

Hypothesis: Lipopolysaccharide (LPS)-mediated microglial activation will decrease PMCA activity and protein levels.

Methods: BV-2 microglia were co-cultured with SH-SY5Y neuroblastoma cells using Dulbecco's Modified Eagle's medium and 10% fetal bovine serum. BV-2 cells were exposed to LPS (100 pg/mL-1 µg/mL) for 24 hours and activation assessed by monitoring the translocation of NF-kB to the nucleus using confocal microscopy. Cell viability was measured by the MTS assay. Total protein in cell lysate was measured by a bicinchoninic acid assay kit. The PMCA protein levels were measured by immunoblotting and PMCA activity by measuring the formation of Pi released on Ca^{2+}-dependent ATP hydrolysis by the Malachite Green method.

Results: Lipopolysaccharide-mediated activation of BV-2 microglia was confirmed by increased NF-kB translocation to the nucleus. Activated BV-2 cells did not alter neuronal viability when co-cultured together. However, there was a significant decline in neuronal PMCA protein levels. Reduction in PMCA protein levels occurred in a dose-dependent manner (40% at 100 pg/mL; 75% at 1 µg/mL LPS). No change occurred in β-actin under these conditions, showing equal loading of protein and the selectivity of the effects of LPS on PMCA.

Conclusion: Our results indicate that activation of microglia causes a reduction in neuronal PMCA protein levels, and this effect is dose-dependent. Loss of PMCA protein compromises the ability of neurons to regulate intracellular Ca^{2+}, which may lead to calcium-mediated toxicity and cell death in PD.

S49

Effects of Hypoxia on the Neuronal Plasma Membrane Ca^{2+}Adenosinetriphosphatase

Brandon Overholt, OMS II; Paul T. Ramlow, MS; Asma Zaidi, PhD

Kansas City University of Medicine and Biosciences College of Osteopathic Medicine, Missouri

Introduction: The plasma membrane calcium (Ca^{2+}) adenosinetriphosphatase (ATPase) (PMCA) uses the energy of ATP hydrolysis to pump Ca^{2+} out of neurons against a 10,000-fold gradient. It plays a critical role in maintaining Ca^{2+} homeostasis, optimal neuronal function, and cell survival. In previous studies, the authors have shown a progressive decline in PMCA activity and protein levels in brain aging and under conditions of oxidative stress. Reduction of PMCA not only disrupts Ca^{2+} homeostasis but also increases the susceptibility of cells to various stimuli that elevate $[Ca^{2+}]_i$. Elevation of $[Ca^{2+}]_i$ has been linked to ischemia-reperfusion injury in stroke. However, the role of the PMCA has not been investigated. The goals of the current study were to determine the effects of hypoxia on PMCA activity and protein levels. Such studies will help understand the biochemistry of cerebral ischemia.

Hypothesis: The PMCA activity will decrease after exposing cells to hypoxia.

Methods: SH-SY5Y cells were cultured in Dulbecco's modified Eagle's medium and 10% fetal bovine serum and differentiated using 10 µM retinoic acid and 80 nM TPA. Cells were exposed to hypoxia (1% O_2) in a Trigas incubator for 4 hours. Cells were collected and lysed using a hypotonic buffer. Total protein was determined using the BCA kit. PMCA was assessed by the Malachite green method, which measures the Pi released from Ca^{2+}-mediated ATP hydrolysis. Immunoblots were performed to assess PMCA protein levels.

Results: Cells exposed to a 4-hour hypoxia showed no evidence of altered cell viability. Measurement

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of PMCA activity, however, showed about a 40% reduction at each of the free Ca^{2+} concentrations tested (0.5-10 µM) (n=5). Immunoblots showed no change in PMCA protein levels or the presence of aggregates and/or PMCA breakdown products. Ongoing studies are being done to reintroduce O_2 to hypoxic cells to determine whether the loss of PMCA activity is reversible or a permanent damage to the protein.

Conclusion: Exposure of cells to hypoxia causes significant decline in PMCA activity. It is likely that free radicals created within the hypoxic cell environment cause oxidative damage to the protein, which results in loss of activity. The observation that loss of PMCA activity occurs before cell death suggests that dysregulation of Ca^{2+} homeostasis preceded cell death and may play a causative role in the cell death process.

S50

Oxidative Stress Is Involved in the Sanguinarine-Mediated Sensitization of Cervical Cancer SiHa Cells to TRAIL

Whitney Wilson, OMS III; Eric Romney, BS; Bernardo Chavira, BS; Anjali Taneja, BS; Vinay J. Nagaraj, PhD

Midwestern University/Arizona College of Osteopathic Medicine, Glendale

Introduction: Cervical cancer is primarily caused by the human papillomavirus (HPV), which transforms normal cervical cells into cancerous cells that are highly resistant to radiation and chemotherapy. 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 DR5 via reactive oxygen species in primary effusion lymphoma cells.

Hypothesis: Since sanguinarine may lead to oxidative stress and upregulation of DR5, it can potentially sensitize SiHa cells to TRAIL and lead to apoptosis.

Methods: Cultured SiHa cells were exposed to sublethal 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.

Results: Treatment of SiHa cells with a combination of sanguinarine and TRAIL led to a significant reduction in cell viability. Significant increase in reactive oxygen species was observed, and caspase activation assays confirmed the induction of apoptosis.

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 precise link between reactive oxygen species and the possible upregulation of DR5 needs further investigation. This knowledge will enable us to devise more effective treatments for patients who have this devastating disease.

S51

Depletion of Intracellular ATP Using a Synthetic ATP-Binding Protein: A Novel Approach to Cancer Therapy

Andrew Fontes, OMS II; Dennis Datuin, BSc; Matt Hamada, BSc; Vinay J. Nagaraj, PhD; Shaleen Korch, PhD

Midwestern University/Arizona College of Osteopathic Medicine, Glendale

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Introduction: The use of chemotherapeutic agents that target key metabolic processes in cancer cells is an important therapeutic strategy. As a result of reduced mitochondrial activity, adenine triphosphate (ATP) is produced mainly by glycolysis and lactic acid fermentation in the cytosol of cancer cells (Warburg effect). Even with reduced production, ATP is still a vital energy carrier that is crucial for various biochemical reactions in cancerous cells. Thus, interfering with the production and availability of ATP offers a new approach to cancer therapy. To assess this idea, a synthetic ATP-binding protein, DX, was tested as a novel cancer therapy.

Hypothesis: Reduced ATP availability, due to the expression of DX in cervical cancer HeLa cells, will interfere with cellular metabolism and significantly affect cell viability.

Methods: For controlled expression, DX was cloned into the pcDNA5/TO expression vector (with an N-terminal FLAG tag), whose expression is driven by a tetracycline-regulated CMV promoter. Cultured T-REx HeLa cells (which stably express the tetracycline repressor protein) were transfected with pcDNA5/TO::DX. As a control for transfection and DX expression, T-REx HeLa cells were transfected with pcDNA5/TO/lacZ and cultured under identical conditions. To determine the subcellular localization of DX, indirect immunofluorescent cytochemical staining was performed on transfected HeLa cells using a monoclonal anti-Flag M2 primary antibody (mouse) and antimouse immunoglobulin G–fluorescein isothiocyanate secondary antibody. The impact of DX expression on cell viability and morphology was assessed using a tetrazolium-based colorimetric cell viability assay and by light and fluorescent microscopy.

Results: HeLa cells expressing DX experienced reduced viability and altered morphology compared with cells expressing lacZ alone. These results suggest that ATP depletion potentiates cell death in HeLa cells. Fluorescence microscopy revealed that the DX-FLAG fusion protein is primarily restricted to the cytoplasm of HeLa cells.

Conclusion: A reduction in intracellular ATP levels mediated by a synthetic ATP-binding protein significantly affects the viability of cervical cancer HeLa cells. The reduction in ATP, and the molecular consequences of this on biochemical pathways and cell viability requires further investigation. We suggest that synthetic proteins, such as DX, could be used to target the metabolism of cancer cells and has the potential for use as a chemotherapeutic agent.

♦S54

Submicron Topographical Patterns Enhance Peripheral Nerve Regrowth Ex Vivo

Casey Sigerson, OMS II[1]; Joshua Gasiorowski, PhD[2]; Michele Fornaro, PhD[3]

[1]Midwestern University/Chicago College of Osteopathic Medicine (MWU/CCOM), Downers Grove, Illinois; [2]Department of Biomedical Sciences, Midwestern University, College of Health Sciences; [3]Department of Anatomy, MWU/CCOM, Downers Grove, Illinois

Introduction: Peripheral nerve damage is a common complication of many types of injuries and disease states. While the peripheral nervous system has been shown to regenerate spontaneously, the extent to which it does so independently is often insufficient to fully restore motor function and sensation. Such loss of capabilities can have a severe impact on the quality of life. Currently, there is a great deal of successful research in improving axonal growth through the use of biochemical growth factors. While these growth factors do cause significant axonal sprouting, the regrowth is often uncontrolled and random in direction. Such growth is inefficient in delivery of neurites to more distant structures. Organized and direct axonal growth should increase the delivery of these neurites and lead to a more functional recovery.

Objective: To control the direction of axonal growth using nano- to micron-scale grooves as topographical cues.

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Hypothesis: Axons will use the biophysical signals as a guide and propagate parallel to them, which will lead to a longer effective axonal length.

Methods: For the purposes of this study we used ex vivo explants of dorsal root ganglia (DRGs) as our experimental model. Cervical and thoracic DRGs were harvested from adult mice and placed in culture plates patterned with varying sizes of anisotropic grooves. Three groove widths were tested: 200 nm, 700 nm, and 2000 nm. A chemically identical flat surface was used as a control. All groups were maintained in serum free medium (SFM) with 5 ng/mL nerve growth factor (NGF) for 6 days. At that point, they were fixed, immunolabeled with nerve-specific markers, and visualized using fluorescent confocal microscopy.

Results: Imaging and analysis significantly demonstrated that axons align and grow in a linear fashion along the 700- and 2000-nm grooves vs the control. No significant difference was seen for the 200-nm grooves. This manner of direct propagation also significantly extended the average radius of growth of the axons in the 700- and 2000-nm test groups. There was at least a 50% increase in the average effective axonal length seen in these groups over the control.

Conclusion: These results can translationally be applied toward novel treatments to directionally and longitudinally enhance spontaneous nerve regeneration across distances greater than those that occur naturally.

S56

Acute Exercise Effects on Carnitine Biosynthesis and Transport in Liver and Kidney

Frank Cusimano, OMS II[1]; Yonas Getachew, MD[2]; Tom Broderick, PhD[3]

[1]Midwestern University/Arizona College of Osteopathic Medicine (MWU/AZCOM), Glendale; [2]Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas; [3]Department of Physiology, MWU/AZCOM, Glendale

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Introduction: Carnitine is an essential cofactor in the oxidation of lipids for energy formation. During exercise, carnitine shuttling of lipids from the cytosol into the mitochondria is enhanced. This is reflected by an increased extraction of carnitine from the plasma. Following exercise, plasma carnitine levels return to normal levels, suggesting that carnitine biosynthesis mechanisms are active.

Hypothesis: The plasma carnitine increase will result from either an increase in the enzymes involved in carnitine biosynthesis or an increase in the reabsorption of carnitine from the urine.

Objective: To study the effects of acute exercise on carnitine biosynthesis and transport.

Methods: Male Swiss Webster mice were exposed to acute exercise consisting of a 90-minute exercise session at 80% VO_2 max. The livers and kidneys were harvested at 4 different time points. Tissue from nonrunning mice served as control. Protein analysis of g-butyrobetaine hydroxylase (BBH), the rate-limiting enzyme in the synthesis of carnitine, and the organic cation transporter (OCTN2), required for carnitine reabsorption from the urine and transport in the liver, were analyzed via Western blot analysis. Gene expression levels of BBH, OCTN2, and other key enzymes were measured by messenger RNA (mRNA) analysis through quantitative real-time polymerase chain reaction (qRT-PCR).

Results: After exercise, there was a 1.5 increase in BBH gene expression at 4 hours and a 1.5 increase in OCTN2 in the liver compared with control. However, no change was seen in the protein expression of BBH and OCTN2 in the liver. In the kidney, there was an immediate 2-fold increase in the protein level of BBH and a 1.4 increase in OCTN2 until 4 hours. Gene expression showed a 1.7 increase in BBH until 8 hours after exercise and no change in OCTN2. CPT-1a, an enzyme involved in the carnitine shuttle, and PGC-1b, a cofactor known to regulate mitochondrial oxidative energy metabolism, were increased 1.5 and 1.8, respectively, with their

peak levels at 4 hours after exercise. No significant change was seen in the mRNA levels of PGC-1a, ALD9a1, TMLHE, PPAR-a, PPAR-g, PPAR-d, and acyl-CoA; enzymes and products involved in the biosynthesis and regulation of carnitine.

Conclusion: The increase in plasma carnitine seen after exercise may be due to the increase in OCTN2 in the kidney or the increase in BBH in the liver and kidney. The biosynthesis of carnitine in the kidney seems to be most responsive to the stress of a single exercise session.

B12*

Drug Delivery Using Layered Double Hydroxide Nanoparticles Based on Zinc and Aluminum for Pancreatic Cancer Therapy

Vinay Nagaraj, PhD; Xiaodi Sun, PhD; Mac Martin, BS; Jiten Mehta, BS; Sandwip Dey, PhD

Midwestern University/Arizona College of Osteopathic Medicine, Glendale

Introduction: Pancreatic cancer is a devastating disease with an extremely high rate of mortality. Current chemotherapy strategies have been largely ineffective due the rapid development of drug resistance in cancerous cells as well as a unique tumor microenvironment that makes drug delivery very challenging. There is a great need for the development of alternative strategies for effective drug delivery that can improve patient outcomes. Nanoparticles, in particular those based on layered double hydroxide (LDH) nanoparticles have great potential as carriers of therapeutic molecules. The authors tested a novel formulation of LDH particles based on zinc and aluminum for their drug delivery capabilities. As proof-of-concept, cultured pancreatic adenocarcinoma BxPC-3 cells were used for the delivery of valproic acid using the novel LDH nanoparticles.

Hypothesis: Zn-Al-based LDH nanoparticles can effectively deliver valproic acid to BxPC-3 cells and affect the viability of the pancreatic cancer cells.

Methods: Newly synthesized Zn-Al-based LDH nanoparticles were interchelated with valproic acid or fluorescein isothiocyanate (FITC). Cultured BxPC-3 cells were exposed to a wide range of nanoparticle concentrations. Cell viability was assessed using a tetrazolium-based colorimetric assay. Nanoparticle uptake was assessed by fluorescence measurements.

Results: BxPC-3 cells treated with valproic acid interchelated LDH nanoparticles showed a significant reduction in cell viability, whereas exposure to nondrug-interchelated LDH nanoparticles did not affect the viability of cells. Fluorescence measurements indicated that FITC-interchelated nanoparticles showed a greater degree of active uptake rather than passive uptake by BxPC-3 cells.

Conclusion: Zn-Al–based LDH nanoparticles have good potential for use as drug delivery agents. Their lack of innate cytotoxicity and ability to be taken up actively by cells indicate that they can be further developed for the in vivo delivery of chemotherapeutic agents.

*This abstract was not submitted by a student.

Medical Education

♦S3

Experiential Learning: An Irreplaceable Tool in Osteopathic Student Education

Timothy J. Bikman, OMS III[1]; John Ford, OMS III[2]; Deborah Schmidt, DO[3]; Lance Ridpath, MS, OMS III[2]

[1]West Virginia School of Osteopathic Medicine (WVSOM), Lewisburg; [2]WVSOM, Lewisburg; [3]Osteopathic Principles and Practice Department, WVSOM, Lewisburg

Introduction: Second-year students at West Virginia School of Osteopathic Medicine (WVSOM) participate in a 10-week osteopathic manipulative medicine (OMM) clinic. The clinic provides osteopathic diagnosis and treatment in an academic setting to community members free of charge. Our

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research addressed how experience with patients affect a student's self-perceived skills, desire to continue education of OMM, and use of osteopathic medicine in clinical practice.

Hypothesis: Experiential learning in preclinical osteopathic medical education improves a student's perception of osteopathic medicine, confidence in its application, and desire for continued learning within the field.

Methods: More than 100 second-year osteopathic medical students from WVSOM participated in a 10-question Likert scale survey before and after their student OMM clinic experience. The survey was anonymously administered via Survey Monkey. Students were divided into groups of 2 and assigned 2 patients from the community to see weekly, for 5 weeks each. The students had 1½ hours to assess, diagnose, treat, and document each visit, all overseen by an osteopathic physician. Data were analyzed using SAS version 9.2. For most analyses, independent 2-sample *t* tests were used. When the data were not normally distributed, the Mann-Whitney 2-sample nonparametric test was used.

Results: Regarding the statement, "I can confidently diagnose somatic dysfunctions correctly and efficiently," the *t* test resulted in a *P* value of <.001. These results were based on a preprogram mean (SD) of 3.56 (0.94) and a postprogram mean (SD) of 3.96 (0.82). The statement, "I can confidently treat somatic dysfunctions" produced similar results with an equivalent *P* value. In response to the statement, "I will apply to a residency program that has a strong osteopathic focus," the Mann-Whitney test produced a *P* value of <.001. These values were based on a preprogram mean (SD) of 2.76 (1.03) and a postprogram mean (SD) of 3.31 (1.06). Similar results were observed regarding the statement, "I will use OMT [osteopathic manipulative treatment] at least once a week as a practicing physician."

Conclusion: This study provided evidence that the preclinical use of OMT increases student's confidence, their desire to continue education in osteopathic residency programs, and their use of OMT in practice. These data suggest that preclinical experiential learning provides significant benefits to osteopathic medical education.

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S53

Model to Predict Student Performance on the Comprehensive Osteopathic Medical Licensing Examination-USA Level 1 Based on the Medical College Admission Test, Undergraduate Grade Point Average (GPA), and Osteopathic Medical School GPA

Lynn Jeffrey, OMS IV[1]; Elizabeth K. McClain, PhD[2]

[1]Kansas City University of Medicine and Biosciences College of Osteopathic Medicine (KCUMB-COM), Missouri; [2]Academic Affairs, Primary Care Medicine, KCUMB-COM

Objective: To investigate relationship between prematriculation and academic variables and performance on Comprehensive Osteopathic Medical Licensing Examination-USA (COMLEX-USA) Level 1 at a single osteopathic medical school.

Hypothesis: There is a positive association between undergraduate grade point average (GPA), Medical College Admission Test (MCAT), medical school first-year GPA, and COMLEX-USA Level 1 performance.

Methods: A nonexperimental design used retrospective review of student cohort's academic data from 2009-2013. Independent variables were undergraduate institutions attended, undergraduate cumulative GPA, science GPA, science hours, first MCAT, highest MCAT, times MCAT taken, and medical school GPA including the first year and the spring semesters of the first through second year. The dependent variable was COMLEX-USA Level 1. Descriptive statistics included frequency, mean (SD), identifying variables by sex and by cohort year. Bivariate correlations and linear regression explored associations and the ability of variables to predict COMLEX-USA Level 1 performance.

Results: A total of 1263 student academic records were analyzed (43.5% female, 56.5% male) from 2009-2013, with academic year cohort range of 239 to 265 students. Undergraduate GPA included cumulative (mean [SD]$\bar{x}$, 3.58 [0.281]) and science ($\bar{x}$, 3.52 [0.259]). 84.7% of students took the MCAT 1 to 2 times, and 14.7% took the MCAT 3 to 4 times (first MCAT score: $\bar{x}$, 24.43 [3.62] and highest MCAT score: $\bar{x}$, 26.37 [2.78]). Medical school means included first-year GPA ($\bar{x}$, 3.00 [0.571]), first-year spring GPA ($\bar{x}$, 3.04 [0.501]), and second-year spring GPA ($\bar{x}$, 3.05 [0.453]). A linear regression model used predictor variables (1) cumulative undergraduate GPA; (2) first MCAT score and; (3) first-year GPA, with the dependent variable COMLEX-USA Level 1. A significant proportion of the total variation in COMLEX-USA Level 1 was predicted by the model. All 3 variables were significant predictors, and the model accounted for 61% of the variance in COMLEX-USA Level 1, $F(3, 673)=350.545$; $P=.000$; $R^2=0.61$. Small negative associations were found between number of COMLEX-USA Level 1 attempts and first-year GPA, undergraduate science GPA, and COMLEX-USA Level 1. Negative associations were also found between number of MCATs taken and medical school GPA, highest MCAT score, and COMLEX-USA Level 1. All associations were statistically significant at a .05 *P* value.

Conclusion: This study validates previous studies supporting associations between undergraduate GPA, MCAT score, medical school GPA, and COMLEX-USA Level 1 performance. This study also identified first MCAT score as an early predictor of future performance. Furthermore, number of MCATs taken was associated with lower MCAT score, lower medical school GPA, and was minimally associated with lower COMLEX-USA Level 1 score. Using predictors of performance can reduce barriers and facilitate early intervention for at-risk students.

Health Policy

S12

Water and Sanitation Status in Rural Honduras: A Comparison Across Honduran Villages Serviced by VCOM Continuous Care

Timothy Layng, OMS III; Jessica Hovancik, BS; Steven Murphy, BS; Gina Meletakos, MS; Dalia Meisha, PhD; Dean Sutphin, PhD; Alexis Stoner, MPH

Edward Via College of Osteopathic Medicine–Virginia Campus, Blacksburg

Introduction: The World Health Organization (WHO) and the United Nations International Children's Emergency Fund (UNICEF) established the Joint Monitoring Programme (JMP) for water supply and sanitation to report and monitor the status of water supplies and sanitation globally, and at the country level. These goals parallel the Edward Via College of Osteopathic Medicine (VCOM) research and public health initiatives to establish sustainable communities and continuous health care in underserved Latin American communities.

Objective: To describe the current water quality and sanitation status among 5 villages surrounding Tegucigalpa, Honduras.

Methods: This case study was performed during a VCOM medical mission trip in April 2014. The sample included heads of households who presented at VCOM medical outreach from the villages of Guajire, Campamento, Comayagua, San Juancito, and El Vino resulting in a convenience sampling. The research adapted a survey from WHO's Core Questions on Drinking-Water and Sanitation for Household Surveys. Additionally, a panel of experts including US and international representatives established validity of the adapted survey.

Results: One hundred seventy-three patients participated. Findings across villages indicated that natives to Comayagua and El Vino traveled the furthest to obtain water, up to 3 hours in some

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cases, whereas a majority of those who live in San Juancito traveled less than 5 minutes. Most residents treated their water before consuming it, and the methods varied within the villages, most frequently adding bleach/chlorine (86 [56.7%]) and boiling (44 [30.6%]). The majority of residents use improved sources of drinking water (136 [78.6%]). Residents from Comayagua (43.5%) and Guajire (33.3%) only had access to unimproved drinking water sources. By comparison, the village of San Juancito, which is the most rural and most sparsely populated, had the highest access to improved water (100%).

Conclusion: Variations among villages require different interventions to make improvements; similarly, within villages, there are differences that require individual attention by the household. The authors recommend new initiatives by VCOM in partnership with the Honduran Ministry of Health to address health disparities associated with current water quality and sanitation and a longitudinal study to measure progress and sustain improvements.

S13

Low Birth Weight in Kansas

Tiffany Toomey, OMS II[1]; Jung WhanYoon, MPH, MS[1]; Kanwar Singh,BA[1]; Kesha Baxi, BS[1]; Alison Scharber, MPH, RDN[1]; Jake Martinez, BS[1]; Emily Freeman, MS[1]; Richard R. Suminski, MPH, PhD[1]; James V. Guillory, DO[2]

[1]Kansas City University of Medicine and Biosciences College of Osteopathic Medicine, Missouri; [2]A.T. Still University–School of Osteopathic Medicine in Arizona, Mesa

Introduction: In the United States, associations between low birth weight (LBW) and infant mortality and morbidity vary among geographical locations. No studies on LBW have been conducted in the state of Kansas, which has compiled a wealth of data on pregnancy and birth outcomes that could elucidate previously unknown factors affecting infant mortality and morbidity.

Objective: To determine the maternal and health care system factors associated with LBW in Kansas, with a primary focus on the importance of private insurance to optimize birth outcomes.

Hypothesis: The prevalence of LBW is significantly lower for women in Kansas having vs not having private insurance at the time of pregnancy.

Methods: Birth certificate data were merged with Medicaid eligibility files for 37,081 single vaginal births occurring during a 1-year period. Univariate associations between maternal characteristics and infant birth outcomes were studied using a χ^2 for categorical variables and a *t* test for continuous variables. Multiple logistic regression was used to determine the independent contributions of variables to LBW. Owing to multiple comparisons, only those variables with a *P* value of .001 or less in univariate analysis were entered into the regression models. Stepwise analysis was used to determine the final best-fit model. Low birth weight was defined as a live birth where the infant weighed less than 2500 g. The use of existing data was approved by the University's institutional review board.

Results: The rate of LBW infants was 5.5% overall, 10.8% for African Americans, and 5% for whites. Mothers without private insurance were 34% more likely to give birth to a LBW infant (adjusted OR, 1.34; 95% CI, 1.13-1.58), and to have comorbidity or to receive late or less prenatal care. Women receiving inadequate prenatal care were more likely to have a LBW infant compared with women receiving adequate plus prenatal care (adjusted OR, 4.40; 95% CI, 3.89-4.98). Mothers receiving adequate plus prenatal care who did not have private insurance had the highest adjusted OR of having an LBW infant (4.48; 95% CI, 3.81-5.27).

Conclusion: Insurance status, prenatal care, and maternal health during pregnancy are critical to the delivery of an infant of normal birth weight in the state of Kansas. This study has important implications regarding current health care reform issues.

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S19

Promoting Exercise and Reducing Sedentary Behavior in Lower-Income, African American Neighborhoods

Emily Freeman, OMS III; Tiffany Toomey, BA; James Yoon, MPH, MS; Kanwar Singh, BA; Kesha Baxi, BS; Alison Scharber, MPH, RDN; Jake Martinez, BS; Richard R. Suminski, MPH, PhD

Kansas City University of Medicine and Biosciences College of Osteopathic Medicine, Missouri

Introduction: African Americans residing in low-income, urban neighborhoods suffer disproportionately from chronic diseases such as obesity and diabetes. Theory posits that this is partly due to relatively low physical activity levels resulting from built environments that inhibit active lifestyles. Attempts to alter aspects of the built environment to promote physical activity in African American populations have achieved partial success.

Objective: To examine the efficacy of Neighborhoods On the Move (NOM) for promoting physical activity among low-income, urban-dwelling African Americans.

Hypothesis: The percentage of residents meeting physical activity guidelines will increase to a significantly greater extent in neighborhoods participating in NOM compared with neighborhoods not participating in NOM.

Methods: A socioecological intervention, NOM uses community-based participatory research methods to promote physical activity, mainly by addressing environmental conditions. A pretest, posttest within and between groups design was used to determine whether NOM had a significant effect on physical activity and sedentary behavior patterns. All participants were adults who signed consent forms approved by the university's institutional review board.

Results: At-home surveys were conducted with 986 residents (93.8% African American; mean [SD] age, 35.9 [15.0] years; 61.2%, less than high school education) from 6 lower-income, African American neighborhoods participating in NOM and 6 matched control neighborhoods. At the 12-month follow-up, residents in NOM compared with control neighborhoods experienced significant increases in minutes per week jogging and weight training and days per week biking and playing sports and significant decreases in per week TV watching. No within- or between-group differences were seen in the percentages of residents meeting physical activity guidelines.

Conclusion: This study indicates that NOM is effective for promoting certain types of exercise and reducing sedentary behavior in African Americans living in low-income, urban areas.

S48

Respiratory Health Among Low-Income Residents of Subsidized Housing Complexes

Kanwar Singh, OMS II; Jake Martinez, OMS II; Kesha Baxi, OMS II; Alison Scharber, Scharber; Emily Freeman, OMS II; Tiffany Toomey, Toomey; James Yoon, DO Candidate; Richard Suminski, DO

Kansas City University of Medicine and Biosciences College of Osteopathic Medicine, Missouri

Introduction: The negative health effects of smoking tobacco are well known. In addition, exposure to second and third hand smoke also causes health problems. Recently, the Kansas City (KC), Missouri Housing Authority developed a policy restricting smoking in its housing developments. The policy was implemented July 1, 2014.

Objective: To compare respiratory health between KC housing authority residents and residents of the Lawrence housing authority where a smoking policy has been in place for 4 years.

Hypothesis: Respiratory health is significantly better in Lawrence compared with KC housing authority residents.

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Methods: Trained researchers delivered the reliable and valid St George Respiratory Health Survey to residences at 3 KC and 2 Lawrence housing developments 1 month before the implementation of the smoking policy in KC. All adults older than 18 years were eligible for the study. The survey asked about acute problems with respiration, such as frequency of wheezing and coughing as well as ability to perform activities of daily living (ADL). Respiratory health scores ranged from 1 to 4, with 1 being poor and 4 equivalent to good respiratory health. For 9 ADLs, participants reported either having trouble (scored 0) or not having trouble (scored 1) doing a given ADL. The %ADL variable was calculated as the number of nontroubling ADLs divided by 9. Independent *t* tests and χ^2 tests were used to compare respiratory health and %ADL between housing developments and between current smokers and nonsmokers. The university's institutional review board approved the research project.

Results: A total of 72 (14% return rate) KC and 66 (21.4% return rate) Lawrence residents returned a completed survey. Smoking rates were significantly different between developments, with 56.9% of KC and 15.2% of Lawrence residents classified as current smokers. Respiratory health scores and %ADL were not significantly different between smokers and nonsmokers or between housing developments. In the KC residents, 73% of nonsmokers supported the smoking policy, and 46% of smokers supported the policy ($P<.05$).

Conclusion: Respiratory health and the ability to perform ADLs were not related to smoking or living in a smoke-free vs smoking environment. The implementation of a smoking policy was related to significantly lower smoking rates.

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S55

Education and Beliefs Regarding Safe Drinking Water and Sanitation Practices Across Selected Communities in Veron, Dominican Republic

Jennifer Kelley, OMS II[1]; Timothy Immomen, BS[1]; Chandra Jennings, MPH[1]; Kristy Fincher, BS[1]; Dalia Meisha, PhD[2]; Dean Sutphin, PhD[2]; Alexis Stoner, MPH[1]

[1]Edward Via College of Osteopathic Medicine (VCOM)–Carolinas Campus, Spartanburg, South Carolina; [2]VCOM–Virginia Campus, Blacksburg

Introduction: The Punta Cana Ecological Foundation is attempting to provide rural village residents with clean drinking water and improved sanitation through a project called Source of Life. While public health education on safe water and sanitation could be helpful, there is a lack of information on current practices and the extent of knowledge the residents possess. This IRB approved study assessed the status of water and sanitation and the extent of public health education in 5 Dominican Republic communities serviced by the Edward Via College of Osteopathic Medicine: Veron, Hoyo de Fruisa, La Cristinita Church, Christian Church Domingo Maiz, and Pueblo Nuevo.

Hypothesis: The communities included in the study lack education and access to safe drinking water and sanitation.

Methods: During a medical outreach trip in July 2014, a convenience sample of adults were given a survey adapted from the WHO's Core Questions on Drinking-Water and Sanitation for Household Surveys and a health assessment survey developed by an expert panel of US and international representatives.

Results: A total of 142 adults completed the survey. Although differences were observed across villages, overall, 34% of participants did not believe their drinking water to be safe. In Domingo Maiz, 63% believed their water to be unsafe, 94% used

unimproved drinking water sources, and 42% reported at least 1 or more cases of a diarrheal disease that year. In Pueblo Nuevo, 36% reported their water was unsafe water, 8.3% of residents were using unimproved drinking water sources, and 82% reported at least 1 or more cases of a diarrheal disease that year. Overall, 27% of residents believe diarrheal disease can be transmitted through unsafe water, yet no respondent at the Veron Clinic site and Hoyo de Fruisa believe that intestinal disease or malaria can be transmitted through contaminated water. More than 50% of the respondents in these 2 villages also reported no access to education on clean water use.

Conclusion: Access to safe drinking water and sanitation varies by community, but all Dominican Republic communities studied have limited access to safe drinking water and limited public health education on safe water practices. Public health education on water and sanitation is recommended to parallel water and sanitation initiatives by the special project in Domingo Maiz and improvements needed in other selected villages in Veron Dominican Republic.

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