## 2018 AOA Research Abstracts and Poster Competition

This issue of *The Journal of the American Osteopathic Association (JAOA)* features abstracts from the posters that were presented at the 61st Annual American Osteopathic Association (AOA) Research Focus Track. This year's abstracts were organized into the following categories:

- basic sciences (see page e101)
- clinical (see page e143)
- health services (see page e193)

This year's AOA Research Focus Track took place in San Diego, California, on Saturday, October 6, and Sunday, October 7, during the AOA's 2018 Osteopathic Medical Conference and Exposition (OMED 18). Abstracts submitted by students into the poster competition (designated with "♠") were judged, and first- and second-place winners were announced at OMED 2018 (designated with "★"). The JAOA did not receive copyright release forms from the authors of abstracts C43, C48, or HS7; thus, those abstracts are not included here.

To enhance the readability of this special feature, abstracts have been edited for basic *JAOA* style only. The content has not been modified; information provided reflects information that was submitted by the primary author, including professional degrees and affiliations. Neither the AOA's Bureau of Clinical Education and Research nor the *JAOA* assume responsibility for the abstracts' content. (doi:10.7556/jaoa.2018.163)

### **Basic Sciences**

### ◆B1—Chronic Diseases & Conditions

## Relationship Between DRG Axonal Location Within Continuous Topographies and Outgrowth

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Significance: Regarding nerve cell growth, studies have demonstrated that biochemical signals play a crucial factor in cell shape, differentiation, cell adhesion, and axonal guidance. However, this growth is also affected by surrounding physical parameters. This is apparent especially during embryonic development, in which axonal nerve growth is influenced by extracellular scaffolds produced by embryonic cells. Unfortunately, patients coping with nerve lesions do not have the same luxury that their younger embryonic selves once had. The ability to direct neurite outgrowth for hopeful reattachment has been extensively studied for apparent clinical purposes. Nano- and micro-patterned substrates have been used as tools to direct neurite outgrowth and demonstrate their capacity to respond to topographic features in their microenvironments. Focused on the effects of biomimetic topography, soluble neurotrophic factors and fixed ECM components on the regeneration of mouse DRG explants, our laboratory has demonstrated a topographical method for influencing the directionality and overall axonal growth length in a given period of time. In this experiment, the DRGs were cultured on plates individually patterned with either a 400 nm, 800 nm, 1400 nm, or 4000 nm pitch size (pitch = ridge width + groove width) using soft lithography techniques. Results demonstrated that for a ridge size of 1400 nm, both axonal outgrowth and conferred directionality were significantly increased. The reason why murine axons prefer to travel along a topography of a certain size is still unclear.

**Specific Aims:** Our laboratory has previously shown that neurotrophic supplementation and biomimetic topography can be used in simultaneity to preferentially guide growth of regenerating axons and increase the total

amount of growth of mouse DRG explants. We would like to further our research by investigating the specific locations that axons are traveling within the continuous topographies, as well as the relationship this has with outgrowth length. Beyond that, we would like to investigate the effect cultured Schwann cells have on axonal growth when placed in conjunction with continuous topography.

Aims: Aim 1: Using SEM, identify whether the DRG axon outgrowths cultured on a 1600 nm pitch size plate have a preferential location. Suspected locations include on top of the ridges, within grooves, and/or suspended between adjacent ridges. From there, we are interested in whether or not axonal growth location has a significant influence on outgrowth length. Aim 2: Utilizing SEM, based on width (W1) measurements taken from axons grown on a 1600 nm (P1) pitch size, and measurements of human DRG's axon widths (W2), an appropriate pitch size (P2) was extrapolated for optimal outgrowth for severed nerve ends that are currently treated with smooth-walled collagen conduits.

Experimental Design: Adult NIH Swiss mice were euthanized and DRG explants were harvested from the animal. Explants were kept in F12 (Gibco<sup>TM</sup>) on ice awaiting plantation. Microgroove surfaces are created in a process of photolithography, the final surface made of Norland Optical Adhesive 81 (NOA81, Norland Products, Inc). Ridge feature size are set at 1600 nm, with 800 nm as ridge width and 800 nm as groove width. DRG explants are anchored on a plastic sterile dish with Matrigel. Matrigel (Corning, Inc) is mixed with serum free media (SFM) in a 1:1 ratio. 10 ug of Matrigel/SFM is pipetted onto the grooved surface per explant. The volume of Matrigel/SFM is distributed on the surface in a circular pattern with a round spatula covering the entirety of the surface.

A single plate holds 3 to 4 explants at each corner of the square microgroove surface. The plate is covered and placed in the incubation chamber at 37°C and 5% CO2 for a minimum of 30 minutes or until polymerized. A 3-mL mixture of SFM and NGF (5 µg/mL) is pipetted on to the surface to nourish the DRGs. The DRGs are returned to the incubation chamber for 6 days at 37°C and 5% CO2. SFM is changed on day 3. A combination of Light microscopy, scanning electron microscopy (SEM), and confocal microscopy were used for growth rate and migration analysis of neuroglia and axonal fibers. On day 6, samples are fixed in formalin and stained for neuron antibodies (anti-β-tubulin, anti-peripherin) as well as cell adhesion molecules (NCAM1). A Nikon Confocal Microscope is used with NIS Element software. DRGs are imaged with the 10x objective. Image is used for quantification of neurites in various directions and at regular distance thresholds. To obtain data on migration, rate of neuronal growth, directionality of growth, and density of growth, a digital "quantification grid" (Q Grid) is layered over the confocal image. For SEM imaging, samples were fixed in 4% paraformaldehyde for 1 hour, rinsed 3 times with PBS, and 3 times for 5 min with distilled water. Subsequently, they were dehydrated with a graded ethanol series of the following dilutions in dH<sub>2</sub>O:  $50\% (1 \times 2 \min) - 75\% (1 \times 5 \min) - 80\% (1-15)$ min) 95%  $(2 \times 15 \text{ min}) - 100\% (2 \times 20 \text{ min})$  and left to dry under the air flow. Samples were then silver-coated to enable or improve the imaging of samples and imaged in SEM to identify the position of growing axons on the topographical surface and measure the averages size of murine axons. For AIM 2, human specimens of DRG were collected from cadavers in the anatomy laboratory. After being fixed in 4% paraformaldehyde, samples are dehydrated, embedded in paraffin, and sectioned (10 µm sections) using a microtome.

Results: Under SEM, axons growing within the 1600 plate had an average width of 555 nm, while those growing on flat plate controls had an average width of 407 nm. All axons growing on 1600 were observed to be growing strictly on ridges; thus, location may play a factor in growth. Conclusion: Axons grown on 1600 nm plates preferentially grew on top of the ridges as opposed to within the grooves. This insight may be beneficial when designing a conduit for patients suffering nerve end lesions. The Cadaver DRG axons had widths of around 2 um, suggesting a topographical conduit with ridge widths of 2.85 um for optimal growth with patients suffering from peripheral nerve lesions.

### ◆B2—Chronic Diseases & Conditions

# **Intracranial Arterial Calcification: A Cadaveric Study**

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Hypothesis: Arteriosclerosis represents the leading cause of mortality in industrialized societies, yet its mechanisms are still poorly understood. An important etiological factor of arteriosclerosis is calcium deposition within the tunica media, internal elastic lamina (IEL), and tunica intima of arterial walls, which can contribute to diminished arterial elasticity. Risk of cerebrovascular events can be independently predicted by calcification of the intracranial internal carotid artery (iICA). Investigating the distribution of calcium in the iICA is therefore an important step in understanding the pathophysi-

ology of arteriosclerosis. To this end, cadaveric arterial tissue representing populations of advanced age were examined. We qualified calcification in the strata of distal iICA, and downstream from it, proximal and distal M1 segments of the middle cerebral artery (M1p and M1d), hypothesizing that prevalence of calcification in vessel wall layers would reflect prevalence in populations of advanced age.

Significance: Although arterial calcification can be interpreted as a biomarker of ongoing atherogenesis, our prior investigations of peripheral vascular disease demonstrated that calcification can be found in the intima, IEL, and media of otherwise non-atheromatous vessels. The link between calcification and atherogenesis has been explored by myriad studies demonstrating a variety of mechanisms, including cell-mediated inflammation and loss of normal signaling between media and IEL or endothelium. Dissociation of near-IEL vascular smooth muscle cells of the tunica media can induce differentiation into migratory and prolific phenotypes, thereby contributing to intimal thickening and atherogenesis. IEL calcification, therefore, may presage atherosclerosis. Insight into this link may allow prophylaxis in vulnerable populations, thereby enhancing the body's intrinsic capacity to heal itself.

Methods: Calcification was examined in 3 intracranial arterial segments: (1) the distal extent of the iICA immediately proximal to the circle of Willis (n=11); (2) the most proximal part of the middle cerebral artery's M1 segment, proximal to the circle of Willis (M1p, n=14); and (3) the most distal part of the middle cerebral artery's M1 segment, adjacent to branches of the insular segment (M1d, n=14). These vessels were extracted from 15 cadaver crania unilaterally on the left side (20% male, 80% female), ages ranging from 63 to 94 years (mean=80.7, median=81.0), and stored in a solution of 1x phosphate buffer serum with 0.02% sodium azide.

Cryopreservation of isolated vascular tissue involved overnight equilibration in 30% sucrose with 0.02% sodium azide, followed by embedding in optimal cutting temperature compound and sectioning into 10 µm slices by use of a cryotome. Samples were mounted onto a slide and then stained with alizarin red to detect calcium. Microscopic images were graded by 2 observers for the frequency of calcium deposition in the media, IEL, and intima, and atherosclerotic lesions were identified based on morphology suggesting intimal thickening or intense, opaque calcium-positive stain suggesting dystrophic calcification. All data were recorded and analyzed in Microsoft Excel.

Results: In the iICA segment, medial and IEL calcification were the most prevalent forms noted (64% of samples contained calcium in either layer). In the M1p and M1d segments, IEL calcification was most prevalent (78% and 93%, respectively), followed by medial calcification (50% and 71%, respectively). In the iICA, M1p, and M1d segments, intimal calcification was least prevalent (36%, 43%, and 43%, respectively). Atherosclerosis was detected in iICA, M1p, and M1d (72%, 72%, and 64%, respectively), but only a subset of these lesions showed dystrophic calcification (14%, 14%, and 0%, respectively).

**Limitations:** Although sample size and underrepresentation of males were not controllable factors, the represented population age was expected to show a spectrum of arteriosclerosis and atherogenic disease progression, thereby allowing us to observe a variety of phenotypes.

Conclusions: Consistent with recent findings, IEL calcification is the most prevalent type in the iICA. While this in itself is significant, to our knowledge, no other study has yet to simultaneously characterize the presence of medial, IEL, and intimal calcification in both atheromatous and nonatheromatous regions of the iICA. Furthermore, we expanded this finding to include proximal and distal portions of the MCA's M1

segment. Understanding patterns of arterial calcification in intracranial arteries may advance our knowledge of early pathogenesis and prophylaxis of cerebrovascular disease.

## ◆B3—Chronic Diseases & Conditions

Effects of Stimulation Magnitude of Cathodal tDCS on Cerebellar and Cerebral Cortices Using an In Vivo Approach and Its Pertinence to Cerebellar Ataxia Treatment Employing a Physiologic Model

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Research Question/Hypotheses: Cerebellar ataxia is a type of neurologic disorder characterized by a lack of coordinated movements due to impaired cerebellar brain inhibition, and it can significantly affect one's quality of life. This form of ataxia can manifest as a result of trauma from stroke, autoimmune attacks, or other various CNS diseases. Previously, noninvasive brain stimulation has been adopted for the management of various diseases related to cognition, emotion, adaptive learning, working memory, and motion. As an effective noninvasive brain stimulation method, transcranial direct current stimulation (tDCS) has been applied for the treatment of cerebellar ataxia in patients and has been shown to have promising results as a form of potential therapeutic treatment. However, the mechanism of cerebellar tDCS at the cellular level remains unclear. This research aims to examine the physiologic activity in the primary motor cortex as the result of tDCS on the cerebellar cortex in the mangement of degenerative movement disorders, specifically cerebellar ataxia.

Statement of Significance: The significance of this research to the osteopathic community involves the elucidation of the cerebellar mechanics affected by tDCS. It has emerged as a potential therapy for cerebellar ataxia in humans (Grimaldi et al, 2014). Animal studies have demonstrated that the cerebellar tDCS is capable of modifying the output of the motor cortex through the cerebello-thalamo-cortical pathway (Ben Taib and Manto, 2009). Exploring the effects of tDCS on the cerebellar and motor cortices can add to the understanding of the cellular mechanisms involved in tDCS therapy. Thus, this research will assist in the optimization of tDCS therapy for cerebellar ataxia.

Methods: Surgery: All cranial surgical procedures were performed according to the Bower lab methods (Bower et al, 1981). Protocols used in this project have been approved by the IACUC of PCOM. Each rat was placed in an induction chamber with isoflurane (4% with oxygen at 1 L/ min by calibrated vaporizer), allowing the rat to lose consciousness without distress. The animal was anesthetized with an injection of ketamine/ xylazine/acepromazine cocktail into the intraperitoneal cavity. Supplemental doses were given throughout the extent of the experiment. The animal was then placed in head-mounting hardware on a custom built surgical setup that includes a heating pad with vital sign monitor. An incision was made in the skin and the soft tissue was removed to expose the skull over the cerebellar and cerebral cortex. Two small holes were prepared, 1 over the cerebellum and the other over the contralateral motor cortex. The dura was excised to expose the brain tissue. The skin posterior to the cerebellum was kept for the tDCS. To generate the tDCS, a metal wire (1-2 mm<sup>2</sup> diameter) was placed on the skin immediately posterior to the hole prepared over the cerebellum. The current was delivered using a stimulus isolator (WPI A365, 100-200 µA) for 20 minutes.

The ground electrode was placed on the contralateral cheek area. Neural Recording: We employed platinum/iridium monopolar electrodes (1 M $\Omega$ , UEPSEGSGXN4G, FHC, Bowdoin, ME). Neural signals were amplified (A-M Systems model 1700), digitized (Digidata 1300A, Axon Instruments), and recorded with Clampex 9 (Axon Instruments). An electrode was positioned into the motor cortex (1.6 mm anterior to the bregma, 3 mm lateral to the mid line, 1 mm depth). A second electrode was positioned into the cerebellar cortex and a single unit Purkinje cell activity was isolated. Then the filter was opened to be 1 Hz - 10 kHz. Recordings were conducted for 10 minutes before tDCS, 20 minutes during tDCS, and 10 minutes after tDCS.

Data Analysis: Data were filtered with a band pass filtered between 0.3-10 kHz. Artifacts were removed manually and spikes were detected using customized Matlab (R2016a) scripts that operate by detecting a threshold calculated by standard deviation. A plot was generated for monitoring the frequency changes of Purkinje cell simple spike activities before, during, and after stimulation. LFPs (1-100 Hz) were examined for the general cerebellar and motor cortical cellular activities. A power spectrum analysis Welch-type was ran on the original unfiltered data with a window of 100k samples (10 seconds) and a window of 100k for discrete Fourier transforms. A surface plot was generated using 1-minute time windows. For the cross-correlation and coherence analysis, nonfiltered signals were used to generate normalized plots using Matlab functions "xcorr" and "mscohere." These methods have been widely used in the data analysis of brain activities (Adhikari et al, 2010; Brazhnik et al, 2012). Results from this analysis were illustrated using average trace and surface plots generated to show the changes before, during, and after tDCS in both frequency and time domains at different intensities (100 and 200 µA).

**Results:** Using normal animal models can provide insight into the mechanisms that underlie tDCS therapy and can be used as a precursor for further research involving diseased animal models. Sprague-Dawley rats (n=10) were used to isolate Purkinje cells (n=14) from the cerebellar cortex as well as to record local field potentials in both the cerebellar and cerebral cortices. Cathodal stimulation intensity was set at 100 µA and 200 μA. The mean frequency of firing rate was analyzed to determine the output of individual Purkinje cells. Some Purkinje cells (n=10) had a decrease in overall firing rate after the stimulation whereas other Purkinje cells (n=4) exhibited an increase in firing rate from the same stimulation. A 1-tailed t test (P=.23) indicated there was no significant difference in firing rates based on intensities. A power spectrum analysis was conducted to study the changes in cerebellar cortical activity, and results from this analysis showed an increase in amplitude at approximately 5 to 10 Hz in (n=7) cells. Other cells (n=2) were observed to have a change in higher frequency around 80 Hz. The remaining cells (n=5) exhibited no significant changes in amplitude.

Conclusion: Overall, cathodal tDCS was shown to cause a decrease in the firing rate of Purkinje cells. Power spectrum analysis revealed an increase in amplitude of low frequency activity of local field potential under cathodal stimulation in some of the cells. Furthermore, cross-correlation and coherence analyses demonstrated that the activity changes of the motor and cerebellar cortices are interrelated. The correlation level decreases with tDCS. The analysis based on current cases indicates that the correlation level is more depressed at an intensity of 200 µA. All of these analyses suggested that the cerebellar tDCS altered activity in the primary motor cortex due to a change in cerebellar output. Future analysis should focus on comparisons between cathodal and anodal direct-current stimulation, as well as alternating-current stimulation, to

determine the most effective form of treatment. In addition, diseased and symptomatic animal models should provide a better understanding of the limitations of cathodal tDCS as a form of treatment for cerebellar ataxia.

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## ♦★B4—Chronic Diseases & Conditions

## Characterizing the Honey-Bee Derived Antimicrobial Peptide Melittin to Eradicate Biofilm-Associated Infections in Chronic Wounds

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Research Question(s)/Hypotheses: Chronic wounds are estimated to cost \$25 billion annually and are very difficult to manage. A major factor contributing to the recurrence of these wounds are infections by multi-drug-resistant pathogens, Pseudomonas aeruginosa and Staphylococcus aureus, which form drug recalcitrant biofilms within wounds. Antimicrobial peptides (AMPs) are considered "nature's antibiotics" and can be found in nearly all classes of life. We identified that the AMP melittin, derived from bee venom, demonstrates potent anti-biofilm activity. Here, we characterized the ability of melittin to eradicate P aeruginosa and S aureus biofilms in vitro. Melittin represents a potential new therapy for biofilm-associated chronic wounds.

**Need-Based Aim:** To develop new therapies for the eradication of biofilm infections associated with chronic wounds.

**Statement of Significance:** The development of new therapies for biofilm-associated infections is a

critical health care need. The re-purposing of naturally made AMPs to meet this need is in line with osteopathic principles of clinical practice and research.

**Methods:** 24-hr biofilms formed by *P aeruginosa* and *S aureus* isolates were tested for susceptibility to melittin using BacTiter-Glo. Biofilm dispersal was measured using crystal violet staining. Cellular permeabilization was quantified using TO-PRO-3 dye, which stains permeabilized cells, combined with single-cell flow cytometry.

**Data Analysis:** Statistical analysis was performed using Graph Pad Prism version 5.0. Either 1-way or 2-way analyses of variance were performed. Tukey's post-hoc test was used for multiple comparisons. Lines and bar graphs depict the mean. Error bars depict the standard error mean (±SEM) or standard error deviation (±SD).

Results: Melittin alone eradicated 99% of cells within S aureus biofilms after 6 hours of treatment. And melittin alone was effective against 4/4 S aureus clinical isolates tested. Moreover, melittin synergized with tobramycin against P aeruginosa biofilms, killing 99% of cells within biofilms after 6 hours of treatment. In addition, melittin in combination with tobramycin was effective against 5/6 CF P aeruginosa clinical isolates tested. Melittin also showed accelerated killing compared with tobramycin, reducing 90% of the cells within biofilms in 2 hours, whereas tobramycin required 4 hours before killing was observed. Finally, melittin caused significant biofilm dispersal and permeabilization of the cells within treated biofilms.

**Conclusion:** AMPs have many advantageous, including rapid onset of action, limited resistance selection, and the ability to synergize with other antimicrobials. We found melittin was a potent anti-biofilm agent against both *P aeruginosa* and *S aureus* biofilms. Melittin is an AMP that could

potentially be used to improve current chronic wound therapies.

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# B5—Musculoskeletal Injuries & Prevention

# Comparative Analysis of Locomotion in an Early Diverging Chameleon

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Background: Chameleons are the only true arboreal lizards; they possess the ability to navigate substrates whose diameter is smaller than the diameter of their body. The extent of arborealism can be seen in the ancestrally arboreal chameleons, such as the veiled and Jackson's chameleons, which descended from terrestrial agamid lizards, similar to the modern bearded dragon. In the evolutionary tree, ground-dwelling chameleons, like the bearded leaf chameleon, diverged before the evolution of true arboreal chameleons that perform semi-erect arboreal locomotion. Ground-dwelling chameleons share the same morphological features that make chameleons different from other lizards, such as 2 independently mobile eyes that can move 360 degrees, 2-toed pincer-like feet, a prehensile tail, and a projectile tongue. We currently lack an evolutionary context to truly understand these adaptations. Although most studies of the chameleon locomotor system have focused on larger, ancestrally arboreal chameleons, the family encompasses great variation in morphology, behavior, and

habitat, including ground-dwelling taxa. Moreover, the extreme arborealism associated with the family is a relatively recent innovation. To investigate how arboreal locomotion first arose and evolved in the chameleon lineage, we first need to understand variation in locomotor abilities among extant chameleons.

Statement of Significance: Much of an organism's body plan and physiology revolves around locomotion. Reptiles and mammals are both known to have evolved from a terrestrial ancestor in which all 4 limbs participated in a sprawling motion. The locomotor traits of therian mammals —comprising placental and marsupial mammals —have a striking resemblance to those of arboreal reptiles. For example, the 2 groups share an upright limb posture, functionally regionalized spine, and highly mobile shoulder girdle. Therefore, chameleon locomotion can be used as a template to understand the transformation in mammalian locomotion from terrestrial to arboreal. In addition, studying the biomechanics of joints in chameleons can help us better understand the structure and function of human joints for different osteopathic manipulative treatment modalities (eg, the chameleon's knee joint has a medial and lateral condyle that is anatomically similar to the human knee joint).

**Specific Aim:** To measure locomotor kinematics of the ground-dwelling bearded leaf chameleon and compare them with ancestrally arboreal chameleons and non-chameleon lizards to understand the evolution of 'erect' arboreal locomotion from the sprawled mode of tetrapods.

**Method:** Four bearded leaf chameleons, *Brookesia superciliaris*, and 1 Jackson's chameleon, *Trioceros jacksonii*, were obtained from a pet company, and the 2 genera were housed in 2 separate vivariums with temperatures ranging from 60-78°F and 60-80°F, respectively. They were given food, water, and calcium supplements

according to their recommended diet. The vivariums were misted daily. Dots of white acrylic paint were applied to the limbs of each animal to act as tracking points. Video recordings of 4 bearded leaf and Jackson's chameleons moving on different substrates varying in diameter from 0.25" to 2" were obtained using 4 synchronized digital cameras (GoPro Hero 6) set at 120 frames per second. The substrate was propped on wooden blocks to ensure that the surface was stable. The speed of the animals was not controlled and they walked at their own pace. The animals were encouraged to walk by tapping their tails with a small paintbrush or cotton swab, if necessary. The cameras were set up around the substrate at different angles and each animal walked on each substrate at least 3 times. The recording space had standardized temperature and it was calibrated by a custom 3D printed frame.

Data Analysis: The video sequences were analyzed using ProAnalyst (www.xcitex.com), a motion analysis software. The software tracked the videos in all 4 cameras to create a 3-dimensional image of the animal's locomotion. The data were used to measure joint angles at touchdown, mid-stance, and lift-off; range of motion; speed; stride length; and duty factor. A linear mixed model was used statistically to compare these variables between the Jackson's and bearded leaf chameleons.

Results and Conclusion: The bearded leaf chameleons preferred to walk on broader surfaces, possibly because of their more sprawling posture. They could grasp onto thinner substrates, but their speed was slower than the Jackson's chameleons and they refused to move forward without external encouragement. They kept their elbow and knee joints primarily in a bent position, giving them smaller elbow and knee angles and larger wrist and ankle angles at mid-stance and smaller ranges of motion, especially in the shoulder and hip joints. Their stride length was proportionally smaller and their duty factor was greater. The bearded leaf chameleon's locomotion can be seen as a model of a transitional stage in the evolution of arborealism. This study is a preliminary investigation of the locomotion of the bearded leaf chameleon. In the future, we would like to increase our sample size and compare it to other chameleon genera and other closely related non-chameleon lizards. Reconstruction of the evolutionary transition of the locomotor system in chameleons allows for a better understanding of the evolution in reptiles as well as the role of convergence and constraints in arboreal adaptation and the various ways animals have adapted to novel environments.

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### ◆B6—Osteopathic Philosophy

# Cannabinoid Receptor Function During Axonal Development In Situ

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Background/Significance: Presently, there is much literature on the endocannabinoid system that supports the osteopathic principle that the body possesses self-regulating and self-healing mechanisms. Many patients seek medical cannabis for its potential therapeutic benefits to manage somatic dysfunction, chronic pain, and a variety of other conditions. Of more concern, this includes morning sickness associated with pregnancy. This remains a pressing issue because the effects of exogenous cannabinoids on fetal neural development remains poorly understood. For the increasing number of osteopathic physicians considering to prescribe and the increasing number of pregnant patients seeking to use medical cannabis, the pos-

sible effects of prenatal marijuana exposure on the developing fetal brain becomes an important area of research in osteopathic medicine.

**Research Question:** This study aims to elucidate the functions of CB1R, the main cannabinoid receptor in the central nervous system, during development of axonal connectivity.

Methods: We investigated the effects of cannabinoids on optic axon growth in intact brains from Xenopus laevis tadpoles. Xenopus embryos containing GFP-expressing optic axons were exposed to either the CB1R inverse agonist AM251 or the selective CB1R agonist arachidonyl-2-chloroethylamide (ACEA). When the embryos reached the young tadpole stage, their brains were dissected and images were captured of control and CB1R-perturbed GFP optic axons and growth cones in situ using a NIKON E800 microscope with epifluorescence attachment.

**Data Analysis:** Using ImageJ, we quantified 10 distinct morphometric parameters of optic axons and growth cones from these images, including aspect ratio of projections, number and undulations of axons, as well as growth cone circularity size, and filopodial number.

**Results:** Application of the CB1R inhibitor AM251 decreased both the number and length of optic axons in the optic tract whereas the CB1R agonist ACEA increased number and length of axons in the optic tract relative to controls (P<.05). AM251 exposure also resulted in larger growth cones with increased filopodial protrusions while growth cones of optic axons exposed to ACEA were smaller and rounder with fewer filopodia compared with control growth cones (P<.05). Additional analysis showed that both AM251- and ACEA-exposed optic axons displayed increased collateral branches and made navigational errors in the optic tract compared with control optic axons (P<.05).

**Conclusion:** Taken together, these data suggest that CB1R regulates optic axonal extension by

negatively modulating growth cone filopodia in situ. Moreover, normal levels of CB1R signaling appear to be required for proper directionality and branching of optic axons in the optic tract. This study can help improve our understanding of the risks of impaired brain development associated with prenatal cannabis exposure. Furthermore, this research can help both osteopathic physicians and pregnant patients make informed decisions regarding medical cannabis use, leading to improved patient outcomes.

# ◆B7—Chronic Diseases & Conditions

## Spinal Cord Neurodegenerative Changes With Post-Polio Syndrome and Dementia

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Research Question(s)/Hypotheses: During a routine anatomy class dissection, a 90-year-old female cadaver was found to have adipose replacement of the right lower extremity musculature. The left lower extremity appeared to be either unaffected or grossly less affected in comparison. A partial past medical history was obtained from the Board of Human Gift Registries following a petition for release of de-identified medical history of the donor. The medical record revealed a history of post-polio weakness with onset at age 22 years that resulted in leg bracing of the affected limb. Also of note was diagnosed dementia, with unknown time of onset or progression. Post-polio syndrome (PPS) is currently recognized as the most prevalent disease of the anterior horn motor neurons. With an aging population and recent outbreaks occurring within US territories, the continued evaluation and approach to treating patients with this syndrome is relevant to current medical practice. The intent of this investigation of the case is to describe the extent of central nervous

system involvement in the lower extremity atrophy presentation.

Methods: Lower thoracic, lumbar and sacral regions of the PPS subject's spinal cord were harvested, cryoproctected, and snap-frozen in isopentane cooled in liquid nitrogen. Spinal cord specimens were cryosectioned at 14 µm and placed on contiguous slides for histological evaluation. Sections were stained by modified Kluver-Barrera method for myelin identification and counterstained with hematoxylin to identify motor neurons. Digital images of sections were acquired using a Leica Aperio system and analyzed using Image Pro Plus software. Hematoxylin staining revealed the presence of large acidophilic particles within the spinal cord of our subject. To determine whether these particles were related to PPS or a feature of normal aging, spinal cord was acquired from 5 control subjects. A partial past medical history was obtained from the Board of Human Gift Registries following a petition for release of de-identified medical history of these donors. None had a confounding medical condition with weakness. One of the 5 controls was diagnosed with dementia and osteoporosis. Sections from the PPS subject and 5 controls were stained using an alcoholic PAS method to establish the identity of the particles as corpora amylacea. Digital images of sections were acquired using a Leica Aperio system and analyzed using Image Pro Plus software.

Data Analysis: Motor neuron numbers and ventral horn area of the PPS subject were assessed for differences between the right and left sides of spinal cord sections from 30 samples taken throughout the thoracic and sacral levels. Data were analyzed for statistical differences using Statistica (StatSoft). To compare the distribution (% area covered) and diameter of the corpora amylacea between the PPS dementia subject and the 5 controls, samples were evaluated in both dorsal and ventral spinal cord areas for 3 sections separated by at least 500  $\mu m$ .

Data were analyzed for statistical differences using Statistica (StatSoft).

Results: In the PPS subject, statistical analysis revealed that significant differences existed in motor neuron numbers between the affected and unaffected sides of the anterior horns, but no differences were detected between the area of affected and unaffected anterior PAS-positive inclusion bodies were observed in spinal cord sections from all subjects. These inclusions were identical to those described in aging human cortex as corpora amylacea (CA). For all subjects there was a significant difference in the distribution of PAS-positive inclusions between the dorsal and ventral regions of the spinal cord, with the dorsal regions being more populated. There were no significant differences detected either in the distribution of CA or in particle diameter between the PPS subject and the controls. However, there were significant differences detected in diameter and distribution between controls and the dementia-diagnosed control and PPS. Conclusion: The observation that motor neuron numbers are decreased with PPS is not unexpected and has been reported previously. However, the lack of any detectable change in anterior horn area is somewhat puzzling. Prior studies have described a decrease in area and the presence of glial scars after polio infection. Our inability to detect these changes suggests that remodeling of the anterior horn occurs after polio. To our knowledge, this is the first report associating a difference in the distribution and size of corpora amylacea within the spinal cord with dementia. Descriptions of these inclusions have been limited to aging cortex and neurodegenerative changes. An increased presence and diameter of these inclusions was not associated with a diagnosis of PPS. These findings have significant implications on the approach osteopathic physicians may take to managing a variety of neurodegenerative disease processes. Further studies will concentrate on determining the composition of the inclusions and whether they differ between subjects with dementia and those without.

Acknowledgment/Funding Source: WVSOM intramural grant.

## ◆B8—Chronic Diseases & Conditions

## Hypomethylating Agent Is Effective in Treating Patients With Brain Metastasis Breast Cancer

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Background Introduction: Breast cancer is the second leading cause of cancer with the highest mortality rate in women in the United States. Late stage breast cancer can metastasize to different locations of the body including lungs, liver, bones, or brain. Breast cancer patients with brain metastasis have a poor prognosis, with a median survival time less than 1 year despite treatment. Current chemotherapeutic agents are largely ineffective against brain metastases of breast cancer. DNA methylation is an epigenetic mechanism used by cells to control gene expression. In normal cells, DNA methylation assures the proper regulation of gene expression and maintains gene silencing. However, abnormal DNA hypermethylation can lead to suppression of tumor-suppression genes and compaction of chromatin, which contributes to the cancer progression. In breast cancer, multiple carcinogenesis-related genes are found to be hypermethylated. DNA hypomethylating agents can activate tumor suppressor genes that are silenced by hypermethylation in breast cancer.

**Hypothesis:** We hypothesize that hypomethylating agents such as azacytidine (AZA) will be effective in the management of brain metastasis breast cancer.

Statement of Significance: Breast cancer is the most common type of cancer diagnosed in women. For breast cancer patients with brain metastasis, their mean survival time is less than 1 year, and current chemotherapeutic agents are largely ineffective. This is an osteopathic consideration that the current therapy is unable to restore the body to homeostasis, which may cause continued devastation of health in patients. In this study, we are testing hypomethylating agents as a new family of chemotherapy drugs in the treatment of brain metastasis breast cancer. Our study suggests that the hypomethylating agent AZA has a positive effect in treating brain metastasis breast cancer. AZA was able to induce more apoptosis and has a lower IC50 value in brain metastasized breast cancer cells compared with the regular breast cancer cells. By having targeted therapy, osteopathic physicians can better connect with and treat their patients with the disease. Targeted treatment options will give patients an improved outlook on their disease and ultimately help them maintain positive social interactions and habits, which are critical for their whole-body health and fit well with the behavioral model of osteopathic care.

Methods and Data Analysis: (1) Cells and chemicals: The brain metastasized breast cancer cell line (MDA-MB-231 Br) and its parental regular triple negative breast cancer cell line (MDA-MB-231) are used in the study. The cells are treated with AZA and subsequent cancer biology-related studies are followed. (2) Cell counting: BioRad TC20TM automated Cell counter was used to measure cell proliferation by assessing the number of live and dead cells. (3) MTT assay: Was used to calculate IC50 values of AZA. (4) Flow cytometry: Was used to measure percent of apoptotic (Annexin-V positive) cells. (5) Western blotting assay: Was used to measure protein expression. (6) Statistics: Statistical significance was analyzed by the t test (2 groups) and 1-way ANOVA with a

Tukey posttest (more than 2 groups), with a P value lower than .05 (P<.05) considered significant. Results: (1) Brain metastasized breast cancer (MDA-MB-231 Br) cells have a different oncologic phenotype compared with their parental regular breast cancer (MDA-MB-231) cells. (i) MDA-MB-231 Br cells primarily reside in brain and MDA-MB-231 migrate to other tissues in vivo; (ii) MDA-MB-231 Br cells grow faster than MDA-MB-231 cells in vitro. (2) Brain metastasized breast cancer cells are more sensitive to AZA treatment. (i) IC50 value of AZA in MDA-MB-231 Br cells is significantly lower than that in MDA-MB-231 cells (48  $\pm$  $4.90 \text{ mM vs } 83.33 \pm 8.82 \text{ mM}, P < .01$ ). (ii) AZA treatment triggers higher percentage of apoptotic cells in MDA-MB-231 Br cells compared with MDA-MB-231 cells. (3) AZA treatment decreases the expression of anti-apoptotic proteins and increases the expression of caspases in MDA-MB-231 Br cells. Treating both cell lines with various concentrations of AZA decreases the expression of BCL-2 and increases the expression of caspase-3 and caspase-9 in MDA-MB-231 Br cells; however, the expression of BAD and BAX remains unchanged in both cell lines. (4) MDA-MB-231 Br cells have higher metastasis potential compared with MDA-MB-231 cells. (i) The expression of epithelial marker cytokeratins is detected in MDA-MB-213 cells but not in MDA-MB-231 Br cells. (ii) The expression of matrix metalloproteinase-9 (MMP-9) is detected in MDA-MB-231 Br cells but not in MDA-MB-231 cells. (5) The DNA methylation status may be different between the 2 cell lines. DNA methyltransferase (DNMT) enzymes catalyze the process of DNA methylation by catalyzing the transfer of a methyl group to DNA. The expression of DNMT3a is detected in MDA-MB-231 Br cells but not in MDA-MB-231 cells. In addition, AZA treatment inhibits the expression of DNMT3a in MDA-MB-231 Br cells.

**Conclusion and Future Plan:** In this study, we are testing the effectiveness of the

hypomethylating agent AZA in the treatment of brain metastasis breast cancer by using an in vitro cell model. We found that the brain metastasized breast cancer cells have a different oncologic phenotype and higher metastasis potential compared with their parental cells. Hypomethylating agents may be effective in treating brain metastasized breast cancer cells as the IC50 value of AZA is lower and more apoptosis is induced by AZA in MDA-MB-231 Br cells. Our future plan includes the study of DNA methylation of cytokeratin-18 and measurement of signal transduction pathways, cell cycle, and angiogenesis upon AZA treatment in both cell lines. These follow-up studies may be helpful in elucidating the molecular mechanisms of AZA in the management of brain metastasis breast cancer.

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# ◆B9—Chronic Diseases & Conditions

# Reactive Bromamines and Loss of PON1 Antioxidant Enzyme Activity From Plasma High-Density Lipoprotein

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Hypothesis: Elevated blood levels of high-density lipoprotein (HDL), the "good cholesterol," decrease risk for cardiovascular disease. One proposed mechanism for this effect links HDL-associated paraoxonase-1 (PON1) antioxidant enzyme activity to protection of low-density lipoprotein (LDL), the "bad cholesterol," from oxidative modification during inflammation. Prior studies in our laboratory have demonstrated that loss of HDL's PON1 activity from human blood plasma during exposure to pro-inflammatory hypobromous acid (HOBr) is exacerbated by the

amino acid taurine (White and Lynch, 2015). The specific aim of the study reported here was to determine whether taurine bromamine and other brominated amines directly promote loss of PON1 activity from HDL in human blood plasma. Methods: Monobromamines (R-NHBr) of taurine, lysine, glycine, cysteine, histidine, tyrosine, and methionine were synthesized by a standard chemical procedure in which freshly prepared HOBr (5.0 mmol/L) was mixed with an excess (450 mmol/L) of the corresponding amine. The monobrominated amines (0-50 umol/L) thus formed were then added to 5-fold diluted human blood plasma and incubated at room temperature for 30 min, after which plasma PON1 activity was measured in a kinetic assay using paraoxon as substrate. PON1 activities are reported as a percentage of that seen in control plasma not exposed to monobromamine. Three independent experiments were performed with each monobromamine, and results are reported as mean ± SD for the pooled data. Statistical analysis of the effects of monobromamines on PON1 activity was performed by ANOVA with Dunnett's multiplecomparison posttest. Results were considered statistically significant when P<.05.

Results: Consistent with our prior study, addition of taurine monobromamine to human blood plasma was associated with a progressive decline in PON1 activity. Thus, whereas addition of taurine monobromamine at concentrations of 10-20 umol/L had little effect on PON1 activity (remained at 82  $\pm$  27 to 99  $\pm$  23 percent of normal), higher concentrations (30-50 umol/L) caused a significant (P<.01) loss of PON1 activity (declined to  $11 \pm 3$  to  $43 \pm 16$  percent of normal). A similar decline in PON1 activity to  $29 \pm 4$  to 38 $\pm$  3 percent of normal (P<.01 compared with control) was observed for plasma incubated with brominated methionine (30-50 umol/L). Brominated histidine also tended to cause a loss, albeit not statistically significant, of PON1

activity, which progressively declined to  $59 \pm 12$  percent of normal at the highest concentration of bromamine tested (50 umol/L). In contrast, addition of monobromamines of glycine, lysine, cysteine, and tyrosine (10-50 umol/L) to plasma had essentially no effect on PON1 activity, which ranged from  $75 \pm 4$  to  $116 \pm 15$  percent of normal (P>.05) in the presence of bromamine.

Conclusion: Our results confirm the detrimental effect of brominated taurine on HDL's cardio-protective PON1 activity under physiological conditions in plasma. Furthermore, we now report the novel observation that at least some other brominated amines (ie, methionine and possibly histidine) can cause a similar loss of cardioprotective PON1 activity from HDL in plasma. These observations may have significance for osteopathic physicians' integrated understanding of the pathologic processes leading to the development of cardiovascular disease, since HOBr is produced by neutrophils at sites of inflammation (Chapman et al, 2009), potentially leading to formation of reactive bromamines (Pattison and Davies, 2004).

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# B10—Chronic Diseases & Conditions

# Using Team-Based Learning in Osteopathic Medical Education to Improve Understanding and Communication Regarding Chronic Diseases

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**Hypothesis:** Team-based learning (TBL) can improve both understanding of chronic diseases

and the ability to communicate to patients about the processes. TBL is one of the most commonly adopted new teaching methods in undergraduate medical education. Originally developed as part of a business education curriculum by Dr Larry Michaelson in the 1970s. it is currently in use in many disciplines. These active learning sessions further enhance communication skills, as modules require both intra- and inter-team communication. TBL also offers an additional opportunity to integrate osteopathic principles into both basic science and clinical topics. Learning modules can be created that challenge students to articulate the roles of structure and function and how they relate to pathophysiology as well as explain the rationale behind treatments based on the emphasized principles of body unity, selfregulation, and the interrelationship of structure and function. At OSU-COM, we introduced TBL into several areas of the curriculum. In this study, we focused on the effect of TBL on high yield areas in endocrine disease pathology: thyroid disease and type 2 diabetes. Students' examination performance and self-perception of their communication skills were surveyed. These TBL topics were selected as critical, chronic diseases likely to be managed by the majority of graduates. In addition, these chronic diseases often require significant education of patients regarding their management. Preparation for this patient education requires both an enhanced disease understanding as well as the ability to communicate effectively. Well-designed TBL modules can better prepare students to provide this education.

**Methods:** The first part of the study focused on objective information regarding the impact of TBL in the form of knowledge retention and application. Data from class examinations were gathered from our assessment program (ExamSoft). Examination performance on TBL

topics was compared with other pathology topics taught with traditional lecture content delivery within the endocrine system. Performance based on question category was additionally stratified. The second part of the study focused on subjective information regarding the impact of TBL on students with particular focus on communication skills. An 8-question survey was sent electronically to all second-year students who had participated in the TBL events as part of the endocrine system (SurveyMonkey). Six questions used a 5-point Likert scale asking students to assess their experience with the TBL sessions. All 6 of these questions evaluated communication skills, 1 involved clinical reasoning, and 1 measured comprehension of underlying pathophysiology. Two additional questions documented students' previous experience with TBL. Data analysis was performed using Microsoft Excel (Microsoft Corporation).

**Results:** An independent sample t test was conducted to compare examination performance on TBL topics to lecture-based pathology topics within the same medical school class. There was no significant difference between the mean (SD) scores for the TBL questions (84.93 [11.5]) and the lecture-based questions (83.43 [9.9]) conditions ( $t_{114}$ =-0.02; P=.207). Within the TBL group, mean examination performance was highest for questions involving "compare and contrast" (89.38), slightly lower for "underlying mechanism" (88.35) and "clinical application" (87.94), and lowest for "recall" (85.92). From the second part of the study, students reported enhanced communication skills, clinical reasoning ability, and disease understanding. 67 of 114 students responded to the survey (59%). No incentive was offered for survey completion. For the 6 questions relating to enhanced communication, 66% of students either agreed or strongly agreed with improved communication ability. Regarding improved clinical reasoning, 72% of students

either agreed or strongly agreed. Regarding improved comprehension of underlying pathophysiology, 58% of students either agreed or strongly agreed. 55% of students reported previous experience with TBL at the undergraduate level and 16% of those with previous graduate school experience having used it in their training. Discussion: A significant difference in examination performance was not observed between TBL and lecture-based topics. These findings are similar to what others have found. Promising, however, was that overall performance was highest on questions involving compare/contrast and recognizing underlying mechanisms of disease processes. These types of examination questions are likely more reflective of the processes applied during the TBL events. The majority of student responses from the second part of the study support improved communication skills and disease comprehension. One of the goals of medical education is to equip future physicians to communicate effectively with both colleagues and patients. A solid understanding of and ability to explain disease processes to patients is especially important with chronic disease management. TBL offers students an environment to discuss and defend ideas with the expectation of deeper understanding under the direction of faculty facilitators. Assessment of improved communication skills, however, is inherently challenging in the short term. Data can be obtained from students' perceptions as was done in this study. A limitation of this type of assessment is the use of subjective criteria to quantify effectiveness. Other studies have also used observational data taken from TBL event facilitators. This added perspective would have been helpful in our current study. We also included examination performance as quantifiable data chosen to represent disease understanding. This assessment, however, can be dependent on the types of questions used on examinations. In our pathology curriculum, we

ascribe examination questions into 1 of 4 categories: underlying mechanism, compare/contrast, clinical application, and recall. The majority of questions used fall into the former 3 categories. We suggest these types of questions offer a better assessment of disease comprehension. While TBL has proven effectiveness at improving student engagement in medical education, we propose that additional dividends include improved communication as well as preparedness to explain disease processes and rationales to colleagues and patients. Results from the second portion of the study support this proposal. We further suggest that improved disease understanding and enhanced communication skills can translate to improved chronic disease management. Opportunities for further study include longitudinal follow-up during clinical training to see if these enhanced skills continue into the clerkship years as could be assessed by preceptors.

Conclusion: TBL is a promising method of teaching osteopathic undergraduate medical education. While increasing student engagement, additional benefits include improved communication skills and disease understanding. These skills may translate to improved chronic disease management as physicians are better prepared to educate their patients regarding their conditions.

# ◆B11—Chronic Diseases & Conditions

## Differential Effects of Beclin 1 on Autophagy and Mitophagy in Cardiomyocytes

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Autophagy is a cellular process in which unwanted organelles and proteins are degraded

and recycled to maintain cellular homeostasis. Mitophagy is a form of selective autophagy that specifically eliminates damaged mitochondria from the cell via the lysosome system to control mitochondrial quality. Autophagy and mitophagy are essential for cell survival in response to stresses such as starvation. How autophagy and mitophagy are regulated for adaptation in different contexts is under intense investigation. Beclin1 is a protein known to regulate autophagy, but its role in mitophagy is not clear. In this study, we determined and compared the ability of Beclin1 to regulate autophagy and mitophagy using rat H9C2 cardiac myoblast cell line. Rat H9C2 cells were infected with an adenovirus encoding either Beclin 1 or beta-galactosidase that was used as a control. After 48 hours, cells were harvested and total and mitochondrial proteins were extracted. Autophagy and mitophagy were determined by western blot analysis of LC3-II, an integral component of autophagic membrane that is commonly used as a marker for autophagic vacuoles at various stages of the autophagic process. Beclin 1 overexpression increased LC3-II levels, which were further elevated by the lysosomal inhibitors in total cell lysates, suggesting that Beclin 1 increased autophagy flux. Surprisingly, however, although Beclin 1 promoted the association of LC3-II with mitochondria, the lysosomal inhibitors did not increase it to the same degree as in cells infected with adenovirus encoding betagalactosidase, suggesting that Beclin 1 reduced the mitophagic flux. These results demonstrated opposite effects of Beclin1 on autophagy and mitophagy, reinforcing the idea that these 2 processes are separable and differentially regulated. Studies are underway to explore the molecular mechanisms that mediate the differential effects of Beclin 1 on autophagy and mitophagy.

# ◆B12—Musculoskeletal Injuries & Prevention

## Establishment of a Viable Murine Dental Pulp Stem Cell Line

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Introduction: Dental pulp stem cells (DPSCs) can be found in the third molar of human teeth-the "wisdom" teeth. The collection of DPSCs is less invasive than other current stem cell lines, and the cells exhibit a high rate of proliferation in culture, which make them ideal candidates for in vitro tissue genesis. Furthermore, routine removal of the third molars in humans makes individualized stem cell therapy a reality for a larger patient population. In this study, we aimed to develop an extraction and media protocol to culture primary dental pulp cells from a murine host and then characterize those cells using flow cytometry and real-time polymerase chain reaction (RT-PCR) for stem cell markers. **Hypothesis:** Using published protocols as a guide for extraction and media preparation, we will culture primary dental pulp stem cells from a murine host.

Significance: Recent research in stem cell therapy has provided new treatment options in the field of regenerative medicine. Stem cells have the unique ability to generate new cells when a tissue is damaged. Adult mesenchymal stem cells have been found in muscle, bone marrow, tendons, umbilical cord, umbilical cord blood, and cartilage. These cells are able to regenerate their respective tissue types. However, current methods of stem cell therapy are functionally hindered by the capacity of mesenchymal cells to grow and differentiate in vivo. For example, in vivo chondrogenesis of mesenchymal stem cells to replace large portions of cartilage is very difficult due to the lack of adequate blood supply to the region.

This poses a problem for the many patients who have traumatic or age-related damage to cartilaginous joints. Multipotent stem cells are able to differentiate into many cell types in 1 class of tissue. Pluripotent stem cells, such as embryonic stem cells, can differentiate into all cell types of the body. Human DPSCs have been shown to be more than multipotent, but not pluripotent, and have differentiated into odontoblasts, adipocytes, myocytes, and neuronal tissue. With further research, DPSCs may become more significant to human application.

Osteopathic Significance: According to the Centers for Disease Control and Prevention, in 2016, 23% of all adults—54 million people—had 1 of the various types of arthritis, the most common being osteoarthritis. Eight million people reported a limited ability to work due to their arthritis. The cost of medical care to treat these 54 million people was \$81 million. Arthritis is treated as a chronic disease for which there is no current cure. Stem cells and the field of regenerative medicine will become more prominent in many chronic diseases, including arthritis.

**Methods:** Dental pulp was harvested from the jaws of discarded laboratory mice who were aged 6 to 10 weeks. The dental pulp cells were grown at 37°C in a 6-well plate containing standard αMinimal Essential Media until cells migrated out of the collagen matrix of the dental pulp. To confirm the presence of DPSCs, we used flow cytometry for CD34 and CD105 stem cell surface markers and generated cDNA for real-time PCR detecting stem cell markers *Sox9*, *NANOG*, *OCT4*, and *NOTCH*. CH3TH10/2 cells, a known stem cell line, were used as a positive control, and MC3T3 osteoblast cells were used as a negative control.

**Data Analysis:** We used multiple t tests to analyze our RT-PCR data. When comparing our DPSCs to MC3T3 osteoblast cells, DPSCs showed a statistically significant increase in stem

cell markers *Sox9* expression (*P*=.0003), *NANOG* expression (*P*=.0048), *NOTCH* expression (*P*=.0001), and *OCT4* expression (*P*=.0411).

**Results:** Primary cells were viewed by light microscopy exiting the dental pulp in culture between days 2 and 7 for all cultures. The pulp cells divided at a rate approximately once per 24 hours and seemed to maintain contact with each other rather than spread evenly on the plates. Flow cytometry confirmed the presence of CD34 and CD105. RT-PCR confirmed the presence of DPSCs expressing significant levels of stem cell markers *Sox9*, *NANOG*, *OCT4*, and *NOTCH*.

Conclusion: Through this work, we have developed a viable murine dental pulp stem cell line that can be used to further study the differentiation of these unique pluripotent cells. Future research will involve the differentiation of DPSCs into chondrocytes and osteoblasts in vitro under the influence of specific media components.

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# ◆B13—Chronic Diseases & Conditions

# 4NQO Carcinogen-Induced Infiltration by Neutrophils in Mouse Liver

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**Introduction:** Liver cancer risk is multifactorial, and some of the risk factors include smoking,

high fat diet/obesity, and sex. Administration of 4-Nitroquinoline 1-oxide (4NQO) in the drinking water mimics the effects of tobacco and is an accepted model for induction of oral carcinoma in mice

Research Question/Hypothesis: We hypothesized that 4NQO can also cause pathologic changes in the liver. In particular, we proposed that administration of 4NQO would cause liver inflammation as manifested by the presence of neutrophils, and this effect would differ between male and female mice and would be augmented by a diet high in saturated fat (HF).

**Statement of Significance:** Results from this study aim to explore the relationship between nutrition, inflammation, and smoking and their relationships to liver pathology. A better understanding will enable improved patient education with regard to prevention of liver cancer in the human population.

**Methods:** Female and male (36 of each gender) C57Bl/6 mice were divided into low fat (LF diet = 10 kcal% fat) and high fat (HF diet = 60 kcal% fat) groups at the age of 5 weeks. The mice were then assigned to 1 of 3 treatment groups for the next 16 weeks: water (H2O), propylene glycol in water (1.25% PG-H2O), or 4NQO dissolved in PG-H2O. After 17 weeks, all mice were given solely water for the next 6 weeks and were then euthanized. The livers harvested. were paraffin-embedded, and sectioned in preparation for immunohistochemical analysis. Anti-Ly6 antibody was used to detect neutrophils. All animal work was in compliance with the Institutional Animal Care and Use Committee at MWU/ CCOM.

**Data Analysis:** Neutrophils were counted in 3 randomly chosen areas per tissue at  $10 \times$  magnification. Analysis using a t test determined no statistical difference between the water and PG controls, which were combined for statistical analysis in GraphPad Prism 7.0.

Results: Administration of 4NOO led to pathological changes in the liver accompanied by an increase in neutrophil numbers (146 average across all 4NQO groups vs 36 average across all control groups). Typically, neutrophils were distributed evenly within the liver parenchyma; however, in 40% of the HF 4NQO male group, neutrophils formed cell clusters. Interestingly, the number of neutrophils in HF 4NQO male mice was higher than in HF 4NOO female mice (264 vs 137, respectively). Additionally, a HF diet augmented the effect of 4NQO in both male and female animals. This trend was more dramatic in male mice (264 in HF vs 101 in LF, P=.09) than in female mice (138 in HF vs in 81 in LF, P=.23). Conclusions: Oral administration of 4NQO resulted in liver inflammation as indicated by infiltration by neutrophils. These inflammatory changes were more significant in males than female mice, suggesting a biological effect for the difference. These effects were amplified by a high fat diet. In general, this suggests that lifestyle factors can prevent or mitigate pathological changes in the liver.

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## ◆B14—Chronic Diseases & Conditions

### Do Acne Bacteria Cause Rosacea?

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**Research Question/Hypotheses:** Rosacea is a long-term inflammatory condition of the skin,

predominantly affecting females, and is characterized by erythema, telangiectasia, and papules following a butterfly-like distribution in the face. While its pathogenesis remains unknown, it is comorbid with Parkinson disease (PD) at a 71% increased risk. This may be due to a yet unidentified common denominator responsible for the inflammation seen in both diseases. The acne-causing bacterium Propionibacterium acnes is increasingly associated with a range of inflammatory diseases, all of which affect epithelial cell types in various locations of the human body such as the prostate, the lung, and even the brain. P acnes accomplishes this through epithelial invasion and intracellular persistence followed by chronic inflammation. We have evidence from work in human cadaveric brains that intracellular bacterial persistence may precipitate PD and we are now hypothesizing that cells of epithelial origin may be affected in the same way in rosacea. Cells of epithelial origin can be distinguished by location size and shape and include neuro-epithelial cells found in association with the mechanoreceptor skin corpuscles (Merkel, Ruffini, Meissner, Pacinian) and free nerve endings. Findings supportive of this hypothesis would provide a superb starting point for the unraveling of the pathogenesis of rosacea as well as shed light on the comorbidity with PD.

**Significance:** Rosacea is a long-term skin condition with a severe psychosocial impact—especially for females who represent about 75% of all affected individuals. The pathogenesis of the disease is completely unknown. This investigation intends to probe for a bacterial origin for rosacea with *P acnes* as the main suspect. Rosacea is frequently treated with tetracycline antibiotics, which are very effective against *P acnes*. This bacterium though is known to persist inside cells of epithelial origin or

extracellular biofilm which could explain sudden flare-ups. Verification of our hypothesis will inspire preventive and treatment options with novel or repurposed bacteriostatic and bactericidal agents. By studying the mechanisms present in our bodies that promote self-healing and understanding how *P acnes* evades these processes, we will be able to tailor treatments that promote holistic wellness. The fact that this skin disorder may have implications toward PD implies an interconnectedness triggers the use of specific osteopathic manipulative techniques, such as lymphatic drainage of the head and neck, to prevent or postpone the development of neurodegeneration.

Methods: Human subject-related work was reviewed and approved by the NYITCOM IRB. We obtained 6-mm paraffin-embedded facial skin punch biopsies (n=3) of patients diagnosed with rosacea (Dermatology Laboratory of New England, P.C.). After paraffin removal and rehydration, immunohistochemistry was performed using antibodies against P acnes, gram-positive bacteria, a-synuclein, late stage inflammatory macrophages, Staphylococcus epidermidis, and Propio-nibacterium freudenreichii. Cell-based experiments were carried out in human peripheral dopaminergic (DA) neurons (SH-SY5Y; ATCC), and human microglia (HMC3; ATCC) infected with various isolates of P acnes (P6, 33179, 266, 12.1.L1) and bacterial controls (S epidermidis, E coli) and scored for their effect on inflammation (C1q, TNF-α. IL-1) and Lewy (α-synuclein) formation using ELISA (n=2). The multiplicity of infection (MOI) ranged from 25 to 0.3 (12 h, 24 h, and 48 h). Using the same cells, bacteria, and reagents, we corroborated ELISA findings through immunocytochemistry on glass coverslips (12 mm).

**Data Analysis:** Using confocal microscopy, we visualized and scored the skin biopsies. Data analysis was performed using Microsoft Excel and

Graph Pad Prism 7 software. Two-way ANOVA for multiple comparisons was used to identify quantifiable differences of the ELISA data.

**Results:** Confocal microscopy clearly revealed P acnes at the center of Pacinian (lamellar) corpuscles and the sensory nerve. Some bacteria were clearly visible intracellularly, while others appeared to arrange themselves along nerve fibers. About half of all Pacinian corpuscles of a patient revealed a large circular area (about one-third of the diameter of the corpuscle) around the sensory nerve with highly-concentrated α-synuclein. At the edge of this structure, mature macrophages were abundant. ELISA and immunocytochemistry on coverslips revealed that infection with P acnes, except for isolate 12.1.L1, caused less inflammation than with bacterial controls (all time points, both cell types). α-synuclein production in peripheral neurons was slightly higher using *P acnes* strains than controls. Other measurements/observations inconclusive.

**Conclusion:** The finding of *P acnes* in Pacinian corpuscles in association with α-synuclein—both known triggers of inflammation—suggests that the bacterium may be involved in the pathogenesis of rosacea and may in fact be a trigger. The finding of acne bacteria in association with abundant α-synuclein suggests causation, which will need to be substantiated further. This work is consistent with other work in the field of PD that suggests the prion-like spreading of α-synuclein from peripheral gut neurons to the brain via the vagus nerve (cranial nerve X). The same may actually be true between tactile corpuscles in the skin and the brain. The finding of common elements between rosacea and PD suggests that they may be involved in the observed co-morbidity between both diseases. If true, α-synuclein deposition in tactile corpuscles of the skin may be an exploitable early biomarker for PD that needs to be paired with an effective preventive

treatment. If *P acnes* turns out to be the ultimate culprit, a tailored antibiotic/antibacterial treatment or vaccination in combination with an immune function-promoting osteopathic approach may be the proper way forward.

**Acknowledgment/Funding Source:** NYITCOM intramural funding to J.R.L.

# ◆B15—Chronic Diseases & Conditions

## Metabolic Responses to Sucrose and Glucose Administration During an Oral Sugar Tolerance Test

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Research Question: Current dietary guidelines recommend restricting saturated fat consumption to reduce cardiovascular and metabolic risk factors. The reduction of fat intake in turn has led to an increase consumption of sugar. Recently, several studies have pointed to the role of dietary sugars, such as high-fructose corn syrup (HFCS) and sucrose, in promoting disorders of lipid and carbohydrate metabolism such as type 2 diabetes and cardiovascular disease. Studies examining fructose, a moiety of HFCS and sucrose, have shown that an increased intake of fructose potentially accounts for the detrimental effects of a high carbohydrate diet. Due to the rapid metabolism by the body, fructose is thought to induce many metabolic changes that can be measured by increased lipogenesis, lactic acidosis, hypertriglyceridemia, high blood pressure, insulin resistance, and increased weight gain. Currently, there is great concern that fructose-containing food, such as sugar-sweetened beverages and some processed foods, may be a contributing factor in the pathogenesis of chronic diseases.

Sucrose and HFCS are both made up of glucose and fructose monomers. Sucrose is a disaccharide of the 2 covalently bound monomers whereas HFCS is composed of glucose and fructose. Understanding the body's response to these sugars will further elucidate their role in chronic disease. In clinical and research settings, the body's response to glucose is measured using an oral glucose tolerance test (OGTT). During an OGTT, 75 g of glucose is administrated to a fasting patient and blood is drawn for every 30 minutes over 2 hours to measure blood glucose and insulin levels. The OGTT can serve as a useful tool for clinicians to diagnose prediabetes, insulin resistance, gestational diabetes, or reactive hypoglycemia. While an OGTT consists of pure glucose, a typical diet consists of sucrose and/or HFCS with minimal ingestion of glucose served alone. Therefore, understanding the body's response to dietary sugars will aid in understanding their role in the aforementioned diseases. In this ongoing study, we aim to determine the metabolic effects on blood glucose, lactate, and insulin levels during an Oral Sugar Tolerance Test, where sugar stands for either glucose (OGTT), sucrose (oral sucrose tolerance test [OSucTT]), fructose (oral fructose tolerance test [OFTT]), or galactose (oral galactose tolerance test [OGalTT]), or oral lactate tolerance (OLTT). Here we examined the difference between an OGTT and an OSucTT on blood glucose, lactate, and insulin levels. We hypothesize that the participants will have a greater initial blood glucose concentration and greater insulin area under the curve (AUC) response to the oral glucose as compared with the oral sucrose load and that lactate will be comparable between the 2 tests.

**Methods:** *Participants.* 3 healthy men aged 18 to 40 years were recruited from the community. Key exclusion criteria included evidence of diabetes

mellitus, liver disease, kidney disease, or thyroid disorders, or taking antidiabetic, hypolipidemic, anti-hypertensive or antidepression medications. Smokers and those with dietary restrictions were also excluded. All procedures followed were in accordance of the Touro University California Institutional Review Board (IRB-M#0716). A signed written consent form was obtained from all participants before screening. Study Design. Participants reported to the Metabolic Research Center at Touro University for two 1-day visits. A randomization scheme with a 16-day washout was used to assign each participant to either an OGTT or OSucTT. Participants arrived after a 10- to 12-hour overnight fast. An intravenous catheter was placed in each participant for repeated blood draws. Blood was drawn for baseline glucose, insulin, and lactate measurements. Participants were given either 75 g of glucose (OGTT) or 67.5 g of sucrose (OSucTT.) Blood was drawn and collected into sodium fluoride/ potassium oxalate (NaF/KOx) for plasma glucose and lactate measurements and into serum separating tubes (SST) for serum insulin measurements at 30, 60, 90, and 120 minutes after sugar dosing. The NaF/KOx tubes were immediately placed on ice and centrifuged at 3000 RPM for 10 min, and plasma was collected. Whole blood, collected in SST tubes, were incubated at room temperature for 30 minutes and centrifuged at 3000 RPM for 10 minutes to collect serum. All samples were stored at -80°C until analysis. A Yellow Spring Instruments 2300 STAT PLUS Analyzer and a PolyMedco Chemical Analyzer were used to measure plasma blood glucose and lactate levels in duplicates for each time point. The Millipore Human Insulin ELISA Kit (EZHI-14K) was used to measure serum insulin levels in duplicates. Statistical Analysis. A probability level of P<.05 was adopted throughout to determine statistical significance.

Results: Blood glucose and insulin levels peaked after 30 minutes in each participant during both tests. Insulin levels remained higher for the OGTT vs OSucTT group without reaching baseline levels at the end of 2 hours. Blood glucose levels between the OGTT, AUC=147.3 mmol/L/ 120 min, n=3 vs the OSucTT, AUC=145.3 mmol/L/120 min, n=3, P<.81. AUC for plasma glucose was similar between the OGTT and OSucTT groups while lactate AUC was higher in OSucTT. Lactate levels during the OSucTT, AUC=295.4 mmol/L/120 min, n=3 vs the OGTT, AUC=200.5 mmol/L/120 min, P<.08. Insulin AUC was higher during the OGTT, AUC=3.3 U/ L/120 min, n=3 compared with OSucTT, AUC=2.1 U/L/120 min, n=3, P<.2. Insulin AUC was higher in OGTT compared with OSucTT.

Conclusion: This study examined the body's responses to sugar consumption. We found a difference between the physiologic response to glucose and sucrose with respect to insulin. Lactate levels were found to be slightly higher in OSucTT but not significantly different, P<.08, while insulin levels were higher in OGTT, p<0.02. Interestingly, blood glucose levels did not differ between glucose and sucrose consumption, P<.81. Future studies include measuring the body's response to a fructose/ galactose/lactate load. Understanding the metabolic response to dietary sugars could inform future dietary recommendations and possibly reduce chronic diseases with nutritional links. Limitations of this study include a small sample size and the testing of only glucose and sucrose.

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# B16—Chronic Diseases & Conditions

# Comparison of Triglyceride Extraction Methods in Plasma and in Triglyceride-Rich Lipoprotein for the Analysis of De Novo Lipogenesis

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Research Question: It is estimated that 4 of the 10 leading causes of death in the United States, including heart disease, certain cancers, stroke and diabetes, are in some way linked to poor diet and lack of physical activity. The metabolic feature of poor lifestyle is identified as metabolic syndrome and refers to the cluster of obesity, hypertension, hyperglycemia, hypertriglyceridemia, and cardiovascular disease, occasionally with secondary manifestations of hyperuricemia, non-alcoholic fatty liver disease (NAFLD), and polycystic ovarian syndrome. The consumption of high fructose corn syrup (HFCS) has been associated with obesity and an increased risk for cardiovascular disease and type 2 diabetes. Fructose, a component of HFCS, and sucrose, table sugar, is metabolized almost exclusively in the liver, and increases the availability of triglyceride (TG) building blocks, dihydroxyacetone phosphate (DHAP), and acetyl-CoA. DHAP can be converted to glycerol-3-phosphate (G3P) and serves as the backbone of TG molecules. Acetyl-CoA is the monomer used to build up fatty acids in a process called de novo lipogenesis (DNL). In the liver, these newly synthesized fatty acids and G3P are assembled into TG and are either stored in the liver or packaged into very-low

density lipoproteins (VLDL) and secreted into the blood stream. These VLDL particles, containing approximately 55% to 80% TG, contribute to postprandial plasma lipid levels and triglyceride-rich lipoproteins Additionally, chylomicrons are lipoprotein particles, containing 80% to 90% TG, secreted by the small intestines that transport dietary fats in the bloodstream and also contributes to postprandial plasma lipid levels and TRL. Using stable isotope tracer techniques, we demonstrated that fructose consumption increases DNL in healthy lean adults. Current processes to measure fractional DNL requires the extraction of TG-containing palmitate from TRL particles through the classical method, an extensive 5-step process: (1) a 17- to 20-hour ultracentrifugation to obtain TG-rich lipoproteins; (2) extraction of lipids; (3) thin layer chromatography (TLC); (4) derivatization to obtain fatty acid methyl esters; and (5) measurement of methyl palmitate by gas chromatography/mass spectrometry followed by mass isotopomer distribution analysis. The purpose of this study is to evaluate different TG extraction methods such as solid phase extraction (SPE) or nonspecific isolation, which either substitutes or eliminates steps in the classical method. We hypothesize that using alternative TG extractions will result in an efficient method for measuring fractional DNL in both plasma and TRL.

**Methods:** *Participants.* 2 healthy males and 1 healthy female, aged 18 to 40 years, were recruited from the community. Key exclusion criteria included evidence of diabetes mellitus, liver disease, kidney disease, or thyroid disorders, or taking anti-diabetic, hypolipidemic, anti-hypertensive or anti-depression medications. In addition, smokers, pregnant women, and those with dietary restrictions were excluded. All procedures

followed were in accordance of the Touro University California Institutional Review Board (IRB-M#0716.) A written consent form was obtained from all participants prior to screening. Study Design. Participants arrived at the Metabolic Research Center at Touro University after a 10- to 12-hour overnight fast. An intravenous catheter was placed in each participant for repeated blood draws. Blood samples were taken over the course of 8 hours. Subjects were fed a meal every hour and a sugar sweetened beverage containing <sup>13</sup>C-sodium acetate every 30 minutes. Blood was drawn every 30 minutes and plasma extracted. TRL was isolated by the ultracentrifugation of plasma at 40,000 rpm for 17 to 20 hours. Lipids were extracted using the 1:3 methanol and chloroform-Folch method. Samples were divided into 3 and underwent the following to isolate TGs: (a) TLC, (b) SPE, and (c) nonspecific isolation (no-TLC.) Additionally, lipids were extracted directly from plasma and divided into 3, and TGs isolated by (a) TLC, (b) SPE, and (c) no-TLC. All samples were derivatized. Fractional DNL was measured and calculated in each sample using gas chromatography/mass spectrometry and mass isotopomer distribution analysis.

Results: Triglycerides were successfully isolated using the nonspecific isolation method, no-TLC, and TLC from both TRL and plasma samples. When all sample groups were compared, fractional DNL-AUC trended in the following order: TRL-TLC > TRL no-TLC > Plasma-TLC > Plasma no-TLC (AUC=1.02, n=3 > AUC=0.92, n=3 > AUC=0.87, n=3 > AUC=0.39, n=3.) As compared with TRL-TLC DNL-AUC, TRL no-TLC resulted in a 10% reduction in DNL-AUC, Plasma-TLC resulted in a 14% reduction in DNL-AUC, and Plasma no-TLC resulted in a 62% reduction in DNL-AUC.

**Conclusion:** DNL-AUC for the classical method, TRL-TLC, was the highest and served as the

basis for comparison because it contained only fatty acids derived from TRL-TGs. Differences in DNL-AUC for each method can be explained by the presence of fatty acids derived from sources other than TRL-TG. Plasma samples obtained using the nonspecific isolation method, no-TLC, was significantly less than those obtained using the classical method. Plasma samples contain fatty acids from phospholipids and cholesterol esters, LDL-TGs and HDL-TGs, along with free fatty acids in addition to fatty acids from TRL-TGs. Interestingly, TRL no-TLC samples and Plasma-TRL samples were similar although the derived fatty acids were from different molecules. TRL no-TLC fatty acids were from VLDL-TGs, chylomicron-TGs, phospholipids, and cholesterol esters, whereas Plasma-TLC fatty acids are from VLDL-TGs, chylomicron-TGs, LDL-TGs, HDL-TGs. With a larger sample size, we hope to generate a factor that can be applied to samples that deviate from the classical method. The omission of 1 or more steps can result in the efficient management of resources. Additionally, plasma samples can be frozen and sent from anywhere in the world, as TRL is generally obtained from fresh plasma. This would diversify DNL research to different populations in various geographic locations that have varying genetic makeup and dietary patterns. In conjunction with the SPE samples, we aim to provide a framework that allows researchers the freedom to choose between methods of sample preparation, ultimately furthering the investigation of DNL and to better understand its role in lipidology and health. Limitations of this study include cohort size.

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# ◆B17—Chronic Diseases & Conditions

# Caenorhabditis elegans as a Model Organism for Emery-Dreifuss Muscular Dystrophy

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Introduction: Emery-Dreifuss muscular dystrophy (EDMD) is a rare and currently incurable disease with the first symptoms usually presenting in the first or second decade of life. Clinical diagnosis of EDMD can be made for patients with the clinical triad: early contractures of elbow flexors, ankle plantar flexors, and spine; childhood onset of humeroperoneal weakness and wasting, and cardiac disease with conduction defects, arrhythmias, and cardiomyopathy. Despite the fact that most EDMD patients remain ambulatory for many years and seldom, if ever, develop profound motor or respiratory dysfunction, their quality of life is significantly impaired and they remain at high risk of sudden cardiac death from heart block and/or progressive heart failure. Currently, there is no disease-modifying therapy for EDMD and management is supportive. A cure is still desperately lacking and research in EDMD includes gene therapy, gene silencing, and cell therapy. To facilitate and broaden the research scope, our work focused on introducing Caenorhabditis elegans as EDMD model organism. C elegans unc-84 mutant worms carry mutations that can be compared with a gene mutation seen in patients afflicted with the autosomal dominant form of EDMD. However, these C elegans EDMD mutant worms do not present with an obvious quantifiable phenotype when compared with wild-type worms. To establish a quantifiable phenotype and establish C elegans as a potential model organism for EDMD, we used the worm treadmill previously developed in our laboratory. Briefly, C elegans, displays a specific locomotion response to various stimuli, including food, chemicals, and electricity. C elegans' response to electricity has been well described and dubbed electrotaxis-the repeatable behavior of crawling toward the negative pole when subjected to an electric field of sufficiently low power so as not to interfere with muscle contraction. We used this behavior to initiate and maintain locomotion to perform exhaustion tests in unc-84 (EDMD mutant worms) to quantify and compare it to wild type. Hypothesis: Unc-84 (EDMD) mutants will have a significant deficit in time to exhaustion and distance traveled compared with wild type C elegans.

Methods: C elegans strains were maintained at 25°C under standard conditions. Hypochlorite synchronized wild type, as well as unc-84 eggs were placed on plates with OP50 bacterial lawn (food) and grown to young adult stage before assaying. The worm treadmill consists of a specially formulated agar based gel and buffer placed in a classic DNA-electrophoresis box, a power source, a microscope camera, and an infrared thermometer to monitor gel temperature. Groups of 50-150 hypochlorite synchronized young adult worms were transferred to the gel, and a voltage of ≥4 v/cm was applied to initiate locomotion towards the anode. The distance and time that the worms were running were continuously monitored. The experiment was ceased and exhaustion was defined when there were no signs of further locomotion in the worms. To assure reliability and reproducibility, all of the experiments were repeated multiple times on separate dates (n=7-13). Hypochlorite synchronized dys-1 mutant eggs were placed on plates with 0.5 mg/mL prednisone mixed into OP50 bacterial lawn (food).

Hypochlorite synchronized wild type, as well as unc-84 eggs, were placed on plates with no drugs added and used as controls.

**Data Analysis:** We collected both the time and distance ran data from multiple repeated experiments (7-13 experiments for each *C elegans* strain/control condition). We plotted and analyzed the data using GraphPad Prism 7 software. To assess statistical significance of the data, we used a 1-way ANOVA followed by Dunnett's multiple comparison test. *P* values lower than .05 were considered significant.

Results: Using C elegans innate electrotaxis behavior and the worm treadmill platform, we ran 2 different unc-84 mutants (CB1174 and CB1410), harboring mutations in different alleles. Despite the fact that crawling on food plates they exhibit no quantifiable phenotype, as we anticipated, on the worm treadmill wild type worms ran significantly longer than the tested unc-84 (EDMD) mutants. Both alleles exhibit a significant deficit in endurance compared with wild type; however, CB1174 strain based on our results has a more robust treadmill phenotype and might be a better candidate for being a EDMD model strain. To explore the potential of our newly established EDMD model to be used for drug screening, we conducted preliminary drug treatment experiments using prednisone as our first candidate compound. Unc-84 mutants treated with prednisone ran statistically significantly longer (up to 60 minutes) and farther than untreated unc-84 mutants.

**Conclusion:** The purpose of this study was to establish *C elegans* as a potential model organism for EDMD research. The worm treadmill is a cost effective and practical platform to be able to run worms to exhaustion. While additional studies are needed to identify potential pharmaceutical candidate compounds, this is an important step toward exploring all possible avenues in our search for the cure for EDMD.

Statement of Significance: Disease prevention is one of the core osteopathic principles. The goal of this project is to provide and validate a model organism that may lead to the development of novel approaches for treating patients with EDMD. During skeletal and cardiac muscle contraction, emerin mediates membrane anchorage to the cytoskeleton—appropriately demonstrating the third tenet of osteopathic medicine: structure and function are reciprocally interrelated. This lack of proper anchoring is one of the main causes of progressive muscle damage occurring in patients with EDMD. The work in this study is conducted to provide further insight into EDMD disease mechanism and potential treatments, guided by the fourth tenet of osteopathic medicine: rational treatment is based upon an understanding of the basic principles of body unity, self-regulation, and the interrelationship of structure and function.

**Acknowledgment/Funding Source:** This study was funded by the West Virginia School of Osteopathic Medicine.

# ◆B18—Chronic Diseases & Conditions

# Rotavirus Mediates Upregulation of Protein Kinase STK11IP in Mammalian Cells Independent of Viral Entry

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**Background/Research:** Virus replication uses host factors and host signaling pathways to provide an environment necessary for replication and infection, respecting nuances and differences among the viral taxonomies. Rotavirus is a triple-layered particle virus with 11 double-stranded RNA segments, each segment carrying its own

distinct function. The outermost layer pertains mostly to host attachment and entry, while the double-layered particle is transcriptionally active in the cytoplasm. Because RNA viral replication occurs in the cytoplasm, a plethora of host protein interactions are likely to occur. Only a few of those viral-host protein interactions are known and described in the literature. Serine/ threonine kinase 11 interacting protein (STK11IP) was chosen as a candidate for further analysis as it controls localization of serene threonine kinase II (STK11), which in turn regulates multiple other protein kinases downstream, in particular, AMP-regulated protein kinase (AMPK). Using a combination of transfection and protein analysis, we attempted to find the mechanism of action of STK11IP during rotavirus infection via bypassing viral entry steps by transfecting purified double-layered particle (DLP). Assessing bypass of viral entry was performed by (1) quantifying immunofluorescence of STK11IP/VP2 in transfected cells with purified DLP; (2) quantifying protein levels in transfected vs un-transfected cells; and (3) performing co-immunoprecipitation with viral protein VP2 in transfected cells.

Significance: Rotavirus infection causes acute gastroenteritis and is the leading cause of diarrhea-related death in the world. Within the United States, children younger than 5 years infected with rotavirus cause over 400,000 doctor visits, more than 200,000 trips to the emergency room, and roughly 20 to 60 deaths yearly. Within West Virginia, enteric illness is the second most common type of disease outbreak, with 3% being of rotavirus origin (2015). Identification of STK11IP's mechanism could point to other compounds to influence the activity of the protein and replication of rotavirus. Understanding STK11IP's functional relationship in viral transcription can provide a model for patient's suffering from chronic illness as well as Peutz-Jeghers and

various pancreatic cancers, where similar mechanisms using STK11 have been noted. Using STK11IP's role paired with osteopathic manipulation could uncover treatments for patients suffering from such disorders.

Methods/Analysis: MA104 (African Green Monkey kidney cells) were maintained in complete medium (M199) with 10% fetal bovine serum, penicillin, and amphotericin B. Simian strain SA11-4F rotavirus infections were performed in serum-free media. Transfected cells were lysed and rotavirus DLPs were purified using AKTA protein purification on a protein A column and VP6 antibodies. DLPs (10μg/μL) were transfected into MA104 cells using lipid SilentFect (BioRad) transfecting reagent to bypass rotavirus' entry process. Cell lines were then incubated, collected, and lysed at intervals of 24, 48, and 72 hours. Lysate samples were quantified at their chronological points of transfection for viral protein levels of VP2, VP6, and host protein levels of STK11and STK11IP. Transfected MA104 cells were also probed for VP2 and visualized with immunofluorescence microscopy.

Results: DLP-transfected whole cell lysates were analyzed by Western blot using rabbit polyclonal antisera against STK11 and STK11IP and polyclonal guinea pig antisera against VP2 and VP6. The results show 45-kDa band consistent with the size of full-length VP6. Whole-cell lysates of transfected cells were noted to have increased levels of protein in DLP-transfected cells were observed under Immunofluorescence and showed a percentage of cells displaying a signal when probed with aVP2.

Conclusion: Our data suggest STK11IP upregulation is induced during rotavirus infection in the absence of viral entry. Increased protein levels are higher at later time points, possibly indicating a role during genome replication and assembly. Ongoing experiments using protein knockdown levels in the absence of viral entry will continue

to further elucidate STK11IP's role and function during viral transcription.

# ◆B19—Chronic Diseases & Conditions

## STK11IP Promotes Rotavirus Replication Independently of Protein Kinase STK11

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Background/Research Question: Viruses use host cell factors and signaling pathways to control the environment for effective replication. Not all viruses have the same approach to this process. Rotaviruses are triple-layered, non-enveloped, double-stranded (ds) RNA viruses, with 11 segments and a life cycle that occurs entirely in the cytoplasm. The replication cycle of rotaviruses certainly requires both its own viral factors as well as host cell machinery. However, few of these processes have been described in the literature. In a previous study, STK11IP was shown to be upregulated during rotavirus infection and to play a role in viral replication. STK11IP became a topic of interest due to its localization of STK11, a master regulator of 12 AMP kinases (AMPK). These AMPK pathways have also been implicated in setting up a permissive environment for viral replication. Using protein analysis and immunoblotting, we studied the relationship between STK11 and STK11IP during rotavirus infection using the following techniques: (1) identify STK11 levels during STK11IP knockdown infection; (2) identify STK11 levels during wild-type infection; and (3) determine viral protein levels during STK11 knockdown infection. Significance: As the leading cause of childhood diarrheal death worldwide, rotavirus infection accounts for over 400,000 doctor visits of children younger than 5 years in the United States. In the West Virginia, enteric illnesses are the second most common type of disease outbreak; rotaviruses are the fourth most common cause of these enteric illnesses. Identification of STK11IP mechanisms as cellular targets may allow the development of treatment modalities to mitigate the involved kinase and alter the course of infection. Additionally, STK11IP and its relationship to STK11 may also be modeled using rotaviruses for other diseases such as cancer or Peutz-Jeghers Syndrome, a chronic disease due to STK11 genetic mutation. Understanding the molecular biology of rotavirus, as well as these chronic diseases, can help further our ability as osteopathic physicians to understand structure-function relationships and better treat our patients.

Methods and Analysis: MA104 cells (African Green monkey kidney cells) were incubated at 37° C in 5% CO<sub>2</sub> complete Medium 199 (M199) supplemented with 10% fetal bovine serum. penicillin-streptomycin, amphotericin and B. Knockdown experiments were performed using SmartPool siRNA to block expression of STK11, STK11IP, with a non-target well for control. Transfection was done using Silentfect Lipid Reagent and OptiMEM medium to allow introduction of siRNA to MA104 cells, which were allowed to incubate for 72 hours. Rotavirus infections were performed using simian strain SA11-4F at a multiplicity of infection of 10 (MOI=10) in serum free M199. Infected and mock (cells treated in parallel noninfected) cell lysates were collected 4 hours after infection and separated using SDS-PAGE gel electrophoresis. Subsequent Western blotting used antibody specific for STK11, STK11IP, NSP2, and β-actin control. Western blots were quantified using Image J, and statistical analysis will be performed using the t test.

**Results:** Rabbit polyclonal antisera were used to probe for STK11. The results showed a 48-kDa band consistent with STK11 that was present in STK11IP knockdown lanes but absent in STK11 knockdown lanes. Reciprocation of this probe,

using rabbit polyclonal antisera for STK11IP, revealed a 121-kDa band consistent with STK11IP present in mock lanes and STK11 knockdown lanes, but diminished in STK11IP knockdown lanes. Several smaller bands were also detected in the STK11IP probe, consistent with prior studies that have suggested multiple isoforms of the protein.

Conclusion: Our data suggest that STK11IP and STK11 can act independently of each other in rotavirus infection, despite their co-expressive relationship. This helps us to understand why STK11IP plays a part in viral load and gives new direction for future studies. However, this is during a short-course infection of 4 hours, which may be a limiting factor; follow-up studies are being done to see if this holds true in longer infections (≥9 hours). Further, this supports our hypothesis that STK11IP promotes viral infection independently of STK11. Prior studies have shown that viral titers are lower in an STK11IP knockdown infection; therefore, further investigation may look at the efficacy of using STK11IP as a cellular target to block virally infected cells specifically. Additional studies are being carried out to understand the different areas of the viral life cycle where STK11IP plays a role.

# ◆B20—Chronic Diseases & Conditions

## Effects of a Drug That Inhibits Peptidyl Prolyl Isomerase Activity on Microbial Viability and Growth

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Research Question(s)/Hypotheses: The overall goals of this project are to determine whether natural products that inhibit peptidyl prolyl

isomerase activity may serve as therapeutic agents for the treatment of microbial infections.

Statement of Significance: With the rise of antibiotic resistance, the use of novel and natural antimicrobial treatments or adjuvants to traditional regimens for infections could improve patient outcomes and reduce health care costs and complications. Peptidyl prolyl isomerases (PPIases) are enzymes that catalyze the cis-trans isomerization of a peptide bond to proline, thus modifying the conformation of target proteins. Three superfamilies of PPIases have been described, which are in part defined based on small inhibitory molecules/ drugs that bind to the proteins. These include the FK506-binding proteins (FKBPs), the Cyclophilins (which are inhibited by cyclosporine A or related molecules), and the Parvulins. Pin1 is a human Parvulin that is highly conserved in bacteria and in fungi. We determined the effects of treatment of Juglone, a natural product extracted from black walnuts and a documented Pin1 inhibitor, on microbial viability and growth.

Methods: Organisms were obtained from American Type Culture Collection and included Candida albicans, Enterococcus faecalis, Bacillus subtilis, Yersinia enterocolitica, and Listeria monocytogenes. C albicans was cultured in yeast nitrogen broth (YNB) + 2% dextrose without amino acids. Cultures were grown at 37° C in a shaking incubator overnight, before experimentation. Complete basal medium was used for growth of E faecalis, B subtilis, Y enterocolitica, and L monocytogenes, which were also grown in a 37°C incubator. Juglone was solubilized in DMSO at a concentration of 10 mg/mL. Serial dilutions were prepared in DMSO. Overnight microbial cultures were diluted 1:100 and tested for effects of drug treatment. Cultures (100 µL) were prepared in 96 well plates, with 6 replicates for each drug concentration. Untreated controls had 12 replicates. To control for absorbance contributions by the drugs used, additional duplicate

wells were included with the indicated drug dilutions without added microbes. A Biotech 96 well plate reader was used to analyze growth of the organisms with the various drug concentrations. All cultures were grown at 37°C for testing.

**Data Analysis:** After overnight growth, the 96 well plates for each organism were read on a BioTek microplate reader with an absorbance of 570 nm. Data related to organismal growth were exported to Microsoft Excel for further analysis. Data were analyzed by subtracting the average absorbance contribution of the drug from the absorbance reading for each well containing the indicated organism. Growth data are expressed as the percent of untreated control wells.

Results: We found that the microorganisms tested exhibited differential sensitivity to Juglone treatment. While E faecalis was insensitive to the inhibitory effects of the drug, *B subtilis* and *Y enterocolitica* were sensitive to Juglone treatment, with 50% inhibition at approximately 4 μg/mL. *L monocytogenes* showed intermediate sensitivity to Juglone, with 50% inhibition of growth at between 62.5 and 125 μg/mL of drug. *C albicans* also demonstrated growth inhibition in with Juglone treatment, but our experiments did not identify a Juglone concentration at which 50% inhibition of growth was identified.

Conclusion: We found that Juglone inhibited growth of some human microbial pathogens. The organisms tested exhibited differential susceptibility to Juglone. *B subtilis* and *Y enterocolitica* were most sensitive based on 50% inhibition at approximately 5 µg/mL. *E faecalis* did not seem to be sensitive to the effects of Juglone. These results suggest that development of drugs that target Parvulin activity may lead to the development of novel antimicrobial therapies. In the future, we will further evaluate the susceptibility of *B subtilis* to Juglone treatment and to explore the possibility that juglone induces sporulation in this species. In addition, another natural product that

has been reported to be an inhibitor of Pin1 enzymatic activity, Epigallocatechin gallate (EGCG), a compound isolated from green tea, will be tested in similar studies.

**Acknowledgment/Funding Source:** This work was supported by a LECOM institutional research award.

# ◆B21—Chronic Diseases & Conditions

# Endothelin B Agonist IRL-1620 Affects the Histopathology of the Site of the Lesion in a Chronic Model of Spinal Cord Injury

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Introduction: Spinal cord injuries (SCI) can permeate many aspects of a patient's life. It can affect a person's mind, body, and spirit. 20% to 30% of patients with SCI have clinical signs of depression. The incidence of SCI is approximately 54 cases per 1 million people, with 17,700 new cases each year. There are on average 288,000 people currently living with SCI in the US. Not only is SCI devastating to the individual, but it is also financially taxing. One year of care can cost up to \$1,102,403.00 and \$4,891,398.00 over a lifetime, not accounting for wage losses and productivity. Most SCI treatment is palliative or symptom-based care, but one of the most promising areas is in stem cell therapy. Although adult neuroregeneration via endogenous stem cells is the subject of extensive research, it is not well used in the clinical management of SCI. Osteopathically, neuroregeneration reinforces the core tenant that the body works to heal itself. Endogenous multipotent neural stem/progenitor cells (NSPCs) are present in the central nervous system.<sup>3</sup> By identifying molecular signaling that corresponds to upregulation of NSPC activity, we will recognize how influence to

differentiation. Previous research has identified protein families associated with neuroregeneration. One of these protein families is the endothelins (ET). One specific ETB receptor agonist, IRL-1620, has been previously studied in Dr Gulati's research as producing neuroprotective properties after cerebral ischemia. IRL-1620 has also been implicated in angiogenesis and neurogenesis by stimulation of neuronal stem cells.<sup>4</sup> In functional studies, previous research has demonstrated that animals treated with IRL-1620 after SCI were able to recover motor function more quickly than control groups. Use of IRL-1620 reduced the area of infarct and oxidative stress while increasing angiogenesis and neurogenesis. Current mechanism hypotheses implicate the Notch signaling pathway as well as the MAP-ERK and PI3K-AKT pathways. Previous research in Dr Fornaro's laboratory has shown an upregulation of PI3K and p-AKT as a result of increased ETB receptor activation in an ex vivo model of SCI treated with IRL-1620 compared with control. Use of IRL-1620 has also demonstrated induction of neurite development and increased cell viability of differentiated neuronal PC-12 cells. IRL-1620 was previously used in other neurodegenerative conditions like stroke, for which it greatly reduced the areas of infarct and oxidative stress. In the animal model of Alzheimer disease, IRL-1620 increased memory recovery compared with control.

Methods: For this project, we used an in vivo model of contusion spinal cord injury in adult male rats. The contusion lesion was performed and animals were either treated with or without IRL-1620 (1nM three treatments after 1, 3 and 5 hr post lesion on day 1). At day 60 after SCI, both groups of animals were euthanized and spinal cords were harvested, fixed in 4% formal-dehyde and cryopreserved. We used samples collected from these animals. Aim 1 required discovering whether the treatment with IRL-1620

affected the size of the lesion and the phenotypes of the cells surrounding the lesions. We hypothesized that the neuroprotective role of IRL-1620 resulted in a reduction of the overall size of the contusion lesion in our rat model of SCI 60 days after trauma. Moreover, we hypothesized a lesser concentration of apoptotic cells in the area surrounding the lesion and the recruitment of microglia and cells of the immune system. Motor function study conducted at 14 and 30 days in animals treated with IRL-1620 indicated improved recovery compared with a vehicle. Both the IRL-1620 and vehicle used the same dosing regimen and were evaluated identically. Spinal cord samples T10-L1 were previously harvested and fixed in 4% formaldehyde, dehydrated in ethanol, and embedded in paraffin. Spinal cords were cut into 10 µm sections using a microtome and stained with hematoxylin and eosin. Sections were imaged with Leica DM 5000 microscope equipment with software for morphometric analysis. Samples included a sham model, 6-hour postcontusion, 60-day postcontusion with IRL-1620 treatment, and 60-day postcontusion without IRL-1620 treatment. After mapping of the lesioned area was completed in Aim 1, Aim 2 required studying these areas in further depth. The morphology of the cells was categorized within the lesion. Using markers for apoptosis, the area of lesion resulting in apoptosis was determined using Bcl2, BAX, and cleaved caspase 3 markers. Healthy tissue was identified using glial cell markers oligo1, oligo2, S-100, and GFAP.

Results: Rat spinal cords from T10-L1 were harvested 6 hours after contusion to assess initial injury, recovery, and morphological changes. Compared with the sham, data analysis included mapping the total area of the spinal cord, area of grey matter, and area of any visible lesion. Additionally, within the total spinal cord area of each section, the percentage of tissue degeneration

was assessed by measuring the area not occupied by spinal cord tissue. Data analysis was completed using Media Cybernetic Image Pro Premier. Samples collected 6-hour postcontusion reflected significant damage compared with a sham model as reflected by a smaller total spinal cord area. smaller grey matter area, and obvious areas of lesions. Furthermore, tissue samples harvested 60 days after contusion treated with IRL-1620 were compared against a 60-day harvest not treated with IRL-1620. Samples treated with IRL-1620 resulted in a smaller lesion area, a larger total spinal cord area, and a larger grey matter area compared with control samples. Upon evaluation of apoptotic markers using confocal microscopy, images collected reveal decreased apoptotic markers present in samples harvested 60 days after contusion treated with IRL-1620 compared with 60-day controls.

Conclusion: Histopathological analysis of SCI after IRL-1620 treatment showed increased neuroprotection and improved anti-apoptotic properties. Additionally, IRL-1620 exhibited anti-apoptotic properties determined by analysis of apoptotic and healthy tissue markers in treated samples compared with controls. Future research includes a mechanism analysis of IRL-1620. Use of IRL-1620 after SCI clinically could greatly improve physical patient outcomes while decreasing emotional hardship and financial losses.

**Acknowledgments:** Previous research in Dr Gulati's and Dr Fornaro's laboratories at Midwestern University provided extensive background necessary for this project.

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## ◆B22—Chronic Diseases & Conditions

## Linking Gross Anatomy With Molecular Diagnostics: LECOM Training Experience

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Research Questions/Specific Aims: The overall goal of this project is to establish training of osteopathic medical students in the anatomic sciences with medical genetics and molecular diagnostics. Statement of Significance: Molecular diagnostics is an emerging area of pathology that applies modern techniques of nucleic acid and protein analysis to diagnosis of human disease. We have implemented molecular diagnostics into a didactic medical school curriculum to facilitate the transition into personalized medicine. This study aims to develop the laboratory infrastructure and methodologies to support genomics research at our institution. Students are trained in gross anatomic pathology as part of their anatomy laboratory curriculum. Having identified lesions or tissues of interest, they then perform laboratory analyses, including tissue staining and immunostaining, as well as genomic DNA isolation and molecular analyses by PCR. Molecular analyses involving genomic sequencing then offers students to bioinformatics as required for data analysis. Exome sequencing specifically targets only the portions of genes that are expressed as proteins, as well as regions of DNA flanking those genes. We chose

to perform exome sequencing to identify polymorphisms in an individual, which may be associated with development of disease, and correlate these findings to more personalized treatment approaches. The DNA sequences obtained were compared with reference DNA databases, and differences are identified as polymorphic. This program offers meaningful research opportunities for osteopathic medical students to develop a deeper understanding of human genetics and the close association of genetics with disease and will enable students to apply molecular concepts throughout their careers.

Methods: A 93-year-old white woman presented in the anatomy laboratory with extensive skin lesions and lymphadenopathy and a diagnosis of seborrheic keratosis was made. Further dissection revealed an intraorbital mass of 8.5 cm×4 cm that extended through the superior orbital fissure to the middle cranial fossa. Pathologic evaluation of H&E sections led to a diagnosis of a grade I meningioma. Tissues were procured from this cadaver, and genomic DNA was extracted using the ThermoFisher Gene Jet Kit. PCR analysis was performed using 50 ng purified DNA per reaction. Primers specific for human and beta-globin were tested as part of the determination of purity of the isolated DNA. DNA isolation from liver, kidney, pancreas, spleen, and 2 independent meningioma samples were determined to be of sufficient quality for further analysis. Through a contract with OtoGenetics Corp (Atlanta, Georgia), human exome sequence analysis was performed with a goal of 30-fold coverage of the human exome. Sequencing and polymorphism analyses were performed using various software packages housed at DNANexus.com. Clinical variant information was obtained from the Online Mendelian Inheritance in Man and NCBI websites.

**Data Analysis:** In analyzing the exome sequence data, we chose to limit our focus at the outset to (1) distinguishing polymorphisms from mutations,

based on potential impact on the expression or function of the gene product and focusing only on predicted high-impact mutations, (2) comparing the 2 meningioma samples to identify mutations that were common to both samples or unique to one or the other, (3) determining whether mutations in the meningiomas were also identified or were not identified in normal tissues (kidney, liver, pancreas, spleen), and (4) identifying any mutations in normal tissues that suggested a constitutional mutation.

Results: The number of polymorphisms identified from any of our DNA samples ranged from approximately 50,000 to 70,000 per sample. We identified high-impact mutations (those predicted to significantly affect protein expression or function) in 17 genes that were common to the 2 meningioma samples, but not identified in the normal tissues that were tested. Some of these mutations are in genes that have been associated with other malignancies, while some are as yet uncharacterized. Our continuing research will characterize these mutations and possible involvement in the initiation or progression of meningiomas. Our analyses also identified a heterozygous nonsense mutation in the CLEC7A gene in normal tissues. CLEC7A encodes a pattern recognition protein that is important in the innate immune response. Mutations in this gene, including the Tyr238X mutation that we identified, are associated with a predisposition to developing cutaneous fungal infections, including candidiasis and aspergillosis. Conclusion: Genomic DNA can successfully be isolated from cadaver tissues and the DNA can be amplified using PCR. It is possible that the multiple cutaneous skin lesions seen in this patient may be associated with constitutional mutation of CLEC7A. There may be an association between CLEC7A haploinsufficiency and the development of these benign skin lesions. CLEC7A is also expressed in microglia of the CNS, and 1 report has suggested that upregulation

of CLEC7A expression is associated with neurodegeneration. Future immunostaining for CLEC7A in CNS as well as skin lesions could help us to understand the role of this gene product in these sites.

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# ◆B23—Chronic Diseases & Conditions

# Pseudolaric Acid B (PAB) Sensitizes Gemcitabine Efficacy Toward Pancreatic Cancer Cell Death by Targeting p53/P-gp Signaling Pathways

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Hypothesis: Pancreatic cancer is one of the deadliest cancers in the United States, with an estimated 53,070 new cases and 41,780 deaths in 2016. The current first-line therapy of pancreatic cancer with gemcitabine yielded a median survival rate of 5.65 months and 18% of survival at 1 year. The major obstacle to successful treatment in patients with pancreatic cancer is due to multidrug resistance (MDR), which is a decreased effectiveness of an anti-cancer drug primarily in the presence of stroma cells, highly resistant cells, and stem cells. The major reason for MDR in cancer is the overexpression of P-glycoprotein (P-gp), a product of the human MDR1 gene. P-gp increases the efflux of anticancer drugs and reduces their accumulation inside the cell. Extensive studies reported that both p53 and multidrug transporters play important roles in chemoresistance. Therefore, our central goal in this project is to identify a novel, nontoxic agent, which can inhibit gemcitabine-mediated pancreatic cancer resistance by modulating the p53/p-gp axis, which would be a potential agent for pancreatic cancer therapy. We have identified a potential agent, Pseudolaric acid B (PAB), which is a diterpene acid isolated from the root and trunk bark of the tree Pseudolarix kaempferi Gordon. PAB has shown great promise as an anticancer agent in several cancer models. PAB was shown to reverse the multi-drug resistance of gastric cancer, as seen by the decreased expression of P-glycoprotein (P-gp). Furthermore, PAB causes G2/M cell cycle arrest by activating ATM/ p53 pathways. Therefore, given these molecular and cellular action profiles, we hypothesize that PAB could be a potential chemotherapeutic agent, which could abrogate the gemcitabine resistance and sensitize pancreatic cancer death. To test our hypothesis, we proposed 2 specific aims: (1) Determine if PAB may reverse the gemcitabine-resistance by regulating the P53/ P-gp axis in pancreatic cancer cells. To test this aim, we plan to examine the efficacy of PAB in gemcitabine treated Panc-1 [P53 mutant] and AsPC-1 (P53 null) cells by evaluating cell proliferation and apoptosis. (2) Determine if mutant p-53 (m-P53)mediated activation P-gp develops gemcitabine resistance in pancreatic cancer cells and whether or not PAB attenuates this process.

**Methods:** Two major pancreatic cancer cell lines Panc-1 and AsPC-1 cells were used to test this hypothesis. *Cell viability* was measured by MTT (3-(4,5-Dimethylthiazol-2-Y1)-2,5-Diphenyltetrazolium Bromide) assay. Briefly, Panc-1 and AsPc-1 cells were plated at 5000 cells per well in 96 well plates. Cells were treated with PAB and gemcitabine alone and combination at specific concentrations for 48 and 72 hours. Panc-1 and AsPc-1 cells were seeded in 6-well plates at 0.3×10<sup>6</sup> cells per well for *apoptosis assay*. Cells were treated with indicated concentration(s) of PAB, gemcitabine, or DMSO. In combination treatments, cells were pretreated with PAB for 24

hours before gemcitabine treatment. Dead and dying cells in both floating and adherent cells were measured in a flow cytometer (ACEA bio sciences) using the Annexin V/FITC kit according to the manufacturer's protocol. *Immunoblots assay:* Cells were exposed to PAB, gemcitabine alone, and PAB+gemcitabine combination or m-P53 SiRNA at definite time periods. Protein expression was determined by western blot analysis.

**Data Analysis:** All experiments were conducted at least 3 times independently. Statistical significance differences were determined by 1-way ANOVA and *t* test.

Results: We evaluated the effect of PAB, gemcitabine, and the combination of PAB and gemcitabine on cell viability, apoptosis, and protein expression in Panc-1 cells. Our results show that PAB inhibited Panc-1 cell proliferation in a doseand time-dependent manner (IC50 ~1.2 µM at 48 h and  $\sim 0.7 \,\mu\text{M}$  at 72 h). Our results also demonstrate that the IC50 value of gemcitabine was significantly decreased when combining PAB with gemcitabine. Furthermore, pretreatment of Panc-1 cells with PAB for 24 hours followed by gemcitabine resulted in significantly increased (2.5 fold) apoptosis compared with gemcitabine alone. Western blot results demonstrated that PAB sensitizes gemcitabine-induced apoptosis with evidence of enhanced cleavage of PARP and increases phosphorylation of p53, suggesting a potential mechanism of PAB to sensitize gemcitabine efficacy in pancreatic cancer.

Conclusion: PAB treatment alone has shown to decrease cell viability and increases the efficacy of gemcitabine toward cell death. Combination regimen of PAB in conjunction with gemcitabine greatly increased apoptosis and phosphorylates p53 in Panc-1 cells. These results demonstrated that PAB sensitizes pancreatic cancer cells to gemcitabine in vitro. The result also suggested that PAB and gemcitabine combination formulation

might be a promising chemotherapy strategy for pancreatic cancer.

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# ★B24—Chronic Diseases & Conditions

### Parkinson Disease: Through the Nose

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Research Question: Parkinson disease (PD) is a progressive, neurodegenerative disease that affects approximately 7.5 million people worldwide over the age of 40 years. Despite the billions of research dollars invested in PD research, the etiology and pathogenesis of PD are still poorly understood. With greater than 90% of cases occurring without any obvious cause, the identification of preventive measures, treatments, and cures are more pressing than ever. Clinically, advanced-stage PD manifests itself through prominent motor symptoms such as bradykinesia, rigidity, postural instability, and resting tremors. In addition, a range of nonmotor phenotypes has been described, ranging from cognitive impairments and constipation to a progressive reduction of smell sensation (hyposmia). On a cellular level, PD is characterized by the intracellular accumulation of insoluble α-synuclein protein aggregates known as Lewy bodies. The substantia nigra pars compacta of the midbrain with its dopaminergic (DA) neurons is the most prominent degenerating structure in PD brains, giving rise to the majority of the motor symptoms. However, the path of cellular destruction

actually begins in the olfactory bulb and the medulla-both of which are areas that accommodate large cranial nerves (CN) reaching into body cavities with high bacterial content (gut, nasal epithelium). The path of cellular destruction and its starting points have actually raised the question whether the disease actually originates outside of the central nervous system (CNS) in the gastrointestinal (GI) tract and nasopharynx and whether it involves bacteria and/or their metabolites (dual-pathway hypothesis). In our laboratory, we are investigating this possibility because we previously found the anaerobic, gram-positive skin pathogen Propionibacterium acnes in high abundance inside neurons of the cadaveric human PD brain. As a result of advanced culturing techniques, we have learned much about the opportunistic behavior of P acnes, which is able to evade immune detection through biofilm and intracellular invasion/persistence, and escape breakdown by macrophages, making it very potent in terms of virulence and invoking and sustaining inflammation. Therefore, P acnes is now considered a prime candidate in the search for the inflammatory trigger in sarcoidosis as well as other diseases with an inflammatory component. Our finding of the pathogen in human PD brains is somewhat of an enigma because the human brain is well protected from pathogens through the so-called blood-brain barrier (BBB). However, the BBB has certain weak spots, along the cranial nerves for instance, along which bacteria may be able to enter the central nervous system (CNS). We therefore hypothesized that Pacnes may be able to enter the CNS via the nasopharyngeal route along the olfactory nerve (CNI). The notion of a bacterial cause for PD is revolutionary as it implies previously unforeseen treatment options. A firm understanding of bacterial entry into the CNS will precipitate

new preventive and treatment strategies such as immune-modulating osteopathic lymphatic techniques as well as pharmacologic approaches.

Methods: This project was approved by the NYITCOM IACUC (2018-JRL-01). A sample size of 10 wild-type C57Bl6J mice were screened for deficits in olfaction using an odor cross-habituation test. Six odors were employed (isoamyl acetate, ethyl valerate, propyl butyrate, s-limonene, ethyl propionate, and ethyl tiglate; all 1:1000) and animal's reaction to those odors tested naively as well as 14 days after intranasal (nasopharyngeal) bacterial inoculation with either P acnes (strain Propionibacterium freudenreichii, or phosphatebuffered saline (PBS) as a control. After olfactory testing, animals were euthanized via transcardial perfusion with 4% paraformaldehyde. Whole heads were harvested for analysis. Holocraniohistochemistry was employed on entire heads to preserve the integrity of olfactory components in relation to the entire brain for sectioning and imaging. Immunohistochemistry was performed on 30 µm cryosections with primary antibodies specific for either gram-positive bacteria, myelin, olfactory marker protein, lectin-1, P acnes, or α-synuclein and conjugated to secondary antibodies with appropriate fluorophores. Images were captured with confocal microscopy. Data Analysis: Data analysis was performed the GraphPad Prism 7 interface.

**Data Analysis:** Data analysis was performed using the GraphPad Prism 7 interface. Quantifiable differences were compared using *t* test with significance set at 5%.

**Results:** The duration of snout-oriented sniffing between pre- and postinjection was compared for each scent for *P acnes*, *P freudenreichii*, and PBS-control groups. Significant differences were appreciated during trial 1 for mice injected with *P freudenreichii* when exposed to isoamyl acetate and propyl butyrate. *P acnes*-injected mice had a significantly longer sniff time before injection for

isoamyl acetate during trial 1. All other recordings were unremarkable. The use of a fluorescent Nissl stain (neurons, axons, nuclei) facilitated identification of all pertinent structures. Unlike P freudenreichii injection, which produced no appreciable pathological differences along olfactory pathways, intranasal injection with P acnes causes loss of myelination around the olfactory nerve with significant destruction of neuronal cell bodies and axons. P acnes injection caused widespread bacterial biofilm inside and aligned in shape with microcapillaries as well as olfactory neurons with olfactory bulb focus. Hot spots of α-synuclein were observed alongside biofilm deposits. None of these findings were present in bacterial controls (P freudenreichii) PBS-injected mice.

Conclusion: Our findings indicate that nasobacterial pharyngeal injection generally permits bacteria (P acnes or P freudenreichii) access to the CNS negatively impacting odor sensation, at least during the chosen time interval. Unlike P freudenreichii, which was mostly neutralized after 14 days without appreciable signs of cellular damage, P acnes persisted in biofilm in the olfactory parenchyma and inside nearby capillaries leaving behind a trail of cellular damage and cell death, especially along the olfactory nerve as it enters the CNS via the ethmoid bone. It must be assumed that this destruction of olfactory neurons has a long-term impact on olfactory sensitivity beyond 14 days, which needs to be tested. In addition to those behavioral aspects, which are intriguingly similar to the hyposmia observed in early PD, damage to the olfactory nerve likely creates additional opportunities for other pathogens to follow suit, exacerbating the situation. Once inside the CNS, it is not hard to imagine that P acnes could migrate deeper into the brain along established cellular paths of PD firmly established by Braak and colleagues. Our finding of  $\alpha$ -synuclein deposition along bacterial biofilm is most intriguing as it implies similarity to the recently discovered antibacterial role of amyloid protein in Alzheimer disease.

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## ◆B25—Chronic Diseases & Conditions

## **Propionibacterium acnes:** The Life of a Central Nervous System Escape Artist

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Research Question and Hypothesis: Parkinson disease (PD) is a progressive neurodegenerative disease that affects approximately 1% of the population older than 60 years. While the pathology is well-established, the ambiguity regarding the etiology and pathogenesis of PD has grossly impeded the ability to develop preventive measures, treatment guidelines, osteopathic manipulative treatment measures, and cures. Previously, our laboratory found evidence suggesting Propionibacterium acnes, an anaerobic bacterial pathogen found abundantly in the human dermatologic microbiota, may contribute to the pathogenesis of PD. In our study, P acnes was detected in the postmortem neurons of midbrains in human cadavers with known cases of PD. Because the bacterium is able to evade microglial immune detection, form biofilm, and precipitate neurological proteins, P acnes may be a source of the chronic neuro-inflammatory state that is characteristic of PD. Chronic inflammation is a promising etiology for the degradation of dopaminergic (DA) neurons within the substantia nigra pars

compacta, although strong evidence linking these features remain scarce. Microglia are macrophages of the central nervous system (CNS) that can polarize to 1 of 2 subtypes, M1 and M2, when exposed to a microbial invader. Upon activation, the M1 class responds first by producing pro-inflammatory cytokines to control the spread of infection and induce extrinsic apoptosis. Once an infection is cleared, the M2 type secretes antiinflammatory substances that counteract the function of M1 cells and promote tissue repair. Interestingly, previous research suggests that Pacnes disrupts microglial allostatic mechanisms by upregulating M1 subtypes, thereby inducing localized and chronic neuro-inflammation. The mechanism behind this disruption, however, remains elusive. In the current report, we hypothesized that P acnes contributes to neurodegeneration associated with PD by evading microglial degradation followed by neuronal invasion, intracellular persistence, and neuro-inflammation.

**Statement of Significance:** The notion of a bacterial cause for PD is revolutionary as it implies previously unforeseen treatment options. A firm understanding of bacterial persistence and neuro-inflammation in the human CNS is going to be vital in the development of effective preventive and treatment strategies, which could encompass immune-modulating, osteopathic lymphatic techniques alongside pharmacologic approaches.

Methods: Intracellular Survival Assay: Human microglia (HMG3) were inoculated with either P acnes (strains P6, P266, 33179 and 12.1.L1), bacterial (Escherichia coli, Staphylococcus epidermidis, Propio-nibacterium freudenreichii), and absolute controls. Extracellular bacteria were extinguished with a high dose of gentamicin after 2 hours followed by a maintenance dosage. Cells were lysed, contents plated, and colony forming units (CFU) counted at 24, 48, and 72 hours. Immunocyto-chemistry on Microglia: Microglia (HMG3; ATCC) were seeded on 12-mm cover-

slips and infected with either S epidermidis, P freudenreichii, or P acnes (strains P6 and 12-1-L1). Infection was terminated with paraformaldehyde (PFA) after 2, 6, or 24 hours. The coverslips were incubated with either primary antibody against gram-positive bacteria, Lamp1 (lysosomal) or Rab5 (endosomal). Appropriate secondary antibodies conjugated to fluorophores, phalloidin (cytoskeleton), and DAPI (nuclei) were used for visualization via confocal microscopy. Animal Models: All animal work was carried out in accordance with the NYITCOM IACUC (protocol: 2018-JRL-01). To investigate the consequences of bacterial brain infection in vivo, P acnes (strains 12-1-L1, P6), E coli, S epidermidis, and P freudenreichii were injected directly into the striatum of anesthetized mice. One group of P acnes-infected animals was treated with minocycline for 1 week starting on the day of infection. At either 24 hours, 2 weeks, or 4 weeks, animals were subjected to a battery of short motor-behavior tests followed by whole brain extraction for 30 µm frozen sections followed by standard and fluorescence immunohistochemistry analysis using primary antibodies against bacteria, DA neurons, inflammation, and α-synuclein.

**Data Analysis:** Data analysis was performed using Microsoft Excel software. Quantifiable differences were compared using the unpaired t test, analysis of variance, and post-hoc analysis for continuous measures. The  $\chi^2$  test and Fisher exact tests compared categorical variables. Significance was set at P<.05.

**Results:** While both *E coli* and *P freudenreichii* were completely neutralized by microglia, *P acnes* 12-1-L1 and, surprisingly, *S epidermidis* showed the highest survival rates overall with a characteristic drop after 48 hours and recovery after 72 hours. Strain P6 survived as well but at a reduced rate. Probing along the endo-lysosomal pathway revealed that while *P acnes* was

effectively taken up by microglia, it typically remained in the endosome following failed lysosomal fusion. Surprisingly, the same was observed for S epidermidis. Qualitative differences between strains P6 and 12.1.L1 and S epidermidis could not be resolved. All other bacteria we completely neutralized inside endolysosomes after 12 hours. All mice injected with bacteria (except minocycline treatment group) displayed some motor dysfunction after 24 hours. Only those animals injected with P acnes (strains P6 and 12-1-L1), still showed reduced motor function after 2 and 4 weeks. These results were supported by immunohistochemistry showing significantly reduced numbers of DA neurons in the substantia nigra pars compacta ipsilateral to the injection of P acnes into the striatum. We also noted persistent P acnes bacteria and biofilm inside capillaries and between cells of the mouse midbrain. Within the biofilm we also identified foci of α-synuclein deposition.

Conclusion: These experiments demonstrate that P acnes is able to escape microglial, lysosomal degradation resulting in invasive colonization of the brain in vitro and in vivo with the ultimate consequence of inflammatory ipsilateral DA neuron loss. Paired with the association of biofilm and α-synuclein deposition, this recapitulates much of the pathology seen in PD brains. The fact that this was all preventable with minocycline indicates a potential opportunity for antibiotics in the treatment/prevention of PD. It also invites a fresh look at targeted osteopathic manipulative treatment, focusing on the metabolic, neurologic, and respiratory-circulatory models to treat patients with neurodegenerative disease. Further research needs to be done to conclude if P acnes can in fact cause PD. With this work, however, we have made significant headway in that direction.

IRB Approval: 2018-JRL-01

## ♦★B26—Chronic Diseases & Conditions

### Modulation of Dendritic Cell Activation and Th1/Th2 Balance by Bacillus subtilis Exopolysaccharide Prevents Allergic Eosinophilia

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Introduction/Hypothesis: The relationship between mammalian host and intestinal microbiota has been linked with the prevention of allergic sensitization. The mechanism by which bacterial flora can potentiate effects on sensitization is unknown. Evidence suggests that the effects are achieved by modulation of the immune system. Previous work from the laboratory found that Bacillus subtilisderived exopolysaccharide (EPS) can prevent allergic eosinophilia in an in vivo murine model. Allergic disease manifests through allergen uptake by antigen-presenting dendritic cells (APC), APC presenting allergen to T helper (Th) cells, Th cell differentiation, and Th influence on effector cells. Atopy and allergic disease is predominantly a Th2-mediated process. The aim of this study was to investigate how B subtilis EPS affects dendritic cell activity and Th cell activation. In a potential pathologically Th2-skewed environment, this line of questioning achieves osteopathic significance by investigating mechanisms of altering T cell response to ultimately return balance and facilitate self-healing.

**Methods:** *T cell activation:* C57Bl/6 murine splenocytes were processed and incubated in Th0, Th1, or Th2 polarizing media in the presence or absence of EPS. Real-time polymerase chain reaction (RT-PCR) analysis using GAPDH (house-keeping gene), T-Bet (Th1 transcription factor), and GATA3 (Th2 transcription factor) probes

were used to determine the effect of EPS on Th-cell differentiation. Intracellular staining and flow cytometry was used to determine Th1 and Th2 cytokine profiles by measuring interferon γ (IFNy) and interleukin 4 (IL-4) production. Dendritic cell activation: C57Bl/6 murine splenocytes were processed and cultured in granulocytemacrophage colony-stimulating factor (GMCSF) to create bone marrow dendritic cells (BMDC). The BMDC were sensitized to ovalbumin (OVA) in the presence and absence of EPS. The cells were introduced to C57B1/6 mice by intranasal lavage, followed by serial challenge with OVA. Bronchoalveolar lavage fluid (BALF) was collected, stained with DiffQuick, and examined microscopically for eosinophils.

**Data Analysis:** *T cell activation:* T-Bet and GATA3 fold induction was determined relative to the internal control of GAPDH. Data were analyzed by *t* test using GraphPad Prism Software. Intracellular cytokine profile data were analyzed using flow cytometric analysis to compare mean fluorescent intensity (MFI) of IFNγ and IL-4 between T cells treated with or without EPS. *Dendritic cell activation:* Eosinophils were quantified as percent of cells in BALF and total cells/mL and were analyzed by *t* test using GraphPad Prism Software.

Results: *T cell activation:* We found that EPS treatment had no significant effect on expression of Th transcription factor GATA3 and T-bet expression. EPS treatment did alter the Th2 response by suppressing IL-4 production, as measured by flow cytometry. The Th1 response, measured by IFNγ production, was unchanged by EPS. *Dendritic cell activation:* Our analysis of BALF from OVA-challenged mice, following intranasal transfer of OVA-sensitized BMDC found that EPS-treated BMDC failed to recruit eosinophils to the same level as non-treated BMDCs.

**Conclusion:** These experiments tested potential targets for exploration into the mechanism of

EPS-mediated immune modulation and high-lighted the importance of Th1/Th2 balance. Our results identify that both dendritic cells and Th2 cells appear to be targets of EPS-mediated immune suppression. Further work is needed to understand how EPS alters dendritic cell and Th2 cell function. Future work is focused on elucidating the extent of EPS-mediated suppression of the immune system and understanding the full mechanism by which EPS suppresses allergic inflammation. The results of our work will bring us closer to understanding the role of bacteria in shaping the health of the immune system.

Acknowledgment/Funding Source: This project was funded using MWU start-up funds awarded to J.A.S. We acknowledge Dr. Katherine L. Knight from Loyola University Chicago for providing EPS for use in this project. Additionally, we thank the Midwestern University Core Facility and Dr Ellen Kohlmeir. IRB/IACUC Approval: #2754, Midwestern

University #2/54, Midwestern

### B28—Osteopathic Philosophy

### Current Trends in COMLEX-USA Level 1 and Level 2-CE Study Resources

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**Background:** The purpose of this study was to evaluate the current trends in study resources used by students to prepare for the COMLEX-USA Level 1 and Level 2-CE. Specifically, we aimed to answer the following questions: how many resources did students use, which resources did they use most often, and which resources did they find most helpful? To our knowledge, there have been 2 studies that have aimed to evaluate study strategies and

resources used by students to prepare for COMLEX-USA Level 1 ("Level 1") and COMLEX-USA Level 2-CE ("Level 2"). A 2013 study<sup>1</sup> found that longer preparation time was correlated with higher Level 1 scores. It also found that the most helpful review book for Level 1 was First Aid for the USMLE, the most helpful practice examination was the COMSAE, the most helpful question bank was COMBANK, and the most helpful lecture video was Kaplan USMLE. Interestingly, those who did not choose COMSAE as the most helpful practice examination were more likely to get a score of 600 or higher on Level 1 compared with those who did choose COMSAE as the most helpful practice examination. A 2015 study<sup>2</sup> found that First Aid for USMLE, UWorld, COMBANK, and Doctors in Training were the most helpful resources for Level 1, and COMAT examinations and clinical rotations were most helpful for Level 2. As more study resources become available each year, this information is apt to change, and we aim to look at the current trends COMLEX-USA study tools. This study is of significance to osteopathic medical students and osteopathic medical educators as an understanding of the most valuable resources will help students potentially improve their performance on the osteopathic medical board examinations. According to the NRMP Program Directors Survey, USMLE Step 1/ COMLEX-USA Level 1 score is the most important factor in selecting applicants to interview across all specialties, and USMLE Step 2/ COMLEX-USA Level 2 score is the fourth most important factor.<sup>3</sup>

**Methods:** This study was approved by the Kansas City University (KCU) Institutional Review Board. Participants were third-year (Level 1 survey) and fourth-year (Level 2 survey) medical students at KCU. This was a cross-sectional design. Students were given the opportunity to

complete an optional anonymous online survey. Participants were asked to disclose their COMLEX-USA Level 1 or 2 score, as well as their USMLE Step 1 or 2 score (if applicable). Popular resources were listed and participants were asked to rank each resource they used on a Likert scale (1 to 10) in terms of how helpful they found that resource to be. Then, they were asked to identify the 3 resources that they found to be the most helpful. They were given the option to write in answers if they used something that was not included in the survey. Resources included various review books, question banks, practice examinations, video/audio lectures, flashcard tools, and review courses. Data were analyzed in SPSS using descriptive statistics.

Results: In total, 60 students completed the Level 1 survey and 66 completed the Level 2 survey. For Level 1, the mean number of resources used was 12.6. Of these resources, the 5 most commonly used in descending order were: First Aid for the USMLE Step 1 (review book), UWorld (question bank), Pathoma (video lectures), Sketchy Medical (video lectures), and OMT Review (review book). The 5 resources rated most helpful in descending order were: UWorld (question bank), First Aid for the USMLE Step 1 (review book), Sketchy Medical (video lectures), Pathoma (video lectures), and COMBANK (question bank). A popular combination of resources commonly used by students for Level 1 studying is UWorld, First Aid for the USMLE Step 1, and Pathoma, commonly referred to as the "UFAP method." In our study, 58 of 60 students used this combination of resources. For Level 2, the mean number of resources used was 8.8. Of these resources, the 5 most commonly used in descending order were: UWorld (question bank), OMT Review (review book), UWorld Self Assessments (practice examinations), Kaplan (question bank), COMBANK (question bank). The 5 resources

rated to be most helpful in descending order were: UWorld (question bank), OMT Review (review book), COMBANK (question bank), OnlineMedEd (video lectures), and UWorld Self Assessments (practice examinations).

Conclusions: We found that students tend to use a variety of resources from several different categories in preparation for Level 1 and 2. OMT Review was a popular choice for both examinations. Our Level 1 results were consistent with the previous 2013 and 2015 studies<sup>1, 2</sup> in that First Aid for the USMLE Step 1 continues to be considered the most helpful review book used by students. UWorld and COMBANK were identified as the most helpful question banks when studying for Level 1. Sketchy Medical and Pathoma video lectures were also very popular and were identified as helpful by the students who used them. For Level 2 resources, question banks or practice examination resources encompassed 4 out of 5 of the most commonly used resources and 3 out of 5 of the most helpful resources, indicating that practice questions are a large part of Level 2 preparation. Because of the competitive nature of residency and the high importance of Level 1 and 2 scores, it is important to examine the current range of resources used by students. Because the amount of resources and categories of media continuously grows, this topic should be periodically revisited to aid students in making effective decisions for test preparation.

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### ★B31—Chronic Diseases & Conditions (AOA OMS Funded Grant)

### Lymphatic Pump Technique Enhances Immunity in a DSS Colitis Model

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Research Question: Inflammatory disease (IBD), comprised of ulcerative colitis and Crohn disease, is known to have a multifactorial process involving the immune, lymphatic, and gastrointestinal systems. It is comprised of both genetic and environmental causes; however, the exact pathophysiology of IBD is unknown. In the gut, the lymphatics have shown to control tissue edema, leukocyte trafficking, and chemokine clearance. Therefore, lymph stasis is thought to be a major contributing factor to the disruption of the normal immune and wound healing response to the tissue damage seen in IBD. If the lymph flow can be restored, then lymphatic remodeling and the body's natural self-healing mechanisms can overcome the innate immune response. We hypothesize that osteopathic manipulative treatment (OMT), specifically lymphatic pumping techniques (LPT), can be used to increase immune cell mobilization, antigen, and cytokine clearance, while also promoting proper wound healing in an IBD mice model.

**Methods:** In this study, we used C57BL6 mice treated with a 3% solution of dextran sulfate sodium (DSS). This method is a well-established model showing similar clinical features to IBD, with minimal risk of mortality. The mice were divided into 4 groups: control

with normal water, control with 3% DSS, anesthesia with 3% DSS, and anesthesia with LPT and 3% DSS. All groups received the respective fluid intake for 4 days, with euthanasia and colon collection following on the fifth day. For the groups requiring treatment, the anesthesia and LPT were performed 24 hours after the initial start time, once daily for the first 4 days. The LPT group received daily treatment by contacting the abdomen and pumping at a rate of 1/sec for 4 minutes. Following euthanasia and colon collection, all samples were divided in half, then half homogenized and half fixed in formalin. Institutional Animal Care and Use Committee (IACUC) approval was given for the project. The homogenized colons were analyzed using flow cytometry, ELISA, and staining for multiple inflammatory markers including, but not limited to, TNF-α, IFN-γ, IL-12, and TGF-β. The fixed colons were stained using hematoxylin and eosin.

**Results:** The histology showed significantly less inflammation and epithelial damage in the LPT group compared with the DSS groups without LPT (P<.01). Additionally, significantly lower levels of TNF- $\alpha$  and IFN- $\gamma$  were found in the LPT group compared with the DSS groups without LPT (P<.01).

Conclusion: These results provide valuable evidence for the potential use of OMT in patients with IBD and the need for human clinical trials. The results also show the importance of the lymphatics in the disease process helping us to better understand this illness. Future research should be aimed at using chronic model IBD mice and human trials.

**Acknowledgment:** Funding for this project was provided by grants from the AOA. We would like to thank the AOA and VCOM for their dedication to medical research and support in this project.

### Clinical

### ◆C1—Osteopathic Philosophy

# Assessing the Attitudes and Habits of Second-Year Medical Students During Board Examination Preparation

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Background: The second year of medical school is an extremely stressful period, as it requires that students not only continue to excel in academic coursework but also begin to prepare for a high-stakes board examination. There is ample research indicating the importance of a well-balanced diet, moderate exercise, and adequate sleep on well-being, productivity, and mental health. To our knowledge, however, the association between lifestyle factors and attitude during board examination preparation among medical students has not yet been studied.

**Objective:** The purpose of the current study is to assess the attitude and habits of second-year medical students at NYITCOM as they prepare for the Comprehensive Osteopathic Medical Licensing Examination (COMLEX-USA) Level I.

**Hypothesis:** A healthier lifestyle among secondyear NYITCOM medical students, marked by a well-balanced diet, moderate exercise, and adequate sleep, will be associated with positive attitudes during board examination preparation, as denoted by lower levels of perceived stress and higher levels of confidence.

**Methods:** An anonymous survey was administered via Research Electronic Data Capture (REDCap) to second-year medical students at NYITCOM shortly before the beginning of their dedicated board examination study period. The

questionnaire included validated survey items on lifestyle factors such as diet, exercise, and sleep, as well as an attitude assessment measuring perceived stress and confidence levels regarding their upcoming board examination. Differences between groups were determined using a  $\chi^2$  test, with P<.05 considered statistically significant.

Results: Ninety-five students responded to the survey; 45.3% of the respondents were female (n=43). Diet, exercise, and sleep habits were not associated with stress levels or confidence in achieving goal score on the COMLEX-USA Level 1. A significant difference in confidence levels was found between male and female students: females reported a higher level of confidence in being able to achieve goal score (P=.03). Further analysis demonstrated that, as compared with males, females performed a greater amount of mild exercise (P=.015) and had a lesser intake of soda and fruit juice (P=.025), as well as a lesser intake of meat, poultry, and fish (P=.003) on an average week. However, among females, there was no significant difference between these variables and confidence levels.

Conclusion: Second-year female students at NYITCOM rated themselves as being more confident in their ability to achieve their goal score on COMLEX-USA Level 1. Although females also appeared to have healthier lifestyle factors, in the female-only cohort, lifestyle factors were not associated with confidence. To better understand other factors that may affect confidence, further analyses are warranted. The goal of futures studies should be to establish whether creating targeted confidence-building interventions will optimize board examination performance. As the interplay between confidence and test-taking performance has not yet been studied, future studies should also consider the participant's actual board score.

**IRB Approval:** NYIT-IRB BHS-1353 (March 13, 2018)

### ◆C2—Osteopathic Philosophy

### Student Perspectives of Simulation-Based Medical Education for Basic Medical Procedures

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Research Questions: The use of simulation-based procedural labs is an integral part of the undergraduate osteopathic medical school curriculum and a method to practice procedures before performing them on real patients. The goal of these labs is clinical skill acquisition in a formative environment. The Principal Investigators had the following aims: (1) Determine the level of confidence osteopathic medical students had in completing procedures introduced via simulation labs, and see if this differed based on year of education at Kansas City University of Medicine and Biosciences (KCU). (2) Determine the frequency with which students in the clinical years performed the procedural skills learned during the preclinical years. (3) Gather learner feedback about methods to improve the delivery of the skills sessions.

Hypotheses: The investigators had the following hypothesizes: (1) Learners would believe simulation is of benefit to introduce various procedures in the preclinical years. (2) Learners would not have frequent opportunities during the clinical years to perform the procedural skills introduced during the preclinical years. (3) Learners would feel 1 session on a particular skill was not adequate to facilitate competency in that skill.

Statement of Significance: The continuing responsibility of physicians to deliver cost-effective quality care with good outcomes and patient satisfaction builds upon habits learned during undergraduate osteopathic medical education. A well-trained osteopathic physician, who is both knowledgeable and skilled and who embodies the tenets of osteopathic medicine will help to broadly

benefit society as a whole, as well as the goals and the reputation of the osteopathic medical profession. First- and second-year osteopathic medical students at KCU use human patient simulators (HPS) for venipuncture, Foley catheter insertion (Foley), nasogastric tube placement (NG tube), intubation, intravenous (IV) and intramuscular (IM) injection, labor and delivery (L&D), and suturing during the longitudinal course Principles of Clinical Medicine. The simulations occur on task trainers in small groups of about 6 students per faculty member, with the exception of the suture labs. The groups typically spend 35-45 minutes with the faculty member per procedure. KCU students are at 26 core sites, and participation in procedures in the clinical setting is variable. It is unclear if KCU students feel that their exposure during preclinical years helps prepare them to perform the procedure on rotations, or if students ever have the opportunity to perform the procedure during clerkships. Time gaps ranging from months to years exist between the simulated procedure and its real-life application, which leads to the question: Is exposure to these techniques in the didactic years too early to be of benefit, given the fact that exposure to a given simulated procedure is often on a single occasion over the course of the students' preclinical years?

**Methods:** Students from all 4 classes at KCU-COM (approximately 1400 osteopathic medical students) were sent a 156-item online voluntary and anonymous survey via SurveyMonkey after KCU IRB approval was obtained.

**Data Analysis:** Data were analyzed using SPSS Statistics (IBM) statistical software using descriptive statistics to quantify survey responses.

**Results:** Of the approximately 1400 students who received the survey, 282 surveys were returned. Of those, 94% were eligible for inclusion in our survey (n=265). For each of the 7 procedural labs taught using simulation, students were asked to rate their skillset immediately after the simulation

session as novice (1), beginner (2), competent (3), proficient (4), or expert (5). Across all 7 procedural simulations, students on average rated their skillset immediately after the lab as beginner (venipuncture, 2.2±1.0, n=228; Foley, 2.0±0.8, n=215; NG tube, 1.9±0.8, n=186; intubation, 1.9±0.8, n=207; IV & IM injection, 2.4±1.0, n=185; L&D, 1.8±0.8, n=130; suturing, 2.3±0.9, n=129). Third- and fourth-year students were asked how many times they performed each procedure while on clerkships. On average, students performed venipuncture, inserted Foley catheters, and intubated patients between 1 and 2 times (Venipuncture, 1.8 times  $\pm 2.1$ , n=95; Foley, 1.7 times  $\pm 1.9$ , n=92; intubation, 1.7 times  $\pm 2.0$ , n=83) during their clerkships. Few students had inserted an NG tube (0.7 times  $\pm 1.3$ , n=68); 49 of the 68 respondents reported never having done so during clerkships. Students reported more frequently administering an IM or IV injection (2.9 times  $\pm 1.9$ , n=67) and directly assisting in the vaginal delivery of a baby (2.9 times  $\pm 1.9$ , n=82). Most students (70 of 81 respondents) sutured 5 or more times during clerkships with only 1 student reporting never having sutured on clerkships. When asked if each lab was adequately carried out, respondent feedback revealed the majority of students strongly agreed, agreed, or neither agreed nor disagreed that it was adequately carried out. Of note, 45.7% of respondents either disagreed or strongly disagreed that the venipuncture lab was adequately carried out while only 14.8% of respondents felt negatively about the delivery of the suture and knot tying lab. For all other simulated procedures, between 22.5% to 28% of respondents felt that the lab was not adequately carried out. Students were asked a variety of questions regarding the delivery of the simulation sessions, responding on a Likert scale ranging from 1-5 with 1 being strongly agree and 5 being strongly disagree. Of specific interest was if students felt they had adequate opportunity to practice the skill during the lab session. The median response for all labs

other than venipuncture was that students agreed that they received adequate opportunity to practice. Conclusion: Students' self-perceptions of their skillsets immediately after the simulation sessions revealed that they viewed themselves as beginners across all simulations. The simulations are of benefit in the sense of gaining a cursory exposure to various procedures, rather than gaining true competency. Students on clerkships did have the opportunity to perform most procedures that were introduced in the preclinical simulation sessions on real patients during clinical clerkships with the exception of NG tube insertion. Students were least satisfied with how the venipuncture lab was carried out, suggesting that students desire more opportunity to practice that skill in a supervised setting before performing it on patients. 26% of respondents on clerkships claimed they had not done the NG tube lab and 19% claimed they had never done the IM & IV injection lab. All students must complete both labs before proceeding to the third year. The data are subject to recall bias, but this also suggests that the NG tube simulation and IM & IV injection simulation are less memorable and, perhaps, unnecessary simulations in KCU's medical education, or the delivery of these sessions needs to be changed.

**Acknowledgment/Funding Source:** We would like to thank KCU for funding for our research, as well as Dr Larry Segars for his guidance in the statistical analysis of the data.

## ◆C5—Chronic Diseases & Conditions

## Prevalence of Prediabetes and Diabetes in Rural Tanzania

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**Background:** Diabetes mellitus has become a pandemic. The World Health Organization has

estimated that the prevalence of diabetes worldwide is 8.5%. Once considered a first-world disease, rates of diabetes are rising dramatically around the globe. While diabetes is clearly rising in third-world countries, the quality and consistency of data is often lacking, especially in more remote and rural areas where rates are harder to capture. For example, the WHO estimates that the prevalence for diabetes is 4.3% for Tanzania (East Africa), yet recent studies' estimates range from 1% to 16%. There are also few data on the prevalence of prediabetes in Tanzania. In the United States, 11% of people progress from prediabetes to type 2 diabetes each year. In this study the authors sought to determine the prevalence of prediabetes and diabetes and the diabetes knowledge among Tanzanian adult citizens.

Statement of Significance: It is important to determine the true prevalence rate of this chronic condition in rural countries like Tanzania. The current estimation is 4.3%, which is relatively low compared with the rest of the world. If there is support that the true prevalence is less than or equal to 4.3%, it would be worth investigating their lifestyle habits and/or genetics. If there is support that the true prevalence rate is greater than or equal to the global or US prevalence, than this determination can help prioritize the need for diabetes screening, prevention, and education programs in the community. By implementing the proper diabetes programs in Tanzania, we could improve people's innate connection between the body, mind, and spirit by preventing or slowing the progression of this insidious disease, thereby allowing the natural mechanisms of self-regulation, self-healing, and health maintenance to do their role.

**Methods:** This study was approved by the Touro University California IRB (# M-1618) and Shirati KMT Hospital. All participants were adult members of the Shirati village community. A tent was set up as part of a medical fair in a daytime

market. There, people could volunteer to participate in the study and provide verbal consent to participate. Subjects were asked their personal information including their age, sex, if they have ever been told that they had diabetes, and if they had eaten in the last 6 hours. If they had eaten in the past 6 hours, they were placed in the "random" glucose pool; if they had not, they were placed in the fasting glucose pool. Participants were also asked 4 multiple choice diabetes knowledge questions. A finger-stick glucose test (Easy Touch Diabetes Testing Kit) was then performed and subjects were further categorized into either normal, prediabetes, or diabetes.

**Data Analysis:** Descriptive analysis was completed on patient data and surveys. Results are reported in terms of total score and means with standard deviation using Microsoft Excel (version 15.31).

Results: In total, 154 people were screened; 25 participants had fasting and 123 had random glucose checks. Six participants had previously been diagnosed with diabetes, 3 were found to be hyperglycemic (with no know previous diagnosis of diabetes) and 24 (16.2%) had glucoses levels in the prediabetes range. The mean age of all participants was 40.7±14.1 years. Mean age of each category are as follows: prediabetes, 44.1±12.9 (n=24); undiagnosed diabetes, 47±5.2 (n=3); previously diagnosed diabetes, 58.5±10.8 (n=6); and undiagnosed/previously diagnosed diabetes, 54.7 ±10.6 (n=9). In participants who had no known history of diabetes (n=148), 121 (81.8%) were "normal" by our glucose parameters (fasting >100 mg/dL; random >140 mg/dL), 24 people (16.2%) fell into the "prediabetes" range (fasting, 100-125 mg/dL; random, 140-199 mg/dL), and 3 people (2.0%) were in the "diabetes" range (fasting,  $\geq$ 126 mg/dL; random, ≥200 mg/dL). The prevalence of diabetes (diagnosed and undiagnosed) based on our sampling was 5.8% (n=154). The collective diabetes quiz score among all 154 participants was

315 of 616 (51.1%). The overall diabetes facts quiz scores for each group are as follows: "normal" range glucose, 243 of 484 (50.2%); "prediabetes" range glucose, 52 of 96 (54.2%); "diabetes" range glucose, 6 of 12 (50%); "previously diagnosed diabetes," 14 of 24 (58.3%).

Conclusion: In the present study, the measured diabetes prevalence in rural Tanzania was 5.8%, which is relatively close to the WHO's estimate of 4.3% and certainly falls in the range of previous estimates (1%-16%) gathered from existing studies. However, rates of prediabetes in this study suggest that diabetes rates will continue to rise. There are a number of limitations to this study, including a small sample size, which limits generalizability. Also, the screening session took place in the middle of a market on a warm day, so the participants had to be able to be at an outdoor market shopping when they came across our screening booth. Additionally, the screening used a single serum glucose measurement, whereas repeated measurements or hemoglobin A<sub>1c</sub> may be more accurate. This study was conducted in a rural part of Tanzania, excluding large urban areas, so our data are not entirely representative of the population. Given the known rapid progression of prediabetes to diabetes, the prevalence of prediabetes (16.2%) in this sample was concerning. The mean age of screened with suspected prediabetes (44.1±12.9) was lower than those with diagnosed/undiagnosed diabetes (54.7 ±10.6). This highlights the need for populationbased screening, education, and prevention programs that strive to identify the disease in its early stages. The undiagnosed diabetes group had a mean glucose measurement of 401±67 mg/dL, whereas the previously diagnosed with diabetes group had a mean glucose measurement of 114 ±21 mg/dL. This mean glucose measurement of the undiagnosed diabetes group makes longstanding diabetes probable. Comparing this mean glucose measurement to that of the previously

diagnosed group, we conclude that the undiagnosed could benefit from a diagnosis to better maintain control of their blood glucose. Across all groups, the diabetes quiz scores were similar but showed remarkably low diabetes knowledge. This too adds support to the need for program implementation. In a future study, we would also strive for a larger sample size and acquire more information about our participant's demographic, such as blood pressure, medical history (eg, chronic kidney disease, hypertension), body mass index, waist circumference, family history of diabetes, birth weight, birth weight of children, diet, smoking history, level of education, and lifestyle habits. This additional information is important to validate our findings and to provide context for who is at risk in this population.

Acknowledgments: Anne Lee RD, CDE (MOBEC), Dorothy Kawira (Palliative Care Department, Shirati KMT Hospital)

## ◆C6—Chronic Diseases & Conditions

### Patterns of Opioid Use During Initial Buprenorphine/Naloxone Treatment in Relation to Changes in Opioid Management Laws in Kentucky

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Background and Objectives: There is limited information on the most commonly used opioid reported at the time of presentation for treatment with buprenorphine/naloxone and the extent to which state policy may impact type of opioid use reported. Our hypothesis is that the current Heroin epidemic affecting Kentucky is linked to the implementation of House Bill One (HB1).

**Methods:** Retrospective study, N=595 from 4 different medical locations from January 1, 2009, to July 1, 2016, that provided buprenorphine/nalox-

one treatment in Louisville, Kentucky. Study aims included identifying the most commonly used opioid at the time of treatment before and after the creation of a state-wide opioid prescribing surveillance system (i.e., the 2012 HB1), and determine the extent to which clinical setting, sex, age, and insurance type impacted type of opioid reported during the intake appointment.

**Results:** Non-heroin opioid use decreased in the academic and private practice settings following passage of HB1, while heroin use increased in all 3 settings. After controlling for clinical setting and demographic characteristics, there was a significant increase in patients who reported using heroin (vs non-heroin opioid) (RR=25.00;  $P \le .001$ ; CI, 12.08-51.73) and a significant increase in patients who reported using opioid agonists (vs non-heroin opioid) (RR=6.56;  $P \le .001$ ; CI, 4.10-10.50) following enactment of HB1.

**Discussion and Conclusion:** After the passage of HB1, there was a significant increase in patients reporting heroin use and opioid agonists compared with non-heroin opioids when presenting for treatment.

**Significance (Data Analysis):** There has been a notable shift in the opioid epidemic, which is evident in outpatient treatment settings.

## ◆C7—Chronic Diseases & Conditions

### Using DCS, an In-Vitro Approach, to Study Firing Rate of Purkinje Cells and Elucidate on Its Applicability in Cerebellar Ataxia

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**Research Question/Hypotheses:** Transcranial direct current stimulation (tDCS), a noninvasive brain stimulation, has been adopted for the management of various diseases related to cognition, emotion, adaptive learning, working memory,

and motion. Cerebellar ataxia is 1 type of neurologic disorders characterized by a lack of coordinated movements due to impaired cerebellar brain inhibition. Recently, transcranial direct current stimulation (tDCS) has been applied for the management of cerebellar ataxia patients. However, the mechanism of cerebellar tDCS at the cellular level remains unclear. Animal studies become important at this stage to answer the question, How does tDCS modify the output of the motor cortex through the cerebello-thalamo-cortical pathway? To understand the mechanism of tDCS to the cerebellar Purkinje cells (PCs), whole cell patch clamp was used to record from these cells. Direct current stimulation (DCS, 200 µA) was delivered at different electrode polarities to mimic the tDCS. The focus of this study is to measure the activity level of PCs under DCS.

Statement of Significance: This research contributes to the osteopathic community by trying to understand cerebellar ataxia, a chronic condition that is widespread, and has significantly reduced the quality of life of affected patients. It explores the effects of tDCS stimulation using in vitro technique on the Purkinje cell firing to elucidate cellular mechanisms involved in tDCS therapy.

Methods: Cerebellar Tissue Preparation: This study follows the protocol (#A14-007) approved by the PCOM IACUC. Sprague-Dawley (SD) rats were used for all experiments. The age of the SD rats was between 14 and 31 days. The purpose of using young pups was to have visible Purkinje cells before the cerebellar matrix is fully developed, which enhances the recording quality. Each rat was placed in an induction chamber with isoflurane (4% with Oxygen at 1 L/min by calibrated vaporizer), allowing the rat to lose consciousness without distress. Anesthetic delivery was maintained for 2-5 minutes until breathing was deep and slowed to 1 breath per second. Rats were then removed from the chamber and weighed in grams. While unconscious, the animal was

decapitated using a guillotine. After the removal of the head, an incision was made using surgical scissors along the midline of the dermis from posterior to anterior exposing the skull. Two parallel incisions were then made along both sides of the ears to allow further access to the brain. The skull was lifted to expose the cerebrum and cerebellum. A scalpel was used to make a coronal cut midway of the forebrain. The forebrain and the cerebellum were then removed from the rest of the brain and immediately placed into ice-cold artificial cerebrospinal fluid (ACSF). A piece of agar block was cut into a "V" shape and glued to the center of the loading block of the vibratome. The cerebellum was sectioned to fit the "V" inlet and glued onto the block in a position to have parasagittal sections collected using a vibratome at 200-300 µm. Slices were transferred to a 37°C chamber that was constantly perfused with oxygenated ACSF.

Recording: In vitro recordings from Purkinje cells were obtained using whole-cell patch clamp technique and visualized using a water immersion lens (×40) and an infrared filter. The ground electrode was placed in the recording chamber and aligned with the tip of the recording electrode. The glass pipette was filled with internal solution for the recordings. The DCS was applied using parallel wires oriented on either side of the slice. Prestimulation, anodal, cathodal, and poststimulation recordings were obtained. Once whole-cell patch clamp recording was established, we kept the membrane potential subthreshold between -60 mV and -75 mV using bias current. A series of current commands (-0.7 to +0.7 at 0.2per step) were given to test the basic property of the cell under the control condition. Then, the membrane potential was kept the same during DCS, and the same current commands were delivered. Spontaneous activity was recorded as well without the bias current.

**Data Analysis:** Recordings in whole cell patch-clamp were obtained using Axoclamp-2B

amplifier. Recordings were run through MATLAB R2016b, and the firing rate of Purkinje cells was determined. The frequency changes of PC action potentials under anodal and cathodal stimulation were compared using a paired *t* test.

Results: Thirteen Purkinie cells were recorded before, during, and after positive and negative polarity DCS to monitor average firing rates. No significant changes were observed in firing rate under either positive polarity (P=.82, n=13) or negative polarity (P=.07, n=11) conditions. No significant changes were observed in spontaneous firing rate under either positive polarity (P=.19, n=7) or negative polarity (P=.82, n=4) conditions. Conclusion: Overall, no significant changes were observed in the firing rate of PCs under DCS. The future direction of this study is to include the orientation of the PCs in the tissue section under the electric field of DCS. This is to test our hypothesis that the dendrite tree of individual PC oriented in each folium determines the final output change caused by DCS.

**Acknowledgement/Funding Source:** We thank Ms Shaunda Bell for her excellent technique assistance at the PCOM-GA campus animal facility. Funding was supplied by the PCOM-GA research division.

### ◆C8—Impact of OMM/OMT

### Using Wearable Technology to Measure the Effectiveness of Osteopathic Manipulative Treatment on Parkinson Disease Motor Symptoms

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**Introduction:** Parkinson disease (PD) is a chronic, progressive disorder characterized by

tremor, bradykinesia, rigidity, dyskinesia, and postural instability. The tremor that presents in PD is typically a rest tremor, meaning it is most apparent when the affected body part is not being engaged in purposeful activity. Tremor affects multiple domains of quality of life, from physical to psychosocial, in a large proportion of patients. Bradykinesia is a global slowing of movements. Dyskinesia consists of abnormal, involuntary movements. The recent development of the Parkinson's KinetiGraph (PKG, Global Kinetics) system, a device to be worn on the wrist, makes objective monitoring of such motor symptoms possible via accelerometric measurements. Long term monitoring of these symptoms is advantageous to account for daily variability commonly experienced in PD. Current treatment options for PD include pharmacologic, nonpharmacologic, and surgical modalities. There is limited data on the effect of osteopathic manipulative treatment (OMT) on tremors and movement in PD subjects. **Hypothesis:** We hypothesize that biweekly OMT sessions over a 6-week period will reduce motor symptoms in patients with PD, namely tremor,

**Statement of Significance:** Directly treating muscular and ligamentous restrictions with OMT may provide motor symptom relief in the PD population and potentially improve quality of life.

bradykinesia, and dyskinesia.

Methods: This study was approved by the NYIT institutional review board. Four PD subjects with balance and motor deficits were randomly assigned into the treatment arm or control arm, with 2 subjects per group. The treatment group received a biweekly OMT protocol for 6 weeks. OMT protocol focused on reducing somatic dysfunctions in the head, spine, and extremities and used primarily muscle energy and articulatory techniques. The control group received biweekly counseling sessions for 6 weeks to account for physician face-to-face time in the treatment arm. Presence of baseline motor symptoms was

assessed using the PKG system, a device worn on the wrist for 6 days before the first treatment (week 1). Following the final treatment (week 6), subjects again wore the PKG device on the wrist for 6 days. Severity of bradykinesia (BK) and dyskinesia (DK) was measured and scored by Global Kinetics. Tremor was measured as the percent of total time with tremor (PTT). Median scores for BK and DK, and PTT from before and after treatment were analyzed using a 2×3 mixed ANOVA approach.

**Data Analysis and Results:** BK values before and after OMT were 37.8 (SE=2.7) and 38.05 (SE=3.15), respectively. BK values before and after counseling intervention were 28.8 (SE=2.3) and 30.2 (SE=0.9). Higher scores represented worse BK. No significant differences were found (P=.489). Pre- and post-OMT DK values were 0.55 (SE=0.15) and 0.3 (SE=0). Pre- and post-counseling DK values were 0.85 (SE=0.15) and 0.45 (SE=0.15). Lower scores represented worse DK. No significant differences were found (P=.698).

Pre- and post-OMT PTT values were 13.3% (SE = 0.7) and 7.5% (SE = 0.6). Pre- and postcounseling PTT values were 11.5% (SE=10.8) and 13.05% (SE=12.05). Comparison of the groups showed improvement in the OMT group over the control group; although that finding was not statistically significant, it may be clinically significant (P=.055).

Conclusion: Results from this study suggest that OMT may decrease tremor severity in PD patients. Limitations of this study include a small sample size and analysis of raw PKG data by a third party (Global Kinetics). The project demonstrates the feasibility of using wearable devices to obtain objective measurements in movement disorders such as PD. Further research is warranted with larger sample sizes to determine whether OMT can produce clinically significant changes.

**Funding Source:** American Osteopathic Association research grant to S.Y. (grant #431607710).

IRB Approval: BHS-975

### C9—Osteopathic Philosophy

### Clinically Based OMM Competency Standards for Physicians in Residencies Designated With Osteopathic Recognition in the Single Accreditation System for GME

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Research Question: How do we create a set of clinically based OMM competency standards to train physicians in residencies designated with osteopathic recognition (OR) in the single accreditation system for graduate medical education (GME)?

Statement of Significance: By 2021, the much anticipated single GME accreditation system will be complete. To date, there are few details about how many programs will be applying to carry on the osteopathic philosophy and practice, or how this teaching will take place. With the granting of OR for either historically DO or MD programs, a set of clinically relevant competency standards for osteopathic manipulative medicine (OMM) will be required. Accreditation Council for Graduate Medical Education (ACGME) and American Osteopathic Association (AOA) program directors were surveyed to gather information to support the construction of said competencies. This research will present a set of proposed, clinically relevant, OMM competencies for physicians in ACGME residency programs acquiring OR.

**Methods:** After permission was obtained from the institutional review board, ACGME and AOA program directors were sent a survey link via email. The survey was created by the researcher and was reviewed by faculty peers for face validity. The primary investigator then created a set of OMM competency standards based on clinical utility as derived from survey data pertaining to common diagnoses and frequently used OMM techniques as cited by participants.

**Data Analysis:** Data were collected and analyzed using descriptive statistics from the surveys completed by participants.

Results: Data were collected from program directors in the general practice fields of family medicine, internal medicine, obstetrics/gynecology, pediatrics, and general surgery. Data were analyzed using descriptive statistics from the surveys completed by participants. There was an overall response rate of 11% (n=236) from all participants. The first question of the survey was a routing question indicating interest in OR, and 52.7% (n=126) of aforementioned participants completed the entire survey. Participants were asked to report the specialty rotations where OMM was most often used in their program. The top 3 responses were family medicine (31%), sports medicine (18%), and internal medicine (13%). In addition, participants were asked to report the most common diagnoses where OMM was used in their program. Low back pain (95.96%), neck pain (86.87%), headache (82.83%), and shoulder pain (76.77%) were cited most often. Lastly, soft tissue/myofascial release (72.9%), muscle energy (71.02%), and counterstrain (60.38%) were the most frequently used OMM techniques reported from participants.

Conclusion: With data gathered from current program directors and with focus on performance of specific osteopathic techniques and common clinical diagnoses, a set of proposed clinicallybased competencies could be used for structuring an osteopathic curriculum within an ACGME combined residency program with OR. This poster provides a set of sample competency standards based on clinical diagnosis.

## C10—Chronic Diseases & Conditions

### Higher Low Molecular Weight Advanced Glycation End-Products in Cord Blood Are Associated With Higher sRAGE

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Background: Advanced glycation end products (AGEs) modification of proteins is implicated in the development and progression of end-organ pathology in diabetes as well as other chronic diseases. Low molecular advanced glycation end-products (LMW-AGEs) reflect AGE catabolism and renal excretion, the latter being characteristically low in the fetus. Fuel metabolism in development and growth is very high and so should be methylglyoxal (MG) fluxes and thereby AGE formation. LMW-AGEs reflect AGE catabolism and renal excretion; therefore, studying them coupled with sRAGE explores the AGE-RAGE axis.

**Hypothesis:** In this study we tested the hypotheses that LMW-AGEs are elevated in cord blood, and this is associated with higher circulating sRAGE as compared with those in maternal blood.

**Methods:** In this cross-sectional study we compared consecutive paired serum from 60 healthy, non-diabetic pregnant women at term aged  $34.1 \pm 4.2$  years and their healthy newborns at term. Total and low molecular weight AGEs were measured by fluorescence. Serum sRAGE was measured by an enzyme-linked immunosorbent assay (R&D Systems Inc).

Results: Soluble RAGE were almost 3-fold higher in neonates than in their mothers: 2.24 (1.85-2.50) pg/mL vs 0.80 (0.70-0.97) pg/mL, P<.0001. LMW-AGEs were higher in neonates than in mothers: 64 (59-68) AU vs 51 (43-59) AU, P<.0001. The ratio LMW-AGEs/total AGEs was almost 3-fold higher in neonates than in their mothers:  $5.30 \times 10^{-2}$  (4.88-5.84) vs 1.96 ×  $10^{-2}$ (1.70-2.38), P<.0001. In cord blood, sRAGE correlates significantly with the ratio LMW-AGEs/total AGEs: Spearman r=0.25, P=.05.

Conclusion: We demonstrate that neonate cord blood contains 2- to 3-fold higher fluorescent LMW-AGEs coupled with 2- to 3-fold higher sRAGE as compared with their mothers. Our findings are in agreement with the present paradigms, giving the kidney a critical role in AGEs disposal and sRAGE a role as a defense mechanism. To be sure, more mechanistic work is needed to examine the sRAGE-AGE axis in the fetus and neonates.

## ◆C11—Chronic Diseases & Conditions

## Interplay Between Holiday Weight Gain, Obesity Knowledge, and Cravings

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Holiday weight gain is a recent consideration in the pathogenesis of obesity. During the holiday season, defined by the 6 weeks in the Western culture between Thanksgiving and New Year's Day, patients are challenged in monitoring food choices. Previous studies have indicated that obesity is no longer considered a simple causative disease, and thus psychological aspects also become critical in patient treatment. Obesity and its pathogenesis should be closely considered in the osteopathic field as it inherently reflects the osteopathic principles and practice of connecting mind and body. The interplay of holiday food cravings, sensory input, and potential consumption become of particular interest. In this study, we specifically focused on the knowledge of patients in the areas of obesity, holiday weight gain, and personal cravings. We aimed to see if age, race, sex, body mass index (BMI), or location were correlated to different levels of knowledge or cravings. Thus, varying levels of each aspect impacts physician goal-oriented care. The institutional review board approved this study. A survey, available both on paper and online, was designed to be objective, specifically modeled after previously established scales and questionincluding the Achievement Goal naires Questionnaire-Revised and Motivation Assessment 2 scale. The survey was broken down into 4 sections, each with a 5-point scale: Demographics, Obesity Background Knowledge, Cravings Knowledge, and Cravings Self-Report. Results were analyzed through IBM SPSS24 software. By using a Pearson correlation and Cronbach coefficient, we evaluated the linear association between variables and the consistency within cohorts. The minimum statistical significance was set at the .05 level, 2-tailed test, for all of the analyses used to compare the craving knowledge ratings with respect to gender, age, and race. The results suggest that the patient population, no matter age, race, sex, BMI, or study site location, is fairly knowledgeable and have holiday cravings which, upon sensory stimulus, result in food consumption about half of the time (P < .05). Furthermore, in order of importance, the senses with the greatest impact on cravings appear to be smell and taste, sight and hearing, and then texture (P<.001). This suggests that there is an underlying cognitive dissonance that physicians must battle when counseling patients during these crucial 6 weeks, paying particular attention to

sensory inputs of smell and taste. In other words, although patients are fairly knowledgeable, sensory inputs and cravings tend to drive the behavior of eating instead. Limitations of this study were temporal and geographical. Rowan Family Medicine has the majority of locations in southern New Jersey, where the population is mostly white middle class. Because the research occurred during the summer, patients may not fully remember their behavior during the holiday season. In addition, some patients were currently undergoing counseling for weight loss, which may have skewed or overestimated the basic level of knowledge. Future research should be conducted closer to the holiday season with a larger sample and include more socioeconomically diverse patients. Also, more investigation is needed to address specific categories of taste and smell such as sweet, savory, bitter, etc. Funding was provided by the Rowan School of Osteopathic Medicine Summer Medical Research Foundation. The success of this study was due, in part, to Robert Steer, EdD, with his expertise in data analysis and to the Rowan Family Medicine staff for their overall guidance.

### ◆C12—Osteopathic Philosophy AOA OMS Funded Grant

### Leveling the Playing Field: Evaluating How Prerequisite Classes Affect Perceived Stress Levels in Medical Students

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Research Question(s)/Hypotheses: As the use of different technology modalities emerge in medical education, the way lecturers teach and students

study must evolve with it. The general body of knowledge that medical students are expected to master in their preclinical years is growing, and adapting to the fast pace of medical education comes with growing pains. We are combating these growing pains by administering a prematriculation course called "Teaching Introductory Study Skills Utilizing Experience" (TISSUE), which enables incoming first-year medical students who have not been in an academic setting in some time to come to campus early and learn how to use the vehicle of the anatomy laboratory. We planned to measure the outcome of the quantitatively qualitatively. course and Quantitatively, we planned to measure the students perceived stress levels with a standardized survey that was validated by the American Sociological Association; qualitatively, planned to measure the course with a free-text postcourse anonymous survey.

Methods: We administered the same Perceived Stress Survey at 5 intervals during the first term of osteopathic medical school for the graduating class of 2021. The survey link was emailed to the class before classes started (survey 1), at orientation (survey 2), and before examination 1 (survey 3), examination 3 (survey 4), and the final examination 4 (survey 5) in Structural Principles of Osteopathic Medicine (SPOM), PCOM's anatomical sciences course. Data were collected via Google Forms and analyzed in SPSS.

**Data Analysis:** We compared the perceived stress levels in first-year osteopathic medical students who participated in the TISSUE program, those who did the PCOM Biomedical Sciences master's degree, and those who did neither. We completed multivariate tests that include Pillai Trace, Wilks Lambda, Hotelling Trace, and Roy Largest Root.

**Results:** Initial analysis of all 5 surveys included a poor sample size because Survey 1 and 3 were done via email without any additional prompting

of the class. As a result, only 64 students completed all 5 surveys and thus could be included in the analysis. Since surveys 2, 4, and 5 were completed during dedicated in-class time there was a much larger compliance, with 213 students completing all 3 surveys. To increase the sample size, we used just surveys 2, 4, and 5, which were coincidentally at the beginning, middle, and end of SPOM, for analysis. The various administrations of the test over time is significant. This means that there is a main effect for time; specifically, collapsing all 3 groups at each time point with a single mean and comparing those means over time yields a significant change. The perceived stress scores actually got higher over time within all 3 groups. The collapsed perceived stress in all 3 groups started as a 22 in the presurvey, increased to a 28 at midterms, and slightly dropped to a 27 before the final. Our analysis of this is that the students are sensitized to their stress levels with repeated administrations of the measure. The repeated measures analysis of time by the groups showed lower stress in both the TISSUE participants and the PCOM Biomed participants, but it was not significantly lower. The average perceived stress levels according to the ASA PSS Scale were 22, 29, and 27 in the control group; 21, 25, and 24 in the PCOM Biomed group; and 21, 27, and 26 in the TISSUE group.

Conclusion: The analysis shows that students significantly get more stressed over time and that there may be a sensitization of students to their stress levels with repeated surveying. Students who participated in the TISSUE program and students who received their MS in Biomedical Sciences from PCOM consistently have lower perceived stress levels overall, but the result is not statistically significantly lower. For the 2022 cohort, the survey will only be administered 3 times, which will hopefully reduce the sensitization bias. The osteopathic philosophy that the body is a unit of body, mind, and spirit tells us

that maintaining a healthy lifestyle and positive mental health is equally as important as the pursuit of academia. Reducing the perceived stress in medical students will lead to an increased ability to learn, which translates to better clinical outcomes.

Acknowledgment/Funding Source: The AOA grant #OMS93. The author wishes to thank the following contributors for their input in developing this program. Osteopathic medical students Kristin Oller, Brandon Twombly, Stephanie Michalik, and Mark Ujevich, who prepared and delivered content in the TISSUE program; Faculty member Ruth Conboy, DNP, and her guest lecture in the TISSUE program, and Drs Mike McGuinness, Ken Veit, and Jay Feldstein for their valuable input in the early stages of development of the program.

### ♦★C13—Osteopathic Philosophy

# Medical Professional Students' Perceived Impact of the Opioid Crisis and Personal Experiences Influence Future Plans Regarding Medical Practice With Opioids

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Research Questions and Hypotheses: Opioid misuse is a growing problem in the United States. Between 21% and 29% of individuals who receive prescriptions for opioids for chronic pain misuse them. In the Midwest, there was a 69.7% increase in opioid overdoses between July 2016 and September 2017, with the highest number in West Virginia. Ohio, West Virginia's neighbor, ranked third in the United States for opioid related deaths in 2016 and has seen a sharp rise in overdoses due to synthetic opioids. Most

research related to the opioid crisis is focused on non-addictive pain management and improving treatments for opioid use disorder. These studies, although valuable, do not address the nuances of the patient-provider relationship or how it affects opioid prescription, opioid use, or patient outcomes. Although there have been multiple calls for the inclusion of pain- and opioid-focused education in medical education, there is limited research related to future prescribers' knowledge, beliefs and postgraduate plans related to opioids. The specific aims of this study were to (1) describe osteopathic medical (DO) students', nurse practitioner (NP) students', and physician assistant (PA) students' perceived impact of the opioid crisis, personal experiences with opioids, and postgraduate plans regarding medical practice with opioids and (2) determine whether personal experiences with opioids influences students' future plans regarding medical practice and opioids. Given that most NP students have previously practiced clinically as registered nurses, we hypothesize that NP students will have different perspectives on the severity of the opioid crisis when compared with PA and DO students. We also hypothesize that personal and clinical experiences with opioids will influence students' decisions about working with patients with opioid use disorder in the future.

Methods: The study was approved by Ohio University's Institutional Review Board (protocol number 18E195). A cross-sectional survey study of 510 health care professional students (ie, NP, PA, and DO students) at Ohio University was conducted between April 23 and May 22, 2018. The Opioid Impact, Beliefs, and Experiences Survey was distributed to all health professional students via the university-maintained listservs and learning management systems. The survey was completed electronically, and participation was anonymous and voluntary. The survey was

developed by a panel of experts at Ohio University and was reviewed to establish face validity and contact validity.

**Data Analysis:** Participants were removed from the analyses if they did not complete all questions in the perceived severity scale, resulting in a final sample of 491 participants.  $\chi^2$  tests were used to parse out differences in personal experiences and postgraduate plans between medical professional programs. One-way ANOVA determined differences in perceived severity of the opioid crisis between medical professional programs.  $\chi^2$  tests were also used to determine whether future plans differed based on personal experiences.

Results: Of the 491 participants, most were female DO students (female=62.7%, age=27.2 ± 5.4 years, 80.4% white, 68.2% DO students, 53.0% plan to work in primary care, 52.1% grew up in area with a population  $\leq 50,000$ ). Overall, students had personal and clinical experiences with opioids (80.0% had clinical encounters with patients who were drug seeking, 84.6% stated that opioid use had impacted their community, 31.3% stated that opioid use had impacted their circle of friends). More NP students had clinical encounters with patients who were drug seeking  $(\chi_2^2=15.0; P=.001)$  and had more experience treating acute overdose ( $\chi_2^2$ =63.2; P<.001) than either PA or DO students. Also, more NP students stated that their nuclear families were impacted by opioids ( $\chi_2^2=13.4$ ; P=.001). NP students also perceived the opioid crisis in Ohio as more severe ( $F_{2.488}$ =7.13, P=.001). Overall, students planned on working with patients with opioid addiction (64.6% believed their work upon graduation would involve dealing with people addicted to opioids, 47.3% felt confident in their ability to deal effectively with people with addiction, 47.3% planned to complete additional training to provide medication-assisted treatment). DO students were significantly more confident in their ability to manage patients with addiction ( $\chi_2^2=7.3$ ; P=.026) than NP or PA students. Students' experiences with opioids influenced their postgraduate plans to work with and their confidence in their ability to treat patients with opioid addiction. Specifically, students were more confident in their ability to treat patients with opioid addiction when they had previous clinical experience with drug seeking or treating an acute opioid overdose  $(\chi_1^2=19.3; P<.001 \text{ and } \chi_1^2=24.6; P<.001, \text{ respect-}$ ively). Additionally, students were more likely to agree that their work upon graduation would involve managing patients addicted to opioids if opioid use had impacted their nuclear family or community ( $\chi_1^2$ =6.4; P=.011 and  $\chi_1^2$ =9.3; P=.002, respectively).

Conclusion: All health care professional students reported a high amount of clinical experience with opioid overdose and drug seeking. Additionally, more NP students had opioid use impact their nuclear family. As we hypothesized, NP students perceived the opioid crisis in Ohio as more severe than PA and DO students. We also found that clinical and personal experiences related to the opioid crisis were associated with postgraduate plans to work with patients with opioid use disorder. The opioid crisis is impacting medical professional students, and school administrators and educators must take this into consideration when developing new opioid-related material and providing wellness resources on campus. Additional research is required to determine the causal mechanisms by which personal experience influences future practice. Future work will also include educational interventions in a simulated clinical setting. Limitations of the current study include the cross-sectional design, which limits the ability to detect causal associations, and the use of a novel survey, which requires additional validity testing.

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### ♦★C14—Musculoskeletal Injuries & Prevention

### The Effects of Head Impacts on Verbal and Visual Memory in Collegiate Mens Lacrosse Players From Pre- to Postseason

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Research Question/Hypothesis: Concussion and mild traumatic brain injury (mTBI) are challenging injuries for physicians to diagnose and manage because of the variability in presentation. In 15- to 24-years-olds, sports are the second-most common cause of concussion. Football is more commonly studied than other sports, even though ice hockey, lacrosse, and other sports have almost as great of a risk of concussion. Because collegiate athletes are pursuing degrees of higher education, concussions and subconcussive impacts can inhibit their ability to learn and be attentive in the classroom. Our study aims to assess changes in verbal and visual memory in Men's Division II collegiate lacrosse players over the season, as they are prone to head trauma from stick checks to their helmets and other sources of contact. We suspected that athletes suffering increased number and/or magnitude of impacts, as measured by accelerometer, would have decreased verbal and visual memory as measured by Immediate Post-Concussive Assessment and Cognitive Testing (ImPACT) at midseason and postseason testing compared with their preseason baseline.

**Statement of Significance:** The purpose of this study was to determine methods of early concussion detection of athletes at risk of developing symptoms from concussion and subconcussive cerebral impairment. By better understanding the patterns of head injuries and symptomatology in

sports, physicians, athletic trainers, and coaches will be more equipped to recognize when athletes are at risk of cognitive injury. Then they may employ appropriate rest and treatment regimens to ensure their long-term mental and physical health. The importance of central nervous system health cannot be overstated in its significance to a holistic approach to patient care and overall wellbeing of the body, mind, and spirit. The mindbody connection is strong, and when the mind is not working at full capacity, the body suffers, and vice versa. Furthermore, with the growing concern over head injuries in sports, it is vital that athletes and their families know they are going to be taken care of and that the necessary precautions will be made to ensure their health and safety while allowing them to continue the activities that provide them joy, stress relief, and comradery.

Methods: We examined 10 male freshmen NCAA Division II collegiate lacrosse players through their preseason into postseason (January-May) using ImPACT testing and Athlete Intelligence Force Monitoring Vector Mouthguards. All participants were randomly assigned a subject number and data collected used that number. Participation was voluntary and recruitment was done by NYIT physicians and medical students, in accordance with the athletic director. Subjects wore the Vector Mouthguard, which contains accelerometers, during all full-contact practices and all 18 games played throughout the season, which recorded number and magnitude of each hit to the subjects' head. These data were automatically uploaded to Athlete Intelligence software via Bluetooth. ImPACT testing was used to measure verbal and visual memory, and the data were collected using their web-based platform at 3 time points throughout the season: preseason (baseline), midseason, and postseason, as well as anytime they were diagnosed with a concussion by team physicians. ImPACT tests verbal memory using a composite of modules including

Word Memory, Symbol Match, and Three Letter Memory and is scored as the percentage correct. ImPACT also tests visual memory using a Design Discrimination module along with a memory paradigm using X's and O's.

**Results:** There was a decrease in both verbal and visual memory over the course of the season. Verbal memory decreased from 83.7 (13.1) in preseason, to 73.0 (14.8) in midseason, and 75.4 (16.5) in the postseason (P=.036). Visual memory decreased from 83.1 (10.5) in preseason, to 73.7 (12.6) in midseason, and 70.2 (17.6) in the postseason (P=.035).

Conclusion: Over the lacrosse season, visual and verbal memory decreased as tested by ImPACT. There was no significant correlation between the worsening of symptoms and the total number of hits taken or cumulative force accrued, which could be to be due to a potential lack of compliance from the subjects in wearing the mouth pieces and or inaccurate interpretation of an impact by the accelerometer. The decreased performance on memory tasks does warrant concern. Further investigation is required to better understand these findings and assess whether a potential link exists between sport-related contact and memory task decline.

Acknowledgement/Funding: We would like to give a special thanks to the physician mentors, Dr Hallie Zwibel and Dr Matthew HellIer. Funding for this study came from the NYIT In-House Grant.

### C15—Impact of OMM/OMT

### Effects of Cranial Osteopathic Manipulative Medicine on Children With Plagiocephaly: Case Studies and Proposed Clinical Trial

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<sup>1</sup>Osteopathy's Promise to Children - An AOA Affiliated Organization, San Diego, California; <sup>2</sup>Private Practice, Solana Beach, California; <sup>3</sup>Private Practice, San Diego, California **Hypothesis:** The application of OMT, with emphasis on osteopathic cranial manipulative medicine (OCMM), will improve the cranial bone symmetry of children diagnosed with plagiocephaly.

Background: Estimates of the occurrence of plagiocephaly, infants with a cranial bone deformity, vary widely. One source reports that plagiocephaly is considered a "rare disease," occurring in fewer than 200,000 individuals in the US.1 However, a multisite clinical trial reported, "Of the 440 infants assessed, 205 were observed to have some form of plagiocephaly. The incidence of plagiocephaly in infants at 7 to 12 weeks of age was estimated to be 46.6%. Of all infants with plagiocephaly, 63.2% were affected on the right side and 78.3% had a mild form." A study from the UCSD Medical School's Dysmorphology Clinic reported, "Seventy-three percent of newborns had at least 1 asymmetry, (10% had more than 1) .... Forty-two percent of infants had facial asymmetry, 62% had head asymmetry, and 13% had mandible asymmetry."3 In 1966, Frymann reported that 88% of the 1250 newborns had some identifiable mal-alignment in the form of cranial bone strain patterns.<sup>4</sup>

**Methods:** Osteopathic physicians at the Osteopathic Center for Children, San Diego, conducted a case series study to investigate the impact of OCMM on 17 infants with diagnosed plagiocephaly.

Materials: We measured head asymmetry using anthropometric caliper and photographic measurement instruments to determine cranial vault asymmetry and calculate the cranial vault asymmetry index (CVAI). The measurements were made at initial visit and then after 5 to 6 cranial OMM visits. OCMM sessions focused on cranial base, occipito-mastoid suture, and temporal bones.

**Results:** Pre- to posttest comparisons showed reduced skull asymmetry, decreased occipital flattening, and increased circumference and cranial

vault index (CVAI). Mean baseline CVAI was 6.1% (grade 3 severity), and mean follow-up CVAI was 3.2% (grade 1 severity). Paired t tests revealed statistically significant differences in CVAI (P<.01) and severity grades (P<.01). No adverse events were reported.

**Conclusion:** Our findings support our hypothesis that OCMM is successful in reducing cranial abnormalities and is a gentle, low-risk treatment for pediatric plagiocephaly.

**Funding:** Funding for this study was provided by Anderson Children's Foundation.

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### ◆C16—Chronic Diseases & Conditions AOA OMS Funded Grant

### An Osteopathic Approach to Leveraging Community Support for Prevention and Management of Chronic Disease in Rural and Appalachian Virginia

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**Research Question(s)/Hypotheses:** Central Appalachian communities continue to experience poor health outcomes in the setting of persistent poverty despite efforts by numerous organizations to address these disparities over the past 50 years.

In 2011, Edward Via College of Osteopathic Medicine initiated a longitudinal study with the goal of identifying demographic, geographic, economic, and social determinants of health contributing to persistently high prevalence of certain chronic health conditions in Appalachian regions in southern Virginia. The overarching goal of this research is to characterize individual communities and target key factors to address in future intervention programs designed to improve the health and well-being of communities in Central Appalachia. Collection and analysis of quantitative and qualitative patient-centered data have been completed and a complementary provider-focused dataset is currently being collected and analyzed. This phase aims to answer questions regarding (1) impact of chronic disease, (2) perceived barriers to improving chronic health conditions in patients and communities of practice, and (3) identification of osteopathic tenets employed in practice. These results, in addition to input collected from focus groups in each area, will ultimately inform the design of targeted interventions in each of the 6 regions studied. This project, which aims to look deeply within and engage with each individual community to formulate problems as well as solutions, is osteopathic at its core.

Methods: Longitudinal and cohort studies were conducted in rural Virginia through analysis of agency mortality data (Virginia Department of Health) and individual electronic health records. Six facilities in 4 health disparity regions of southern Virginia were identified and agreements to participate confirmed for a cross-sectional study. An IRB-approved protocol provided for the systematic random selection and de-identification of protected medical records of admitted patients aged 18 years or older. An interdisciplinary team designed, pretested, and revised a survey tool in Qualtrics, LLC, specifically for the efficient extraction of data from selected records with a focus on 9 chronic diseases and a nonchronic

disease (mild mental illnesses) using International Classification for Disease codes. Cases were further reviewed for family histories, lifestyle behaviors, social history, physical examination notes, and clinical and laboratory test results. Interdisciplinary steering committees were formed to include health care providers and interested parties in each distinct region to provide feedback toward the development of a 35-item survey to be distributed to providers across the 6 regions and to later convene as focus groups in each region to further provide complementary qualitative data.

Data Analysis: Longitudinal data (1960-2012) were obtained from the Virginia Department of Health (n= $\sim$ 60,000). Cohort data were extracted from 2012 inpatient electronic health records from 6 hospitals. Records were selected via systematic randomization (n= $\sim$ 1400). Data analysis controlled for age, gender, and ethnicity. Data compared southwest Virginia to comparison areas and identified social, behavioral, environmental, and clinical confounders. Nine chronic disease mortality conditions and 1 nonchronic, external cause of death were studied. Statistical analyses included paired t tests, Pearson correlations, Rao-Scott  $\chi^2$ , and Nagelkerke (NK) analyses; significance was  $\alpha$ =0.05 using SPSS software.

Results: Results for the electronic health record reviews indicated inpatients in southwest Virginia had greater likelihoods of diagnoses with neoplasms (9.40% vs 7.50%, NK=3.6) (*P*<.01) and diabetes (30.40% vs 13.90%, NK=4.3) (*P*<.0001) compared with their eastern Virginia counterparts. Prevalence of mental disorders was 42.80% in southwest Virginia and 30.30% in eastern VA (NK=16.8) (*P*<.0001). Overall rates of chronic bronchitis were increased in the coal mining region of southwest Virginia when compared with eastern Virginia (29.90% vs 1.50%, NK=21.5) (*P*<.0001) while individuals employed as coal miners had lower rates of hypertension,

heart disease complications, and asthma than non-coal miners. Although inpatients in southwest Virginia were less likely to experience kidney disease than inpatients in eastern Virginia (9.30% vs 10.10%), kidney disease was most prevalent in the south side region at 18.40% (NK=9.4) (P<.0001). Smoking and alcohol use status yielded no statistically significant differences between regions. Preliminary analysis of qualitative data collected from interviews with primary care providers in the single region of Buchanan County indicates that physicians in this region experience difficulty in securing referrals to specialists, patient compliance, patient transportation, and balancing best practice with the financial constraints of the patient population. Preliminary analysis also indicates that physicians are very receptive to assistance in addressing these issues.

Conclusion: While each of the 6 regions of southern Virginia studied is similar in the presence of poor health outcomes and poverty, the quantitative results from the review of electronic health records highlight the unique and complex interplay between demographic, geographic, economic, and social determinants of health faced by each community. Providers have indicated that they are struggling to provide optimal care and are open to assistance. It is our hope that identifying and addressing each region as a unique entity will allow for the design of lasting and meaningful interventions that maximize the inherent strengths and minimize the weaknesses of each individual community. Considered as a pilot project, this study will continue to offer valuable insight into next steps to include development of a reproducible modular system to facilitate the efficient and thorough assessment of needs to inform individualized interventions toward improved health outcomes in any community.

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Association for their generous support of this research through a student research grant.

## →★C18—Chronic Diseases & Conditions

### Assessing the Impact of Rock Steady Boxing on Depressive Symptoms in Parkinson Disease

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Background: Recent literature suggests that depression is one of the most common psychiatric disorders associated with Parkinson disease (PD). Rock Steady Boxing (RSB) is an exercise regimen that aims to improve quality of life for patients with PD. The preliminary results of several clinical trials have shown that RSB is successful in improving various motor symptoms of PD. To our knowledge, however, the impact of RSB on depressive symptoms among PD patients has not yet been studied.

**Objective:** The purpose of the current study is to assess the impact of Rock Steady Boxing on depressive symptoms in a cohort of patients with PD.

**Hypothesis:** Participation in Rock Steady Boxing will decrease depressive symptoms in patients with PD.

**Methods:** Prior to enrolling in RSB classes at the Adele Smith Parkinson's Disease Treatment Center of NYITCOM, PD patients were administered a baseline Patient Health Questionnaire-9 (PHQ-9). The PHQ-9 was then readministered at subsequent 12-week intervals, with the final assessment conducted at 36 weeks. Differences between assessments were determined using a paired samples *t* test, with *P*<.05 considered statistically significant.

Results: Six participants (all male; mean age, 70.3 y) completed the 36-week assessment. At the 36-week assessment, there was a positive correlation between participation in Rock Steady Boxing and reduction in depressive symptoms. (r=0.909; P=.012). An itemized analysis of the PHQ-9 was conducted, which showed a positive correlation between participation in RSB and reduction in feeling tired or having little energy (r=0.908; P=.012). However, there was no significant difference between the mean total score, or mean fatigue score, of the PHQ-9 at baseline and at 36 weeks.

Conclusion: After 36 weeks of participation in Rock Steady Boxing, there was a positive correlation between participation in RSB and reduction in depressive symptoms; specifically, participants reported feeling less fatigued. However, on further analysis, there was no significant difference in depressive symptoms among participants. This discrepancy is likely due to our small sample size; thus, future studies should evaluate a larger patient cohort. The goal of future studies should be to establish whether Rock Steady Boxing can improve the psychological well-being of patients with PD.

**IRB Approval:** NYIT IRB BHS-1210 (September 13, 2016)

### C19—Impact of OMM/OMT

### The Effect of Osteopathic Manipulation on Anxiety and Depression in Medical Students

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**Introduction:** Whether it is termed a mental illness, stress-related condition, psychiatric issue, or functional disorder, psychological dysfunction

of individuals in today's society may be more frequent and incapacitating than any other disease or disorder. Medical students enrolled in colleges of osteopathic medicine (COMs) are not exempt from this phenomenon. Prior available studies suggest that the suicide rate among medical students is higher than in the age-matched population and that a reported that 3% to 15% of medical students have suicidal ideation during medical school training. Clearly, there is a high prevalence of stress, anxiety, depression, and burn-out in medical students. One of the tenets of osteopathic medicine is that the human being is a compilation of body, mind, and spirit. Researchers would like to investigate whether faculty at COMs can assist in improving the overall well-being of enrolled medical students. Specifically, researchers hoped to investigate osteopathic manipulative treatment (OMT) as it relates to the soma (body) and how it can affect a patient's mood (mind) and beliefs (spirit).

**Hypothesis:** The goal of this study was to determine whether OMT assists participants in experiencing a change in mood, particularly in reference to depressive and anxious symptoms using the Beck Depression Inventory and the Spielberger State-Trait Anxiety Inventory surveys, respectively.

Methods: This study was approved by the Touro IRB commission in 2018 (#1737). First- and second-year students enrolled at TouroCOM's Middletown Campus in New York, aged 21 to 45 years, were invited to participate in the study. No prior history of anxiety, depression, or having received OMT in the past were accounted for and no other particular criteria were used to exclude participants. In total, 20 participants were in the control group and 31 were in the experimental group. The study had a total duration of 5 days. Participants in both groups completed 2 surveys: the Beck Depression Inventory and the Spielberger State-Trait Anxiety Inventory to

evaluate characteristic attitudes and symptoms of depression and measure of state and trait anxiety, respectively, on day 1 and day 5 of the duration of the study. The treatment group received osteopathic evaluations, diagnosis, and manipulative treatment to correct their somatic dysfunctions. optimize neuromusculoskeletal function, and decrease their somatic dysfunction severities on day 1 and day 3. No OMT was provided to the control group. Participants in the experimental group completed their surveys before receiving OMT. Data were analyzed using SPSS 24.0 software. Predefined thresholds ( $\alpha$ ) for P values were set at .05. Pearson correlations and paired t tests were conducted, as well as  $\chi^2$  for inferential results.

**Results:** Statistical analysis revealed P values of .017 and .045 relating state anxiety and trait anxiety, respectively. These results were statistically significant, suggesting an impact of OMT on reducing anxiety, with a greater effect on reducing how the individual anxiously responds to stressful situations (state anxiety). However, the role of OMT in decreasing depression symptoms remains to be seen, as results yielded a P value of .278.

Conclusion: The decrease in reported anxiety symptoms may be due to improvements in the function of the autonomic nervous system as well as a regulatory effect on the hypothalamuspituitary axis and its actions in response to stressful situations. A direct correlation can be noted between the beneficial effects of treatment of the body and the effects on the mind and spirit.

Limitations of this study include the small quantity of participants, certain personality traits associated with medical students, and the short time frame over which measurements were taken. Future work includes increasing the patient participation pool, expanding to subset populations with mental health conditions, and measuring the effects of OMT over longer periods.

Mental health researchers have long known that stress plays a strong role in various forms of anxiety and depressive disorders. Findings suggest a strong influence of the patient's physical body on the patient's overall anxiety state and a venue for additional treatments to standard of care, including OMT, to positively affect a patient's mood. OMM-trained faculty employed at COMs are in a unique situation in which they can contribute to improving student's overall well-being by engaging the tenet of osteopathic medicine stating that body, mind, and spirit are all integrated as 1 element.

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## ◆C20—Chronic Diseases & Conditions

# Quality of Hypertension Care: An Improvement Initiative in 2 Outpatient Health Care Centers

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**Purpose:** Improving hypertension control is an important public health goal; however, despite active research and many inexpensive treatments available, significant barriers remain in primary care practice. Our primary objective was to identify areas for improvement of hypertension care and to implement changes in practice to improve outcomes for patients with hypertension. We also aimed to evaluate whether project participation influences osteopathic physicians' attitudes in

treating patients with hypertension and physicians' adherence to current clinical guidelines.

Hypothesis: We hypothesized that increased physician knowledge and adherence to clinical guidelines would lead to an improvement in blood pressure control, patient compliance, patient satisfaction and long-term complications of hypertension. The hypertension quality improvement (QI) initiative was designed based on a national Performance Improvement -Continuing Medical Education program developed by the American Academy of Family Physicians (AAFP). Bird et al (2013) observed improvement of diabetes performance measures as a result of a similarly designed QI. Our primary research question was, Will the hypertension QI initiative, which consists of creating a patient registry, peer education presentation, and electronic medical record (EMR) improvements. result in increased provider knowledge and compliance with current hypertension guidelines, improving quality of hypertension care in the Academic Health Care Center of NYITCOM? Secondary research questions sought to determine whether project participation influenced physicians' attitudes and improved adherence to clinical guidelines in treating patients with hypertension.

Methods: We conducted nonexperimental pre- vs postdesign quality improvement study by assessing 16 specific measures of hypertension care for ambulatory patients with the history of hypertension at baseline and 3 months after implementation of the QI initiative. The study was conducted at 2 health centers affiliated with NYITCOM. De-identified data were collected from 100 medical records, randomly selected from the practice's EMRs, and compared with a national sample of peer data. The intervention was based on the AAFP METRIC Performance Improvement module and consisted of creating a computerized registry, making system improvements to the EMRs, and conducting peer educa-

tion workshops on current best practices. We administered a pre- and postintervention survey, developed by the AAFP, to primary care physicians to assess attitudes toward hypertension care. Data Analysis: Statistical analysis was performed using SAS 9.4. Comparisons between pre- and postintervention clinical data for both NYITCOM and national data were performed using a  $\chi^2$  test. Additionally, comparisons between NYITCOM and national data were performed to assess whether there were differences between the groups. Results were considered statistically significant when P < .05. Aggregate Practice Assessment Questionnaire responses at baseline and on follow-up were grouped into reflecting negative, neutral, and positive attitudes, as described by Bird et al (2013). Differences between groups were assessed using a  $\chi^2$  test.

Results: Improvement was demonstrated in several primary outcomes measures: an increased number of patients were counseled on sodium intake (P=.005), physical activity (P=.001), alcohol consumption (P=.03), and weight reduction (P<.0001). No improvement was demonstrated in the number of patients counseled on the DASH (Dietary Approaches Stop Hypertension) diet, smoking, or target blood pressure goals, or in the number assessed for diabetes, hyperlipidemia, obesity, renal disease, or cardiovascular disease. Pre- and postintervention data from the 7-item provider survey administered to the primary care physicians did not show statistical significance in the number of positive or neutral/negative responses.

Conclusions: The QI initiative improved provider knowledge and compliance with hypertension guidelines in several areas; however, more work is required. Implementing peer education workshops on a regular basis, as well as continued improvements in the electronic medical records, may improve quality of care of patients with hypertension.

### C21—Osteopathic Philosophy

### The Osteopathic Military Tradition: Knowing When the Physician and the Team Are Trained

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Hypothesis: A.T. Still established the military tradition among his followers. Military and medical training has never relied more on simulation than it does now. The objective marker for the quality of simulation training, especially expensive high-acuity, high-risk training needs to be established. The hypothesis that hyper realistic simulation allows us to evaluate objective hormone and cardiac human factor data are the basis of the current research. To accomplish this goal, we produced an artificial environment that duplicates, as close as possible, real environments.

Methods: Second-year military medical students engaged in a weeklong surgical simulation exercise in conjunction with the training of Federal Firefighters, California Highway Patrol, Local SWAT, US Border patrol, and military personnel. 108 students lived in a movie set modeled as if they were deployed to an (over 4 years) Afghan village at Stu Segall Productions for the entirety of the exercise. Similarly, members of 6 Forward and Fleet Surgical teams trained in this environment. Salivary hormone and heart rate variability data were gathered to show stress and habituation. Salivary hormones were evaluated

by the methods described by Granger et al. Heart rate variability was measured continuously to the 1/1000th of a second using Firstbeat BG continuous technology.

Results: Data from 45 second-year military medical students shows habituation, as defined by salivary amylase data on every day of the training compared with pretraining levels. Statistical significance for each day was between P>.002 and .004. Because of the team dynamics, amylase data are presented in a different format. Salivary a-amylase (sAA) data are represented as deltas, which are calculated as the percent change from the "pre" time point. In a  $2(SIM) \times 3(TIME)$ repeated measures ANOVA, there was a main effect of SIM (P<.05) and a marginal main effect of TIME (P=.07). In SIM1, there was a 9% decline in sAA from pre- to posttraining (pre-post), which continued in a downward trajectory at 20 m (-21%) and 40 m recovery (-20%). There was a difference pre-post vs pre-20 m (P<.05) and a marginal difference in pre-post vs pre-40 m (P=.06). For SIM6, sAA levels appeared more stable across the entire epoch (small decreases from 4, 3 to -3%, respectively). No differences were observed between time points. In comparing sAA responses between SIMs, SIM1 vs SIM6 were different at pre-20 m and pre-40 m (P < .05).

Conclusions: Salivary a-amylase (sAA) data from the trauma team training, represented as deltas of the percent change from the "pre" time point, indicate habituation to stress. Similar changes in alpha amylase, as evaluated daily and seen in the first medical students, also show a habituation to

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### ◆★C22—Impact of OMM/OMT

### Managing Tremor in Parkinson Disease Using Osteopathic Manipulative Medicine

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**Background:** Tremor is a common symptom of Parkinson disease (PD), presenting as an obstacle to daily functioning and gradually decreasing quality of life and independence of its patients. PD patients have increased difficulty using objects and decreased writing movement speed. Spiral tracings are effective measurements of tremor and correlate significantly with the unified Parkinson disease rating scale (UPDRS) findings. Tremors during spiral tracing decreased after medication intake, suggesting that spirals/graphical tasks might be more sensitive in diagnosing tremor than the UPDRS. Pharmacologic treatment may control tremors, but short- and long-term use are not without side effects and symptoms may persist. Decreasing the severity of tremors through osteopathic manipulative medicine (OMM) may help reduce medication intake and serve as a safe alternative management option in patients with PD.

**Hypothesis:** OMM will reduce severity of tremors in PD as measured by spiral tracing and hand-drawn straight line tests.

**Statement of Significance:** OMM applied to restricted and stiff regions of PD patients may show improvement in tremor symptoms with little to no side effects. Reduction in tremor may drastically increase quality of life in this population.

**Methods:** This study was approved by the NYIT institutional review board. Six individuals with PD and tremors were equally divided into 2 groups: 1 receiving OMM and the other receiving counseling twice per week for 6 weeks. Both groups performed spiral tracing and straight line drawing tests before and after intervention at visit 1 (week 1), visit 12 (week 6), and at week 10 after a 4-week washout. These tests were evaluated for time (duration of task completion) and accuracy (number of deviations from the tracing outline). The OMM group received a 30-minute OMM session using muscle energy, myofascial, and articulatory techniques targeting the head, spine, thoracic cage, and extremities. The counseling group attended 30-minute 1-on-1 counseling sessions on a variety of topics pertaining to PD. The tests were scored by 2 to 3 graders and the scores were averaged.

**Data Analysis:** Means for number of deviations and length of time were analyzed using a  $2\times4$  mixed ANOVA approach.

**Results:** The week 1 presession loose spiral mean (SE) number of deviations for OMM group and counseling group were 27.7 (5.1) and 20.5 (7), respectively; the mean (SE) times in seconds for OMM group and counseling group were 48.0 (30.0) and 30.5 (5.5) seconds, respectively. The week 1 postsession loose spiral mean (SE) number of deviations for OMM group and counseling group were 27.8 (2.7) and 15 (1.5), respectively. The week 6 presession loose spiral mean (SE) number of deviations for OMM group and counseling group were 18.1 (4.3) and 16.5 (2.4), respectively; the mean (SE) times for OMM group and counseling group were 37.2 (9.4) and 23.9 (4.2) seconds, respectively. The week 10 loose spiral mean (SE) number of deviations for OMM group and counseling group were 21.2 (5.0) and 18.5 (2.3), respectively; the mean (SE) times for OMM group and counseling were 42.3 (27.8) and 27.3 (10.8) seconds. No significant differences were found between the group or weeks for number of deviations (P=0.635) or time (P=0.293). The week 1 presession tight spiral mean (SE) number of deviations for OMM group and counselling group were 35.8 (6.8) and 38.5 (15.5), respectively; the mean times for OMM group and counselling were 66.7 (35.7) and 61.5 (2.5) seconds, respectively.

The week 1 postsession tight spiral mean (SE) number of deviations for OMM group and counselling group were 30.1 (5.7) and 31.8 (5.8), respectively. The week 6 presession tight spiral mean (SE) number of deviations for OMM group and counselling group were 26.1 (3.4) and 22.3 (1.0), respectively; the mean (SE) times for OMM group and counselling group were 81.3 (23.8) and 47.7 (8.4) seconds. The week 10 tight spiral mean (SE) number of deviations for OMM group and counselling group were 20.6 (1.1) and 27.0 (5.3). No significance differences were found between the group or weeks for number of deviations (P=0.215) or time (P=0.298).

The week 1 presession line mean (SE) times for OMM group and counselling were 67.2 (35) and 25.9 (1.8) seconds, respectively.

The week 6 presession line mean (SE) times for OMM group and counselling were 54.2 (25.3) and 21.8 (5.2) seconds, respectively.

The week 10 line mean (SE) times for OMM group and counselling were 70 (37) and 28.8 (5.5) seconds, respectively. No significant differences were found between the group or weeks for time (P=.889).

**Conclusion:** OMM did not significantly reduce the severity of tremors in patients with PD. Limitations include human error in grading, small sample size, learning effect, and daily symptom variability. Future studies including a larger sample size should be completed to confirm these findings.

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IRB Approval: BHS-975

## C23—Chronic Diseases & Conditions

# Intermediate Risk Pulmonary Embolism Morbidity and Mortality Benefit From ICU Admission

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**Hypothesis:** Patients with a diagnosis of intermediate risk pulmonary embolism in the emergency department (ED) at Charleston Area Medical Center admitted to the intensive care unit (ICU) will have a lower mortality and morbidity rate compared with the non-ICU setting.

**Objective:** Acute pulmonary embolism is a potentially life-threatening disorder that carries a high morbidity and mortality. Pulmonary embolism is the blockage of 1 or more of the pulmonary arteries due to blood clot, fat, or air. Research evaluating the level of care required for intermediate pulmonary embolism management has been limited.

Methods: A retrospective medical record review of patients admitted to the Charleston Area Medical Center from the ED was performed. Patients included were those aged >18 years with the diagnosis of pulmonary embolism. Mortality, morbidity, vital signs, RV:LV ratio, and rate of ICU admission were collected. Analyses were done to compare the frequency and outcome of ICU vs Telemetry bed admission.

**Results:** A total of 385 patient medical records were reviewed and included in the study. Results revealed that patients with intermediate pulmonary embolism are 6.2 more likely to get admitted to the ICU compared with patients with mild pulmonary embolism (P<.05), with no significant difference in mortality.

Conclusion: Despite being 6.2 times more likely to be admitted to ICU compared with patients with mild pulmonary embolism, our study shows no benefit in mortality from ICU admission for patients with intermediate pulmonary embolism. The osteopathic significance of this study will allow emergency medicine providers a holistic approach in determining the level of care regarding treatment modalities for a patient with an intermediate risk pulmonary embolism to prevent an in-hospital mortality. Further research is required to define a guideline to determine the level of care needed for patients with intermediate pulmonary emboli.

IRB Number: 18-426 (approved April 19, 2018).

### ◆C24—Pain Management

## **Public Perceptions on Prescription Opioid and Heroin Abuse**

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Introduction: Osteopathic physicians must be a part of the conversation regarding the opioid epidemic facing the United States. According to the National Survey on Drug Use and Health (NSDUH), 11.8 million people were estimated to have misused opioids in the past year. The vast majority of these people abused prescription opioids (POs) and the number of heroin (illicit opioid) users was in the hundreds of thousands (NSDUH, 2016). According to a study conducted by Kolodny et al (2015), consumption of Oxycodone alone increased by 500% from 1999 to 2011, and that number continues to rise. PO abuse appears to be a potential precursor to heroin abuse, with 4 out of 5 Americans reporting having misused PO before heroin (Muhuri, 2013).

Lang and Rosenberg (2017) showed that heroin is perceived as more addictive than alcohol and marijuana, and people are least willing to associate with heroin abusers. As follow-up to the Lang and Rosenberg study, the aim of our research was to assess whether heroin is publicly perceived as more addictive and less socially desirable than PO, despite both drugs being derived from the opium poppy plant and having similar pharmacologic effects (NIDA, 2018). We additionally assessed whether gender contributes to perception of addictive potential and desired social distance from people who display addictive behaviors. Our research also investigates the differences in perception between appetitive addiction (ie, behavior seeking to fulfill hedonistic motives) and compulsive addiction (ie, subjective loss of control brought about by strong physiologic dependency) related to heroin and PO abuse.

Method: Via social media and direct email invitations, participants were asked to complete an online survey. At the end of the survey, each participant could opt into a random drawing for a \$50 Amazon gift card. Study participants were older than 18 years and primarily residents of the intermountain western United States. Participants were randomly assigned, based on birth month, to answer questions relating to 1 of the study's target addictive substances (PO, heroin). A total of 131 participants (33 men, 99 women; age, 30.02 y,  $\sigma_X = 11.35$ ) completed the heroin survey items, and 113 participants (36 men, 77 women; age, 33.08 y,  $\sigma_X$ =12.86) completed the PO survey items. Participants self-reported their demographic characteristics and completed the following measures: Social Distance Scale for Substance Users (Link et al, 1987), Perception of Addiction Potential Scale (Konkoly et al, 2015), and Subjective Definitions of Addiction Scale (Chassin et al, 2006).

**Results:** According to an independent-samples t test, heroin (M=4.67;  $\sigma_X$ =0.55) was viewed as

more addictive than PO (M=4.24,  $\sigma_X=0.79$ ;  $t_{243}=$ -5.00; P < .01) on a 1-to-5 scale with 5 being the most addictive. Participant preference for social distance from heroin and PO users was compared using the Social Distance Scale for Substance Users, with a lower value indicating less social acceptance. Participant mean rating of social distance from heroin users was 1.41 ( $\sigma_X$ =0.36), whereas participant mean rating of social distance from PO users was 1.63 ( $\sigma_X$ =0.46) ( $t_{243}$ =4.20, P < .01). This suggests that participants show more willingness to associate with PO users than with heroin users. There was no statistically significant difference between men and women's willingness to associate with heroin users; however, men were found to be more willing to associate with PO abusers than women, r=-0.20, P=.03. Using responses to the Subjective Definitions of Addiction Scale, an independent samples t test was conducted to assess compulsive and appetitive drive to consume opioids and heroin. For opioids, there was a significant difference in mean scores in regard to perceived compulsive drive (4.20;  $\sigma_X$ =0.79) than appetitive drive (3.79,  $\sigma_X$ =0.83) ( $t_{224}$ =3.82; P<.01). For heroin, the perception of a compulsive drive to consume heroin (4.31;  $\sigma_X = 0.66$ ) was significantly different compared with appetitive drive to consume heroin  $(3.92; \sigma_X=0.77) (t_{260}=4.41; P<.01)$ . The higher means for compulsiveness indicates that participants perceive the addictive nature of opioids and heroin as a subjective loss of control with strong physiologic dependency, and not a behavior related to fulfilling hedonistic motives.

Conclusion: Understanding that the public perceives heroin as more addictive than POs and also desires greater social distance from heroin abusers is valuable information for an education campaign to fight opioid addiction. Education efforts that explain that POs are derived from the same source, produce similar pharmacologic effects, and are comparable in addictive potential to heroin are needed so that the public can be similarly cautious of addiction to prescription opioids as they currently are of heroin. Due to the increased social distance women desire from opioid users, it may be necessary to acknowledge their concerns for addiction potential as well as stress the importance of their support for those who are beginning a PO regimen for pain treatment. We propose that this educational gap be addressed by using an osteopathic model of pain management, which may also lead to an effective way to combat the opioid epidemic. Cavilieri (2005) proposes a nonpharmacologic approach to pain treatment, which includes education, cognitive-behavioral therapy, and osteopathic manipulative treatment (OMT). While these adjuvant therapies may not eliminate the use of POs, they have the potential to decrease the frequency and dosage required for pharmacologic pain management. McReynolds (2005) found osteopathic manipulation to be as effective as its pharmacologic counterpart in relieving acute pain. Licciardone (2013) suggests that osteopathic physicians who practice manipulative medicine are well prepared for guiding patients entering the realm of chronic pain management. Methods specific to the osteopathic model, such as cognitive behavioral therapy and OMT, are evidence-based and provide a safe and effective alternative source of pain management (Cavalieri, 2005). Although an osteopathic physician is an essential part of a solution, an effective health care team working holistically with the patient to deliver Cavalieri's forms of therapy provide a possible mechanism to provide patient education as well as eventually help mitigate the opioid epidemic. Overall, our results align with and extend Lang and Rosenberg's study and provide new insight into the public's perception on addiction. We believe the results of our study may be helpful in educating the medical community and the general public. This responsibility likely falls on those with the power to prescribe pain medications. During these discussions, it is important to keep in mind the findings that women are less likely to associate with PO abusers. While it is not entirely certain whether this implies that men and women should be educated differently, it does call for further research into men and women's varied perceptions on addiction. By altering the public perception and increasing the regularity of osteopathic care models, the opioid epidemic may be combated with this novel approach.

### ♦★C25—Impact of OMM/OMT

### The Effect of Osteopathic Manipulative Medicine on Oxidative Stress Following Mild Traumatic Brain Injury: A Pilot Study

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Introduction/Specific Aims: Concussion, a form of mild traumatic brain injury, occurs after a primary mechanical injury to the head or body. Secondary nonmechanical damage follows, including changes in cerebral perfusion and metabolism. Hypoperfusion results in accumulation of toxic mediators, including reactive oxygen species, leading to the breakdown of the bloodbrain barrier and progression of neuroinflammation. This secondary process is thought to lead to the emergence and perpetuation of concussion symptoms after injury. Previous studies have found osteopathic manipulative medicine (OMM) to be effective in improving concussion-like symptoms, including dizziness, nausea, and imbalance. OMM uses manual techniques to address musculoskeletal restrictions, or somatic dysfunctions, which can arise after injury.

By removing biomechanical barriers in mTBI patients, OMM could lead to improvements in cerebral glymphatic circulation increasing clearance of oxidative stressors. 8-hydroxy-2'-deoxyguanosine (8-OHdG) is a urine biomarker produced by the oxidative damage of DNA by reactive oxygen and nitrogen species. OMM has the potential to address 8-OHdG and other toxic mediators present in the nonmechanical phase of mTBI. Through randomized controlled trials, the effect of OMM on the markers of oxidative stress can be investigated, allowing for a better understanding of its role in the management of concussion.

**Research Question/Hypotheses:** To determine the effect of OMM, as compared with a control group receiving concussion education, on cerebral oxidative stress, as measured by levels of 8-OHdG.

Methods: This study is NYIT Institutional Review Board approved, BHS-1139, and is registered at clinicaltrials.gov (NCT02750566). This randomized controlled trial investigates the effectiveness of OMM in treating mild concussion symptoms over a 1-week period after diagnosis. Subjects presenting at the NYITCOM Academic Health Care Center for concussion evaluation were recruited for this study. Subjects aged 18 to 50 years, with a diagnosis of concussion, cleared of life-threatening injuries by a neurologist, were included in the study. Exclusion criteria included subjects with contraindications to OMM, history or current diagnosis of spinal cord injury, or a neurodegenerative condition, pregnancy, inability to complete assessments, as well as loss of consciousness for greater than 2 minutes, witnessed seizures, or intractable vomiting following head injury. Following informed consent, subjects were randomly assigned to an OMM or control group receiving concussion education. All subjects received intervention on the initial visit (visit 1) after enrollment and at follow-up 48 to 72 hours later during visit 2. A third visit, 1 week after visit 1, was used for final data collection. Subjects in the OMM group received physician-directed osteopathic manipulative treatment. Physicians were directed to assess and treat somatic dysfunctions potentially contributing to concussion symptoms, with focus on the cranium, thoracic and lumbar spine, ribs, and pelvis/sacrum. The OMM group subjects all received key techniques to decrease craniocervical restriction and improve lymph drainage in the head and neck. Control subjects received concussion education, standardizing 30 minutes of face-to-face time with a physician between groups. Data collected included urine samples taken from groups prior to intervention on visits 1, 2, and 3, as well as after intervention on visit 1. Urine samples were analyzed through competitive enzyme-linked immunosorbent assay using colorimetric detection for levels of 8-OHdG.

**Data Analysis:** Analysis included 5 subjects, 4 who received OMM and 1 control. Statistics were performed on IBM SPSS Statistics 24 and  $\alpha$  was set at .05. Independent t tests were performed to determine any differences in initial 8-OHdG levels between groups. Mann Whitney U testing was performed to analyze mean differences between preand postintervention 8-OHdG levels over visits 1, 2, and 3.

Results: No significant differences in initial preintervention 8-OHdG levels were found between the OMM group and control subject (*P*=0.936). From pre- to postintervention on visit 1, an average increase in 8-OHdG levels was seen in both the OMM group (0.20 ng/gCr) and control subject (0.03 ng/gCr). A further average increase in 8-OHdG levels was seen from visit 1 to visit 2, OMM group (1.57 ng/gCr) and control subject (0.06 ng/gCr). The control subject on visit 3 had a further increase in 8-OHdG from visit 2 of 0.17 ng/gCr, resulting in an overall increase of 0.26 ng/gCr from preintervention on visit 1. The OMM group on visit 3 had an average decrease

in 8-OHdG from visit 2 of 0.11 ng/gCr, resulting in an overall average decrease of 0.02 ng/gCr from preintervention on visit 1. Mann Whitney U testing revealed no significant differences in the average changes of 8-OHdG over the 3 visits between groups (P=1.000).

Conclusion: The results of this pilot study demonstrate an interaction between OMM and 8-OHdG levels. While no significant difference in 8-OHdG levels were found between the OMM group and control subject over time, an average decrease in 8-OHdG was seen in the OMM group while the control subject had an overall increase. Owing to these results, further study with larger populations including moderate and severe concussions is warranted. Included in further study, the correlation between 8-OHdG levels and symptom number and severity should also be implemented. The implications of certain OMM techniques, such as dural venous sinus drainage, known to address specific therapeutic models and their relationship to oxidative stressors, can also be investigated. Through this process, the mechanism behind OMM's role in management of concussion can be established, allowing for the understanding of specific techniques addressing mTBI pathophysiology, which will supplement the body's innate capacity to heal itself.

### ◆C26—Impact of OMM/OMT

### Medical Student Use of Osteopathic Manipulative Medicine (OMM) in Outpatient and Inpatient Clinical Rotations

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**Introduction**: During the first 2 years of osteopathic medical school, students learn osteopathic manipulative medicine (OMM) in the classroom and laboratory setting. They practice skills on their fellow students, most of whom are in good health, or on standardized patients, who typically present with complaints that mirror those of patients in a standard outpatient setting. Third and fourth-year clinical rotations serve as an opportunity for students to practice the aforementioned skills on real patients, with a variety of chief complaints and pre-existing conditions, in a multitude of different settings. A prior study found that despite receiving little to no OMM training in inpatient settings, third and fourth-year students were able to decrease patients' pain via OMM treatments in hospitals and outpatient clinics.

Hypothesis: We predict that student-performed OMM is safe and effective in clinical rotations in both inpatient and outpatient settings. We also hypothesize that third- and fourth-year students will be more comfortable performing OMM techniques in an outpatient setting based on their training in medical school. Therefore, we predict that techniques performed in an outpatient setting will lead to greater decreases in patient-reported pain, as compared with those performed in an inpatient setting.

**Statement of Significance**: OMM is a cornerstone of osteopathic medical education. The findings of the current study may help to shape future educational structure and to encourage OMM use during clinical rotations

Methods: This study was approved by NYIT's Institutional Review Board. Third and fourth-year students at NYITCOM are required to submit logs of patient encounters during which they use OMM on rotations at local hospitals and outpatient clinics. Information collected on OMM encounter logs includes: class, rotation, OMM technique(s) used, and a pre- and posttreatment patient-reported pain scale out of 10. Logs from the family medicine and ambulatory medicine rotations were classified as "outpatient." Logs from internal medicine and surgery were classified as "inpatient." Logs

from psychiatry, pediatrics, OB-GYN, electives, sub-internships, and radiology were excluded from this analysis, as these rotations have both inpatient and outpatient components and the logs did not capture the specific setting of OMM treatment. Change in pain was calculated as the difference between the pretreatment pain scale and the posttreatment pain scale.

**Data Analysis:** Data were analyzed using IBM SPSS with  $\chi^2$  tests for categorical comparisons and t tests for the scalar data.

Results: 9168 logs were completed between June 7, 2016, and June 13, 2018. A total of 6126 logs were included in this analysis, 72.6% of which were classified as outpatient (n=4448) and 27.4% of which were classified as inpatient (n=1678). Significantly more patients tolerated treatments than not (99% vs 1%, P<.001). There was no significant difference between the types of techniques used by students on outpatient and inpatient rotations (P<.05). There was a statistically significant difference between pretreatment pain scores scores (P < .01). posttreatment pain Treatments conducted in an inpatient setting led to significantly larger changes in pain than those conducted in an outpatient setting (4.37, SD 2.26 vs 3.01, SD 1.75, P<.01).

Discussion: The findings show that student-performed OMM is generally safe and well tolerated. The results above indicate that the techniques used in an inpatient setting lead to greater decreases in patient-reported pain than those used in an outpatient setting. This can potentially be due to inpatient care providing situations where OMM can be more effective. Overall, the results of this study indicate that our teaching methods and OMM are generalizable and effective among various disciplines. Future curricular planning should seek to broaden the scope of the chief complaints that are used to teach techniques, as to guide students in being equally effective in both

outpatient and inpatient settings. Limitations of this study include the accuracy of student logs, a potential bias because students more comfortable performing OMM would be more likely to do so in an inpatient setting, and a lack of reporting of ineffective treatment or treatments performed past the required number of OMM logs.

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#### ◆C27—Impact of OMM/OMT

#### The Effect of Osteopathic Manipulative Treatment on Reactive Oxygen Species in Parkinson Disease

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Introduction: Parkinson disease (PD) is the second most common neurodegenerative disorder and causes many symptoms, including bradykinesia, tremor, postural instability, and musculoskeletal stiffness. Neurodegeneration is commonly associated with an increase in inflammation and oxidative stress, demonstrated by higher systemic levels of reactive oxidative species (ROS) thought to originate from mitochondria in underused skeletal muscle tissue. ROS are characterized by an unpaired electron, produced by both exogenous and endogenous sources and involved in pathological processes. Due to their reactivity, they modify cellular components such as nucleic acids, proteins, and lipids. Lack of homeostatic balance between production and defense mechanisms is detrimental. The effects of ROS, cumulatively known as oxidative stress, are often measured by the interactions of ROS on specific molecules. Dityrosine (DT), a cross-linked dimer form of tyrosine, is a stable molecular result of oxidation by ROS, lending to its use as a clinical biomarker. Another biomarker, malondialdehyde (MDA), is used to demonstrate the effect of free radical oxidation on lipids.

Osteopathic manipulative treatment (OMT) aims to reduce somatic dysfunctions, free musculoskeletal restrictions, and increase fluid circulation. The goals of OMT use in PD are reducing stiffness, increasing muscular activity, and decreasing inflammation. These changes may lead to decreased ROS production and increased ROS clearance.

**Hypothesis:** Biweekly OMT over 6 weeks will reduce oxidative stress in PD compared with biweekly counseling by decreasing the processes that generate DT and MDA.

**Statement of Significance:** OMT may reduce molecular damage caused by excess oxidative species generated in PD.

Methods: This study was approved by the NYIT institutional review board. PD subjects with balance and motor deficits were randomly assigned to the intervention arm (n=10) or control arm (n=9). The treatment group received a biweekly OMT protocol for 6 weeks. The OMT protocol focused on reducing somatic dysfunctions in the head, spine, and extremities and used primarily muscle energy and articulatory techniques. The control group received biweekly counseling sessions for 6 weeks to account for physician face-to-face time in the treatment arm. Subjects returned after a 4-week washout at week 10 for measurements once again. Blood samples were taken before and after the intervention at visit 1, week 3, week 6, and week 10. Oxidative stress was quantified by detecting plasma concentrations of DT and MDA via ELISAs.

**Data Analysis:** Mean (SE) concentrations of DT and MDA were compared temporally and between OMT and counselling groups via a  $2\times5$  mixed ANOVA and t test approaches.

**Results:** Week 1 presession concentrations of DT for the OMT group and counselling group were 3.7 (0.29) nm/dL and 3.6 (0.55) nm/dL. Week 1 postsession concentrations of DT for the OMT group and counselling group were 3.8 (0.43) nm/ dL and 3.5 (0.53) nm/dL. Week 3 concentrations of DT for the OMT group and counselling group were 3.5 (0.66) nm/dL and 3.8 (0.84) nm/dL. Week 6 concentrations of DT for the OMT group and counselling group were 3.8 (0.32) nm/dL and 3.0 (0.2) nm/dL. Week 10 concentrations of DT for the OMT group and counselling group were 2.8 (0.32) nm/dL and 2.9 (0.33) nm/dL. No significant differences were found between groups or weeks (P=.18). Week 1 presession concentrations of MDA for the OMT group and counselling group were 1.6 (0.43) nm/dL and 1.8 (0.53) nm/ dL. Week 1 postsession concentrations of MDA for the OMT group and counselling group were 1.5 (0.43) nm/dL and 2.1 (0.68) nm/dL. The OMT group had lower MDA in the acute setting compared with counselling (P=.337). Week 3 concentrations of MDA for the OMT group and counselling group were 2.0 (0.56) nm/dL and 2.1 (0.55) nm/dL. Week 6 concentrations of MDA for the OMT group and counselling group were 1.9 (0.60) nm/dL and 1.8 (0.48) nm/dL. Week 10 concentrations of MDA for the OMT group and counselling group were 2.7 (1.1) nm/dL and 1.8 (0.60) nm/dL. No significant differences were found between groups or weeks (P=.536).

Conclusions: This study suggests OMT did not affect the plasma concentrations of DT and MDA in our sample population, however, OMT may have a beneficial effect on MDA concentrations acutely. Limitations of this project include that blood samples were drawn at different times of the morning between and within subjects. Another aspect not controlled for is the morning activities of the subjects before blood draw. The sample size is also small. Further studies should be completed to overcome these limitations and

perhaps investigate other biomarkers of oxidative stress.

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# C28—Chronic Diseases & Conditions AOA Funded Grant

#### Glycemic Control, Self-Care, and Psychosocial Issues in Adults With Diabetes in Rural Appalachian Ohio

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Background: Diabetes in the United States has reached epidemic proportions, and the people of Appalachia have been disproportionately affected by this disease. In rural southeastern Ohio, diabetes rates far exceed both the national (19.9% vs 9.4%) and state prevalence (11.0%). Here, diabetes patients are more likely to be diagnosed late, have low empowerment and health literacy, and higher rates of diabetes complications. Nearly one-third of residents live below the poverty line and suffer from high unemployment, food insecurity, and lower access to health care. Despite these health disparities, the impact of diabetes is understudied in this region.

**Statement of Significance:** Diabetes is both a physical and emotional health problem. Assessment of diabetes reflects the first tenet of osteopathic philosophy, that the person is a unit of body, mind, and spirit. Therefore, the management of diabetes necessitates an understanding of the bidirectional relationship between a patient's diabetes (ie, body) and psychological well-being (ie, mind and spirit).

**Specific Aim:** We aimed to assess the physical and emotional health of patients with diabetes living in rural Appalachian Ohio.

**Methods:** We conducted a descriptive crosssectional survey-based study to assess diabetic patients' glycated hemoglobin, frequency of selfcare, diabetes self-efficacy, diabetes distress, depressive symptoms, and coping styles.

**Data Analysis:** Descriptive statistics were calculated for sociodemographic characteristics, and t tests and  $\chi^2$  tests were conducted to assess differences by gender, age, and type of diabetes. Multivariate regression models examined the main effects of psychosocial issues on glycemic control.

Results: A total of 175 adult diabetes patients completed the surveys (56.6% type 2 diabetes, 43.4% type 1 diabetes; duration, 10.5±9.3 y; mean HbA<sub>1c</sub>, 7.3±1.4%, 49.7% on insulin; age, 37.1±17.3 y; 61.1% female; 83.7% white; 43.4% with college degree or more; 98.8% insured). On average, participants felt 75.7±16.7% confident in their ability to carry out diabetes self-care but completed 56.7±19.2% their self-care tasks. Participants expressed 42.9±20.9% emotional coping and 56.0±16.2% self-controlled coping skills. Overall, 14.4% of participants showed symptoms of severe depression; 25.7% of participants with type 1 diabetes and 29.9% with type 2 diabetes exhibited high diabetes distress. Interestingly, diabetes self-care, self-efficacy, diabetes distress, depressive symptoms, and coping styles did not differ by age, gender, or type of diabetes. Adults self-reporting severe depressive symptoms were more likely to report high diabetes distress for type 1 ( $\chi^2=12.361$ , P<.001) and type 2 diabetes ( $\chi^2$ =30.334, P<.001). Multivariate regression analyses found high scores of type 1 diabetes distress (standardized b= 0.325, P=.037) were independently associated with higher HbA<sub>1c</sub> levels after controlling for depressive symptoms (standardized b= -0.038, P=.809), age (standardized b=-0.200, P=.093), and gender (standardized b=0.212, P=.071). This model accounted for 19% of the variation in HbA<sub>1c</sub>. Multiple

regression analyses using the same model found no association between type 2 diabetes, distress, and HbA<sub>1c</sub>; the lack of significance may be explained by well-educated, working adults with private insurance.

Conclusion: Adults with diabetes in rural Appalachia Ohio experience high rates of diabetes distress and severe depression comparable to other US regions. Despite expressing moderating high diabetes self-efficacy, adults carried out slightly more than half of their diabetes self-care behaviors. Diabetes education interventions that incorporate cognitive behavioral and problem-solving techniques would benefit adults with depression and/or diabetes distress in this region.

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#### ◆C30—Osteopathic Philosophy

#### Integration of Pressure Sensors in Lumbar Palpation Education

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Introduction: Palpatory skills are necessary in the field of osteopathic medicine and are important for diagnosing and examining somatic dysfunctions. Osteopathic students practice and refine their palpatory skills throughout the 4 years of medical school, starting in a laboratory setting and then continuing to improve with real patients in clinical rotations. As a result, research related to palpation and pressure is useful in the field of osteopathic medicine. To determine how to avoid inflicting pain, previous research in related fields of study have evaluated how much pressure can induce pain in muscles. A recent study found that

subjects who use equal force in both contact points (left and right hands) tend to have higher diagnostic accuracy than those who have unequal force. The study used the TekScan pressure sensor to measure force applied while diagnosing a lumbar segment. The TekScan system has been used to gauge pressure in various areas of medical research and to assess palpation forces when diagnosing somatic dysfunction. This study examines the effects of integrating the TekScan in lumbar palpation education.

**Hypothesis:** Students who use the pressure sensors during a lumbar diagnosis workshop will use more bilaterally equal and less force overall when diagnosing the lumbar segment and thus will be more accurate than students who do not have pressure sensor exposure.

Methods: This study was NYIT institutional review board approved. Matriculated first- (OMS I) and second-year (OMS II) osteopathic medical students were recruited for the study. Thirty-two students participated in this study. Students were randomly assigned to 2 groups. Both groups received a 10-minute didactic on the lumbar spine, including lumbar diagnosis. Afterward, both groups had 15 minutes to practice lumbar diagnosis with an attending helping to guide their practice time. The students in the experimental group had a TekScan sensor available for practice to ensure that they were using equal pressure in both palpating thumbs. The students in the control group were instructed to attempt to use equal pressure during palpation; however they did not have access to a TekScan sensor. Participants were asked to diagnose an L5 lumbar segment on a model patient after their workshop. The model patient had his/her L5 lumbar diagnosis confirmed by 2 NMM/OMM board-certified attending physicians before diagnosis by the participants. A TekScan sensor was placed over the model patient's L5 region to capture the pressure and time to diagnosis. Subjects were instructed to

record an L5 diagnosis using proper osteopathic terminology. The magnitude of force exerted on the TekScan sensor upon palpation, as well as the amount of time elapsed during the course of palpation, were measured by the sensor. Palpation by the subject was recorded in real time using the TekScan Pressure sensor. An attending physician checked the L5 diagnosis after the students completed their diagnoses to make sure it had not changed.

**Data Analysis:** Independent samples t test was performed to analyze differences in average force between left and right hand based between the 2 groups. Independent samples t test was also used to measure magnitude of force used by the control and experimental group and well as time to diagnosis.  $\chi^2$  analysis was used to determine if there was a relationship between the groups and correct diagnosis.

Results: Thirty-two subjects were included in our analysis (25 OMS I and 7 OMS II). The difference in average force applied by the left and right hand by the subjects was an average of 285.7 g in the control group and 128.8 g in the experimental group. This demonstrates that the students exposed to the TekScan as an educational tool applied a lower average force compared with the control group. However, the difference in groups was not statistically significant (P=.059). The control group had an average of 36.15 seconds for diagnosis, while the experimental group had an average of 28.196 seconds for diagnosis, which was also not statistically significant (P=.116). There was no statistical significance between either group getting a correct diagnosis. Additionally, there was no statistical significance between either group in relation to the magnitude of pressure applied.

**Conclusion:** Our findings demonstrated that the TekScan-exposed students used a more equal force between left and right hands. While this was not statistically significant, the TekScan may

increase diagnostic capabilities of osteopathic medical students. These results suggest that students who received table training with the TekScan learn to better apply equal pressure when diagnosing a lumbar somatic dysfunction. Since these results are trending toward statistical significance as subject numbers increase, further studies are needed to increase the sample size. There was no statistically significant difference between either group with regard to assessing for a correct diagnosis. This could be due to some confounding variables such as prior student diagnostic exposures, comfort of palpating through the plastic sensors, and proper contact with the correct level. Additional research needs to be conducted to further determine the potential benefits of using pressure sensors in osteopathic diagnosis education.

IRB Approval: NYIT IRB 1338

# C33—Chronic Diseases & Conditions

#### Evaluation of Health and Lifestyle Characteristics With an Emphasis on Their Relationship to Blood Glucose in Indigenous Populations in and Around Tacloban City, Leyte Philippines

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**Background:** The Philippines is a sovereign country composed of 7107 islands in the Western Pacific Ocean. Tacloban City, located on the island of Leyte, is one of the most resource-poor areas of the Philippines and was devastated by Typhoon Haiyan. Dr Zyss has spent considerable time working in and around Tacloban City.

Based on his personal observations, we wanted to perform osteopathic history and physical examinations, including a survey to evaluate lifestyle characteristics and the possible impact of Typhoon Haiyan on this population. Special emphasis was placed on screening for chronic diseases like diabetes, hypertension, oral health, and diet.

Objectives: The specific goals of this study were as follows: (1) To provide health screening and education to patients and to follow up with their primary care physicians. (2) To identify untreated or undertreated diseases in patients and direct them to care. (3) To identify common chronic conditions in this population so preventive health measures, including developing educational materials, fundraising, and further studies could be undertaken, in an effort to reduce morbidity and mortality in these patients. (4) To understand the impact, if any, of Typhoon Haiyan on these patients.

Methods: IRB approval was obtained prior to starting the study. Patients aged 18 years or older were invited to participate by word of mouth in and around Tacloban City. Consent was obtained from each participant prior to being enrolled. All documents were available in English and Tagalog. Staff, who were fluent in both Tagalog and English, were available during the study. Each patient was assigned a unique identifier. The individual osteopathic history and physical examination containing 25 items and a free text area for optional additional information were collected. The survey questions of health and lifestyle were filled out and collected at the time of the physical examination. Random fingerstick blood sugars and chemical urinalysis using a rapid 10 analyte dipstick were performed. All components of the study were performed or supervised by a licensed osteopathic physician. Some data were converted into diagnostic categories using the American Heart Association guidelines for blood

pressure, vision screening using the American Ophthalmologic Association guidelines, and body mass index (BMI) before analysis. The data were analyzed using primarily descriptive statistics.

Results: All 107 participants were from the Philippines; 81 were women and 26 were men. For reported level of completed education, 33 completed elementary school; 41, high school; 1, technical school; and 31, college or university. For reported employment status, 11 worked full time; 22, part-time; 70, unemployed; and 1, retired. Mean height was 60 in and mean weight was 126 lb. By BMI, 8 were underweight (BMI less than 18.5); 51 had normal weight (BMI 18.5 to 24.9); 39 were overweight (BMI 25.0 to 29.9); and 9 were very overweight (BMI ≥30). For blood pressure, 31 had a normal blood pressure (systolic <120 and diastolic <80), 18 had elevated blood pressure (systolic 120-129 and diastolic <80), 12 had hypertension stage 1 (systolic 130-139 and diastolic 80-89), 38 had hypertension stage 2 (systolic >140 and diastolic >90), and 7 had a hypertensive crisis (>180/120). Patients with hypertensive crisis were triaged for immediate care. Pulse pressure ranged from 17 to 132 (mean, 54). 40 patients reported taking medications, of which 26 were antihypertensive and 6 were for glucose control; 67 patients reported no medications. Oral health was assessed visually for 106 participants and rated as very poor (n=19), poor (n=65), good (n=18), very good (n=2), and excellent (n=2). 6 patients had no missing teeth, 9 patients were missing all 32 teeth, 14 patients were missing 6 teeth, the remaining 73 patients had variable numbers of missing teeth. Vision screening with no corrective lenses, mild or no visual impairment better than 20/70, OD=77, OS=80, moderate visual impairment 20/70 to 20/200, OD=15, OS=12, severe visual impairment 20/200 to 20/400 OD=0, OS=0, could not read the chart, finger counting

or 20/400 or greater, OD=9, OS=10. 6 patients had their vision corrected with glasses to mild or no visual impairment. 4 patients had vision corrected with glasses to moderate visual impairment 20/70 to 20/200. Unexpectedly, 5 patients had a pterygium on 1 or both eyes. Chemical urinalysis suggested urinary tract infection in 11 patients, while 9 patients had >2000 mg/dL reading for glucose. Of the 104 patients questioned about tobacco use, 19 responded positively. The average number of people in a household was 5 but ranged from 1-13 (n=103). Patients were asked about physical activity divided into 3 categories. Vigorous physical activity average was 1.9 d/wk for an average of 105 min/d. Moderate physical activity average was 3.5 d/wk for an average of 123 min/d. Patients (n=105) were asked if they used alcohol: 51=yes, 54=no. Rice is the main component of the diet; patients (n=105) reported consuming and an average of 4.19 cups/d and 23.81 cups/wk. We were interested in understanding the effects of Typhoon Haiyan on the diet. When asked about the availability of fresh vegetables and fruits, 58 and 64 patients reported a decrease in availability, respectively, after Haiyan (n=105). When asked whether they consumed more processed foods after Typhoon Haiyan, 31 reported an increase and 54 reported a decrease (n=85).

Conclusion: The population was predominantly female, and many were unemployed. Major health issues include hypertension, hyperglycemia, obesity, poor oral health, and visual impairment. The population had a relatively sedentary lifestyle. Many of them had the same health and lifestyle issues found in resource-rich countries. The Typhoon disrupted much of the farmland and destroyed many residences. This preliminary study provides information that identifies many health issues that can be addressed through preventive measures. Osteopathic physicians treat the whole person and consider diet,

exercise, and mental health. This study will provide justification to raise funds to be used for preventive care, treatment, and further study, thus improving the health and quality of life in this resource-poor population.

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#### ◆C34—Osteopathic Philosophy

#### Where Comfort and Confidence Diverge: Missed Opportunities for Sexual and Gender Minority

#### **Competency in Osteopathic Education**

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**Research Question/Hypotheses:** If research shows that medical students lack sexual health competency, can optional training improve their knowledge base, and if so, how would such training affect their understanding of patients who identify as sexual and gender minorities?

Statement of Significance: To address growing health disparities among patients of sexual and gender minority (SGM) persons, the Association of American Medical Colleges (AAMC) recommends that medical schools incorporate sexual health competencies into their curriculum. 1,2 The Commission on Osteopathic College Accreditation standards lack recommendations for the inclusion of SGM-related health care competency in osteopathic curriculum. 3,4 Recent studies of medical student competency in SGM care further validate these concerns by showing a lack of knowledge and understanding in treating patients of SGM. 5-10 At NSU-KPCOM, students

care for patients in Florida's Miami-Dade and Broward Counties, which outrank entire states in incidences of new HIV infections among patients who identify as men who have sex with men (MSM). Safe Zone trainings (https://thesafezoneproject.com/) can improve both knowledge and understanding of SGM communities. This study investigated the efficacy such training to improve SGM health competence of medical students residing within Miami-Dade and Broward Counties.

Methods: IRB exemption obtained after standard forth protocols set by NSU-KPCOM. Recruitment via email and social media obtained 236 participants who then completed anonymous online surveys administered through Google Forms. Competency was measured through responses on Likert scale measurements of thirteen questions related to SGM patient care before and after the training to identify overall changes in knowledge or understanding. Surveys remained open for submission 1 week before (n=115) and for 1 week after (n=121).

**Data Analysis:** Preliminary analysis of the survey data sought to isolate participants who attended the training and were medical students. Of those students, 78 completed pretraining surveys and 73 completed posttraining surveys. This variation identified a need for additional exclusion criteria to remove those who did not attend both trainings from further analysis. This led to a net total of 42 participants who met all inclusion criteria, compared with a negative control group (n=70) to examine survey bias.

Results: The key outcomes found subtle differences before and after the training in both domains of knowledge and understanding. Also, almost 10% reported in the comments section of both surveys that while they felt comfortable treating SGM patients, they did not feel confident in doing so, revealing a discrepancy between

comfort and confidence that was later evaluated in the posttraining survey. Lastly, more than 90% of participants expressed that the training is relevant enough to be incorporated into their required curriculum, identifying a desire to learn more about the health disparities of SGM communities.

Conclusion: This study reveals that incorporating SGM health care competency into osteopathic medical curriculum can improve NSU-KPCOM student's awareness of local resources, knowledge, and understanding of SGM communities. This curriculum must be regularly assessed to maintain efficacy for patient care. A 1-hour training session can affect both the knowledge and understandings of students who attend, compared with those who did not. Additionally, this study shows that most students feel neither confident nor comfortable enough to refer SGM patients to local resources. Perhaps this explains why over 90% of participants declared that the Safe Zone training is relevant enough to be incorporated into their required curriculum. Further studies may reveal factors influencing the differences in confidence and comfort in patient care.

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### ♦★C35—Musculoskeletal Injuries and Prevention

#### **Health Behaviors of eSport Athletes**

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Introduction: eSports is a form of electronic gaming, also known as professional or competitive video gaming, that has grown substantially in the past decade. A total of 22 US colleges have established varsity gaming teams over the past 3 years, often offering at least partial scholarships and backed by coaches and game analysts, much like other competitive college teams. As of now, there is little objective clinical research on observing the exercise habits, physical aches, and gaming history of these individuals—each of these being major

contributors to osteopathic care using the osteopathic models of care.

**Hypotheses:** We hypothesize that eSport athletes will be performing lower amounts of physical activity than the recommended activity by the Centers for Disease Control and Prevention (CDC) and American College of Sports Medicine (ACSM) and that these players will have a higher percentage of reported physical pains and fatigue in their eyes, back or neck, wrist, and hand than the general population.

**Statement of Significance:** The information gained from this study may help guide osteopathic physicians in treating common complaints of amateur and professional eSport athletes.

**Methods:** This study was approved by the NYIT institutional review board. Surveys were sent to 50 eSport participants from 5 different universities asking about activity related to playing games, physical discomfort, and medical history.

**Data Analysis and Results:** Most eSport athletes practice between 3 and 10 hours per day. The most frequently reported complaint from the players we surveyed was eye fatigue (56% of individuals). 42% of eSport athletes had back or neck pain. 36% of eSport athletes had wrist pain. 32% of eSport athletes had hand pain. 30% of participants do not perform exercise. Less than half (46%) of participants take a standing break after every 1 hour of play and 22% take a standing break after every 2 hours of play. 10% of participants are playing for 5 hours or more without breaks.

Conclusion: The study shows these athletes are prone to back, neck, wrist, and hand pain and eye fatigue. These areas are aptly treatable using osteopathic manipulative treatment across multiple models. There is no fully dedicated guidelines for prevention of eSport injury. This study provides baseline data that can be used to develop injury prevention protocol for these athletes.

IRB Approval: BHS-1357

#### ◆C38—Impact of OMM/OMT

#### Osteopathic Manipulation Increases Cognitive Ability in Patients With Chronic Pain: A Rationale for a New Approach

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Research Question: Elderly patients frequently complain of a decline in cognitive ability and pain. A recent systematic review and meta-analysis suggest that chronic pain is associated with memory deficits. Osteopathic Manipulative Treatment (OMT) has been shown to alleviate pain. Therefore, does OMT have the potential to improve cognitive function in patients with chronic pain?

**Hypothesis:** Patients receiving OMT for pain will demonstrate improvements in cognitive function and reductions in pain and inflammatory biomarkers.

Clinical and Osteopathic Significance: The health care system is faced with an increase in the elderly patient population. This unique patient population frequently experiences cognitive decline and has chronic pain. Because these patients require greater care, they can deplete medical and financial resources. As osteopathic physicians, we understand the interconnectedness of body systems and how to diagnose and treat somatic dysfunction. Identifying the source of pain and treating it with OMT may reduce the prescription of opioids and facilitate the body's ability to heal itself. Most importantly, if OMT can improve cognitive function in these patients.

it will increase their quality of life and reduce health care costs.

**Methods:** Midwestern University Institutional Review Board approval was obtained (MWU #2761). Patients were recruited and consented at our Multi-Specialty Clinic. Self-identified pain scores, neurocognitive function tests, and salivary biomarkers were measured at admission and after approximately 6 weeks of standardized OMT. These parameters were re-measured after 4 weeks without OMT (washout). Inflammatory biomarkers (tumor necrosis factor  $\alpha$  [TNF- $\alpha$ ], interleukin-1 [IL-1], IL-6, IL-8, and cortisol) were measured with high sensitivity enzymelinked immunoassay kits (Millipore Sigma).

**Data Analysis:** Primary outcomes included neuropsychological, clinical, and physiological domains. Nonparametric repeated measures and correlations were used to index the effect of OMT over consecutive assessments with SPSS software.

Results: In this preliminary study, 15 patients received an average of 4 OMT sessions over 5.7 weeks. With each office visit, OMT significantly reduced patient-assessed pain (10-point scale) supporting previous literature. After an average of 6 weeks of OMT, pain was significantly reduced from 5.3 to 3.4 (P<.05), which was durable at follow-up (P < .05, average of 4 weeks without OMT). Significant gains in attention (measured by the number of seconds it takes to connect random numbers in numerical order) decreased from an average of 36 seconds to 26 seconds (P < .05). Verbal memory (recall of word list) increased significantly from 18 to 25 words (P<.05), which was durable at follow-up (P<.05). Similar gains were observed in executive function (Stroop Test, P<.01). Biomarkers for inflammation had significant patient-to-patient variation illustrating the diversity of the patient population, pain duration, and pharmacologic treatments.

There was a trend for OMT to reduce IL-1 (530  $\pm 517$  to  $96\pm 66pg/mL$ ) and cortisol (0.16 $\pm 0.06$  to 0.12 $\pm 0.03ug/dL$ ), but not IL-6 or TNF- $\alpha$  concentrations.

Conclusion: This proof-of-concept study suggests OMT improves neurocognitive parameters and reduces pain acutely and up to 4 weeks after treatment (washout). Study limitations include small sample size and lack of control groups. Ongoing research is incorporating osteopathic physician controls (osteopathic philosophy, no OMT) and allopathic physician controls to strengthen conclusion validity.

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# ◆C39—Chronic Diseases & Conditions

#### Diabetes Self-Efficacy Predicts Self-Care Among Adults With Type 1 and Type 2 Diabetes

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Background and Significance: There are over 30 million people living in the United States with diabetes. In Southeast Ohio, diabetes rates are more than 2 times the national average (19.9% vs 9.4%). Diabetes self-care requires more than simply following a prescribed regimen; there are difficult behavioral changes that people need to make to manage their diabetes. Self-efficacy has been shown to be useful in successfully making these changes. Despite the importance of self-efficacy for behavioral change, the impact of diabetes self-efficacy on diabetes self-care and

glycemic control has not been studied in the Appalachian region.

Research Questions and Hypotheses: The specific aims of this study were to (1) describe the population in southeastern Ohio with types 1 and 2 diabetes and (2) determine how self-efficacy is related to self-care and glycemic control. Given the association of self-care, self-efficacy, and glycemic control, we hypothesize that a patient's self-efficacy score would be predictive of his or her self-care and that patients with high self-efficacy would have good glycemic control.

Methods and Data Analysis: The study was approved by Ohio University's Institutional Review Board (IRB number 17X234). A crosssectional survey study of 175 students, faculty, and staff from Ohio University was conducted. The survey was anonymous and completed electronically. Participants were removed from the analyses if they did not complete all questions in the Confidence in Diabetes Self-Care (CDIS) Scale and the Self-Care Inventory (SCI) Scale, which left 94 participants. Diabetes self-efficacy was assessed using the CDIS scale; diabetes self-care was assessed using the SCI Scale version 2. To assess glycemic control, participants were asked their recent hemoglobin  $A_{1c}$  (HbA<sub>1c</sub>). Independent samples t tests were used to determine differences in self-efficacy, self-care, and glycemic control between type 1 and type 2 diabetes groups. Pearson's correlation was used to determine relationships between self-efficacy, self-care, and glycemic control. A linear model was used to determine whether self-efficacy was predictive of self-care.

**Results:** The sample was primarily comprised of female participants with type 1 diabetes (HbA<sub>1c</sub>,  $7.6 \pm 1.6$ ; age,  $29.5 \pm 14.1$  y; female, 59.6%; type 1 diabetes, 68.1%; duration,  $11.1 \pm 8.1$  y; college degree or more, 38.3%). Participants with

type 1 diabetes had higher self-care inventory scores than participants with type 2 diabetes  $(t_{92}=3.26, P=.002)$ , but patients with type 1 diabetes also exhibited poorer glycemic control  $(t_{92}=2.32, P=.023)$ . Overall, there were negative, albeit statistically insignificant, relationships between self-efficacy and HbA<sub>1c</sub> and between self-care and HbA<sub>1c</sub>. These negative trends were more pronounced in participants with type 2 diabetes. According to a linear model, diabetes selfefficacy was a positive predictor of perceived selfcare  $(F_{1.92}=53.01, R^2=0.37, P<.001)$ . Diabetes self-efficacy was a stronger predictor of self-care in participants with type 1 diabetes than in those with type 2 diabetes  $(F_{1.62}=42.84, R^2=0.41,$ P < .001 and  $F_{1,28} = 11.85$ ,  $R^2 = 0.30$ , P = 0.002, respectively).

Conclusion: These results suggest that increasing diabetes self-efficacy improves self-care, and this improvement is more pronounced in individuals with type 1 diabetes. However, individuals with type 1 diabetes had poorer glycemic control, and the negative relationship of self-efficacy and HbA1c was weaker in this group. Although high diabetes self-efficacy translated to high self-care in the type 1 diabetes group, it did not translate to improved glycemic control. Additional research is required to investigate other factors that could be influencing glycemic control in this population. Future work will also include qualitative interviews to elucidate causal relationships. The current study is limited by a small sample size taken from a university setting. Additionally, self-report items like HbA<sub>1c</sub> may have been influenced by recall bias.

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# C41—Chronic Diseases & Conditions

# Adverse Childhood Experiences (ACEs) Screening in an Outpatient Pediatric Practice: A Quality Improvement Project

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Background: Adverse childhood experiences (ACEs) are associated with chronic health conditions, increased risky behavior, and negative health outcomes in adulthood. The cumulative exposure to toxic stress leads to neurodevelopmental changes that can drastically affect a person's health. The effects of these exposures are evident even in early childhood. Despite a growing body of evidence to support the longterm impact of ACEs, there is still a lack of evidence to support screening for ACEs, especially in early childhood. Organizations such as the American Academy of Pediatrics (AAP) support screening for ACEs in the pediatric population to help identify at-risk children and provide the support and resources necessary to prevent these negative outcomes through instilling resilience. The focus of Osteopathic medicine is to improve health by focusing on the whole person, yet many pediatricians, both osteopathic and allopathic, do not routinely screen for ACEs.

**Hypothesis:** The following paper describes a quality improvement (QI) project using the Plan, Do, Study, Act (PDSA) cycle, which implemented ACEs screening at a pediatric clinic and subsequent referral to behavioral

health providers for patients at risk of developing negative long-term health outcomes. Screening results were followed to determine whether the patient population correlated with nationally recognized statistics.

Methods: Plan: Initial investigation into the most effective and efficient form to use for screening revealed no currently validated form for pediatric patients. The most widely used form, and closest to being validated, is the Center for Youth Wellness ACE questionnaire (CYW ACE-Q), which was used in this project. As a QI project, institutional review board approval was not required. There was concern for inadequate support from the pediatric psychology department for referrals once screening was initiated. An initial data-gathering phase was run to determine the approximate number of referrals that would be generated through the screening process. For 2 months, the survey was distributed by the front desk and patients were asked to anonymously fill out the screening form. These screening forms were collected by the nursing staff. At the end of the 2 months, it was determined about 10% of patients would have received a referral to pediatric psychology, which was determined to be sustainable. Do: Screening was initiated on November 1, 2017, and information was collected from November 1 until May 2018. Nursing staff were educated on the screening process and asked to hand out the appropriate questionnaires to patients. All patients aged 3 to 18 who were seen in the continuity clinic were asked to be screened. Providers would then review the questionnaire and document results in their note using a standard provided format. If results of the screen revealed a score of 4 or higher, the patient was considered at risk for negative longterm health outcomes, and a referral to pediatric psychology was offered.

Results: Study: During the study period, 2858 total patients were seen. Of those patients, an ACES score was documented on 810 patients. This represented a screening rate of 28%. 94 new referrals to pediatric psychology were generated, which accounted for about 60% of those with a score  $\geq 4$ . Another 11 patients (7%) declined a referral, and the remainder (51 patients; 33%) were already seeing psychology or psychiatry. In this study window, 3% of the total number of patients seen were referred to behavioral health services. Of note, there were an additional 88 patients, or about 11%, who qualified for referral but were already seeing someone within psychology or psychiatry. The Z score was calculated to determine the significance between the national 12.5% and our 19% for those with the  $\geq$ 4 ACEs and found a Z score of -5.42 (P < .05), which rejects our initial hypothesis that our population would be similar to the national data. The Z score was also calculated for those with ≥1 ACEs (national 67%, our population 56%) and determined to be 6.46 (P < .05), also showing a significant difference in our population. Of note, these comparisons are to adult data and not pediatric specific data. Act: During the study period, there were multiple PDSA cycles run to improve screening rates. These included education of all the resident physicians, reminders placed on the computers, discussions with the department head about attending physicians, nursing staff education, and calculating individual documentation rates and posting those. No intervention made much difference in documentation rates, which stayed approximately 28% to 30% throughout. Results revealed that the individualized approach (calculating individual percent documentation) appeared to have the most impact on providers, however, further data are necessary to corroborate this finding.

Conclusion: The initial ACEs study documented that 67% of people have at least 1 ACE and 12.5% (1 in 6) of the individuals have an ACEs score of 4 or higher. This is statistically different from our study findings of 56% and 20% (1 in 5), respectively. Our patients are more likely to experience a greater number of toxic events if they had any, but we did have more patients who had experienced no adverse events compared with national norms. One explanation for this difference may be that physicians are biased in documenting higher scores, specifically if the patient needs to be referred to psychology. The need for a referral may improve documentation rates of ACEs as placing the referral acts as a reminder to the physician to document the ACEs score. Another important consideration for this difference from national data is the comparison of pediatric patients to data gathered in adults. ACEs data represent a cumulative exposure in the first 18 years of life, but if documented at a younger age, a patient may screen with a lower number as they have not had the opportunity to be exposed to as many events. However, this is precisely why we feel intervening early is critical for these children. Several limitations were revealed during the project. At this time, there is paucity in previous research in the pediatric population to compare with results of the present study. With only about 30% of encounters being documented, there may be biases in the data. Despite limitations in the present project, the results emphasize the importance of screening for ACEs. Knowledge of the relationship between high ACEs and negative health outcomes creates an important role for the pediatric provider. To avoid negative health outcomes, pediatricians must consider all factors that affect emotional and physical well-being of children during well child examinations. As osteopathic physicians, we strive to take the whole patient into account when providing medical care; the ACEs survey is another tool to help

provide high quality preventive care. Implementation of ACES screening allows us to identify at-risk children early to help alleviate the effects of toxic stress on neurodevelopment, educate families, and provide support to help improve home environments. Data from the current QI project not only support the need for ACEs screening in primary pediatric offices, but also the need for integrated behavior health services in pediatric clinics.

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#### ◆C42—Osteopathic Philosophy

# **Choosing Primary Care: How Influencing Factors Differ By Gender**

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**Hypothesis:** We hypothesized that gender and other key motivating factors would differ substantially between osteopathic medical students pursuing a career in primary care compared with those pursuing non-primary care.

Significance and Background: As health care reform continues in the United States, 2 common goals have been to implement strategies to improve health outcomes and decrease overall health care costs. Substantial evidence has shown that regular access to primary care is a critical mechanism available to achieve these goals. However, increasing access to primary care is proving difficult with the shortage of primary care physicians and rapid attrition of the current workforce. Osteopathic medical schools have become a major supplier of the general physician

workforce. Today, 1 in 4 US medical students matriculates from an osteopathic medical school, and more than 5,400 new osteopathic medicine physicians graduate annually from an American Osteopathic Association-accredited college of osteopathic medicine. Furthermore, osteopathic medical schools are responsible for training a large portion of primary care physicians, with an estimated 56% of current osteopathic physicians practicing in a primary care specialty. Considering the increasing number of graduates from osteopathic medical schools and the critical need for primary care physicians in the United States, we aimed to understand the possible motivations for osteopathic medical students to pursue a primary care specialty.

Methods: We analyzed responses from the annual American Association of Colleges of Osteopathic Medicine (AACOM) graduate survev (2007-2016). Primary care was defined as pursuing a career in family medicine, general internal medicine, general pediatrics, or geriatrics. Non-primary care included all other specialties. Self-reported factors including (1) intellectual and technical content, (2) debt level, (3) lifestyle, (4) prestige/income level, and (5) personal experience and abilities were summarized, and their subjective value was contrasted between those pursuing primary care vs those who were not. The influence of gender on the decision to pursue a career in primary care was also analyzed. This study was approved by our Institutional Review

**Data Analysis:** The distribution of responses for each of the 5 self-reported factors across a 5-point Likert scale (major influence, strong influence, moderate influence, minor influence, no influence) was summarized.  $\chi^2$  analyses were performed to evaluate differences between those planning to enter a primary care specialty compared with those who were not. We assessed the association between gender

and each influencing factor using linear regression. In addition, logistic regression was used to assess the association between gender and choosing primary care.

Results: Survey responses increased from 2403 in 2007 to 4191 in 2016 as the matriculating osteopathic class size increased nationwide. Although participation in the survey was optional, response rates ranged between 72% and 77% from 2007 to 2016. In the total population, women comprised the highest percentage of graduates pursuing a career in primary care (57.7%) when compared with men (42.3%), and gender was found to be associated with differences in choosing a specialty (P < .0001). In addition, women were 1.75 times more likely to choose primary care than males were (95% CI, 1.62-1.89). Over time, the percentage of women entering primary care increased (35.1% in 2007 to 40.0% in 2016) while the trend in their male counterparts remained relatively stable (21.1% in 2007 to 26.8% in 2016). In the results of the logistic regression, women remained more likely to select primary care than men were each year of our analyses. For example, in 2007, women were 2.02 times more likely to choose primary care (95% CI, 1.68-2.42), and in 2016 this odds ratio dropped slightly to 1.89 (95% CI, 1.66-2.16). In the linear regression, gender had a significant effect on each of the 5 influencing factors (P<.0006 for all). Among the self-reported factors, lifestyle was the most important factor each year for all students (P<.0001). For students entering primary care, the percentage of students stating lifestyle was a "major influence" increased gradually from 60.1% in 2007 to 75.3% in 2016. A similar trend was observed among students entering nonprimary care specialties with increases from 57.5% in 2007 to 63.3% in 2016. Students entering primary care were more likely to report prestige and income level to be "no influence" or a "minor influence" compared with students entering non-primary care (P<.0001). Debt level was more likely to be a "major influence" to students choosing to enter non-primary care specialties than it was to those entering primary care (P<.0001), and this percentage of non-primary care students has grown from 22.9% in 2007 to 30.6% in 2016. The intellectual and technical content of the specialty was of great importance to slightly more non-primary care students (average of 35.5%) than it was to primary care students (average of 27.9%). Finally, students entering primary care and non-primary care both reported similar frequencies across the Likert scale when rating the importance of one's personal experience and abilities in choosing a specialty.

Conclusion: Our results indicate that gender may play a substantial role in influencing a graduate's choice of specialty, and women seem to drive the trend toward primary care. Furthermore, each of the 5 factors analyzed were significantly different between students entering primary care and students entering non-primary care specialties. Lifestyle was deemed a major influencing factor each year, and respondents suggest that debt level is a strong influencing factor among students pursuing non-primary care specialties. Although this study had a large sample population and included data spanning 10 years, we were limited within the confines of the predetermined survey that is disseminated annually by AACOM. Consequently, we were unable to investigate whether other potentially important factors may influence specialty choice. Further analyses should be done to understand how these and other factors in medical education and training influence students' choice of specialty, especially in light of recent findings indicating that the percentage of females entering osteopathic medical school has been declining since 2004. Previous thinking on education

methods, student experience, and the stress of debt must be scrutinized and potentially upgraded to encourage the next generation of physicians to meet the health care needs of a changing nation.

# C44—Chronic Diseases & Conditions

#### Virtual Reality Physical Activity Intervention for Chronic Low Back Pain: Initial Findings From a Feasibility Study

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Objective: Within the United States, low back pain (LBP) is the leading cause of pain and second-leading cause of disability, as well as one of the most common reasons for seeking medical care. While most acute LBP remits within a few weeks, up to 10% of individuals develop a chronic pain condition characterized by long-term pain, disability, and resource cost. Research has supported that maladaptive beliefs about pain and physical activity (eg, pain-related fear) contribute to poor outcomes following back injury. The current pilot study examined the safety and feasibility of an interactive virtual reality (VR) cognitive-behavioral intervention designed to challenge fearful pain beliefs and gradually promote physical activity. This can be an addition to osteopathic manipulative medicine to aid in reduction of chronic LBP.

**Design:** Thirty-four individuals (17 female; mean age, 46.2 y) with chronic LBP and high maladaptive pain beliefs completed a physician screening, as well as standard measures of average pain intensity, pain-related fear, and disability both before and after a 3-day laboratory-based intervention protocol.

**Results:** Repeated-measures analyses indicated no significant elevation in pain-related fear (F=1.4, P>.05) or disability ratings (F=0.3, P>.05) and a significant decline in average pain intensity (F=4.0, P<.05). Self-report data were consistent with physician observation/screening. Mean (SD) scores on the treatment evaluation inventory (34.7 [5.6]) suggested above-moderate treatment acceptability and overall positive interest in the intervention.

Conclusions: Findings support the safety and feasibility of a VR gaming intervention model designed to deliver cognitive behavioral treatment for maladaptive pain beliefs while promoting physical activity among individuals with chronic LBP. The tested model represents an early prototype of the intervention, which is ultimately intended to provide a flexible interactive platform across clinical and home settings.

# ♦C45—Musculoskeletal Injuries and Prevention

#### The Effect of Subconcussive Impacts on the Neurocognitive Function of Men's Collegiate Lacrosse Players From Pre- to Postseason

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**Hypothesis:** There are 1.6 to 3.8 million sport-related concussions per year. Men's lacrosse is a high-contact sport that has been historically underrepresented in concussion research. Previously, scientists believed that impacts of high magnitude causing clinically overt concussions were the primary cause of neurocognitive decline and chronic traumatic encephalopathy (CTE). However, recent studies have demonstrated that repeated head

trauma, regardless of clinically evident concussions, may be the primary cause of CTE.<sup>2</sup> We sought to determine specific thresholds for non-clinically overt, or subconcussive, head trauma that cause neurocognitive impairment. To assess neurocognitive function, the C3Logix computer-based assessment was used. Specifically, the "Trails A" component, a validated trail-making assessment of psychomotor speed and visual processing speed, was measured in seconds during preseason, midseason, and postseason testing. Additionally, impacts were measured by the Athlete Intelligence Force Monitoring Vector Mouthguard. The mouthguards contain an accelerometer located at the molars to accurately record any impact, measured in G-force, above a userdefined threshold.

We hypothesized that athletes suffering from an increased number of impacts and collision events throughout the season, as measured by the mouthguards, would have decreased neurocognitive function as measured by Trails A.

Statement of Significance: The purpose of this study was to determine the significance of detecting subconcussive neurocognitive impairment, thus gaining a better understanding of the injury patterns caused by head impacts in Men's Collegiate Sports. The data collected using the tools listed below allow for clinicians and athletics personnel to detect head injuries earlier and more accurately, therefore treating the athletes more efficiently. Athletic trainers, coaches, and physicians can better maintain each individual athlete's well-being using a baseline and follow-up tests, rather than generalized thresholds which may overlook athletes with atypical symptoms of head injury. Osteopathic physicians aim to treat the body, mind, and spirit of their patients. The negative effects of subconcussive impacts on neurocognitive function can decrease an athlete's ability to perform well on the field and in the classroom, leading to frustration, which can increase

stress in everyday life. This stress may be exacerbated if an athlete relies on his or her athletic scholarship to pay for college tuition. Therefore, if these subconcussive impacts are properly recognized and managed, the physician will help the athlete achieve his or her full potential on the field as well as address and relieve associated stress.

Methods: We studied 10 male NCAA Division II Collegiate Lacrosse Players throughout their freshman year season using preseason, midseason, and postseason testing (January - May). All participants were randomly assigned a subject number, and data collected used that number. Participation was voluntary and recruitment was done by New York Institute of Technology physicians and medical students, in accordance with the athletic director. Subjects wore the Vector Mouthguard during all full-contact practices and all games played throughout the season. The mouthguard recorded the number of impacts to the subjects' heads as well as the magnitude of each impact. The data were automatically uploaded to Athlete Intelligence software. The accelerometer threshold was set to 5G. Subjects were evaluated using the C3Logix Concussion Assessment Trails A test in the pre-, mid- and postseason.

**Data Analysis:** The data were analyzed by comparing the athletes' mean scores of Trail A between pre- and postseason with paired samples t test and correlating it with the amount of impacts with forces of >15G, >25G, >50G, and >80G received throughout the season with computation of Pearson correlation coefficients. All analyses were performed using IBM SPSS Statistics 23 and statistical significance was determined by a P value of <.05.

**Results:** The results showed that the athletes' neurocognitive function has improved from preseason (21.0 [3.1]) to postseason (17.5 [2.5]) as a whole (P<.001). There was a strong positive correlation (r=0.76; P=.011) with impacts >15G, and also a

strong positive correlation (r=0.67; P=0.036) with impacts >25G.

Conclusion: There was a significant positive correlation between the change in time to complete Trails A, from pre- to postseason, as tested by C3Logix, and the total number of impacts >15G and >25G that the athletes sustained throughout the season. We expected that the time to complete Trails A would increase as the number of impacts throughout the season increased, but instead we witnessed an overall decrease in time. However, when the time to complete Trails A was correlated to the number of subconcussive impacts experienced by each athlete, an increase or less of an improvement in time to complete Trails A was associated with a higher number of subconcussive impacts. These results are concurrent to those from past research, emphasizing the importance of receiving multiple, smaller force blows to the head. This will allow athletic trainers, coaches, and physicians to better prevent, diagnose, and manage head injuries that were previously overlooked. The decrease in overall time for Trails A throughout the season can be attributed to a learning effect with subsequent administrations of the test, similar to the one found with King-Devick.3

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#### C46—Osteopathic Philosophy

#### Patient Perceptions of Osteopathic and Allopathic Physician Communication Style and Empathy and Reported Satisfaction with Low Back Care

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Significance: The osteopathic tradition promotes physician behaviors and attributes believed to improve health outcomes for patients. Physician attributes such as open communication, patient involvement, and empathy are reflective of key aspects of the interactions between physicians and patients in the contemporary health care environment. Researchers in the osteopathic field often seek to measure these attributes, test their association with the osteopathic practice of medicine, and measure the relationships between these ideal physician attributes and patient outcomes.

**Hypothesis:** We hypothesize that patients of osteopathic physicians will report more favorable perceptions of physician communication and empathy, as well as greater satisfaction with medical care, than patients of allopathic physicians.

Methods: The patients in this study were recruited from the Pain Registry for Epidemiological, Clinical, and Interventional Studies and Innovation (PRECISION Pain Research Registry) at the University of North Texas Health Science Center from April 2016 through June 2018. Eligible patients were adults with subacute or chronic low back pain who reported having either an osteopathic or allopathic physician as the main provider for their back care. At baseline, each

patient completed a series of validated research instruments relating to their low back pain and the physician who provided medical care for it. The Physician Communication Behavior Questionnaire was used to measure: patient participation and patient orientation; effective and open communication; emotionally supportive communication; and communication about personal circumstances. Physician empathy was measured primarily with the Consultation and Relational Empathy Measure and secondarily with the Jefferson Scale of

Patient's Perceptions of Physician Empathy. Patient satisfaction was measured using the 8 dimensions within the Patient Satisfaction Questionnaire with 18 items, and with the Scale of Patient Overall Satisfaction with Primary Care Physicians. Differences between osteopathic and allopathic physicians on each measure were assessed using the t test. The sample size was sufficient to detect at least "medium" differences between physician groups (Cohen's  $d \ge 0.50$ ) with

Table.

Patient Assessments of Physician Communication Behavior and Empathy, and Satisfaction With Low Back Care According to Type of Physician Provider<sup>a</sup>

	Mean (SE)		
	DO (n=96)	MD (n=212)	P Value
Physician Communication Behavior <sup>b</sup>			
Patient participation and patient orientation	66.3 (3.1)	65.0 (1.9)	.73
Effective and open communication	69.6 (3.0)	68.5 (1.9)	.75
Emotionally supportive communication	76.7 (2.5)	74.2 (1.8)	.42
Communication about personal circumstances	58.6 (3.2)	55.6 (2.2)	.44
Physician Empathy			
Consultation and relational empathy <sup>c</sup>	40.8 (1.1)	38.6 (0.8)	.11
Patient perception of physician empathy <sup>d</sup>	19.9 (0.5)	19.5 (0.3)	.53
Patient Satisfaction <sup>e</sup>			
Communication	4.0 (0.1)	3.9 (0.1)	.63
General satisfaction	3.7 (0.1)	3.5 (0.1)	.09
Technical quality	3.7 (0.1)	3.7 (0.1)	.72
Interpersonal manner	4.2 (0.1)	4.0 (0.1)	.13
Financial aspects	3.6 (0.1)	3.6 (0.1)	.69
Time spent with physician	3.7 (0.1)	3.6 (0.1)	.47
Accessibility and convenience	3.7 (0.1)	3.6 (0.1)	.36
Overall satisfaction with physician	58.3 (1.3)	57.3 (0.9)	.52

<sup>&</sup>lt;sup>a</sup> DO denotes osteopathic physician; MD, allopathic physician. Higher scores represent better communication skills, greater physician empathy, and greater patient satisfaction.

b Based on the Communication Behavior Questionnaire.

<sup>&</sup>lt;sup>c</sup> Based on the Consultation and Relational Empathy Measure.

<sup>&</sup>lt;sup>d</sup> Based on the Jefferson Scale of Patient's Perceptions of Physician Empathy.

All patient satisfaction scales were based on the Patient Satisfaction Questionnaire-18, except overall satisfaction with physician. The latter was based on the Scale of Patient Overall Satisfaction with Primary Care Physicians.

 $\alpha \le .05$  and  $\beta \ge 0.99$ . The study was approved by the North Texas Regional Institutional Review Board. Results: A total of 308 patients were eligible for the study, including 208 women (67.5%) and 270 patients (87.7%) with chronic low back pain. The mean (SD) age of patients was 54.3 (11.3) years. A total of 96 patients (31.2%) reported having an osteopathic physician as their main provider for back care. Although patients of osteopathic physicians generally reported more favorable perceptions of physician communication and empathy and greater satisfaction with back care than did patients of allopathic physicians, none of the results achieved statistical significance (Table). A post-hoc analysis of these results found that physician group differences for consultation and relational empathy (Cohen's d=0.20) and general satisfaction (Cohen's d=0.20) would be classified as "small," with the physician group differences on the remaining 12 measures classified as "trivial" (Cohen's d<0.20).

**Discussion:** Our findings indicate that differences between osteopathic and allopathic physicians in their communication styles and empathy were not likely to be clinically relevant. Correspondingly, differences in patient satisfaction between the physician groups were also small or trivial. Although previous research has shown that there appears to be a distinctive osteopathic approach to treating patients with low back pain, the present findings suggest that factors other than the patient-physician interaction are more important in defining the "osteopathic difference." Less reliance on pharmacotherapy, use of osteopathic manipulative treatment, and continuity of care may be more reflective of the osteopathic difference in treating patients with low back pain. The strengths of our study include a pragmatic design using patient-reported data within a communitybased research registry and adequate statistical power. A potential limitation is that patientphysician interactions were not video- or audiorecorded to corroborate the reported findings or to discern more subtle differences between the physician groups not captured by patient selfreport instruments. The next step in our research will be to identify other factors that may represent mediators or moderators in explaining the relationship between osteopathic treatment of low back pain and patient outcomes relating to pain intensity, back-related functioning, and health-related quality of life.

Conclusion: The overall findings of this study indicate that differences between osteopathic and allopathic physicians with respect to communication style and empathy were not likely to be clinically relevant in treating patients with subacute or chronic low back pain, and that differences in patient satisfaction between the physician groups were correspondingly small or trivial.

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#### **Health Services**

#### +HS1—Osteopathic Philosophy

#### The Influence of Medical School Debt on Specialty Choice: An Analysis of Colleges of Osteopathic Medicine

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Research Question(s)/Hypotheses: This study seeks to determine the association between medical school debt and specialty choice among graduating osteopathic medical students. Additionally, the authors aim to determine if the relationship (if any) between level of debt and specialty choice among graduating osteopathic medical students is likely to change as the impact of the single accreditation system (SAS) is fully felt.

Statement of Significance: Although there have been several decades' worth of studies on medical students regarding the influence of medical graduate debt on specialty choice, the impact of debt levels on graduating medical students' selection of a specialty is generally thought to be minimal. However, previous studies have primarily focused on allopathic medical students, while little literature exists on the impact of debt on osteopathic medical students. Studies on allopathic students may not be generalizable, as levels of debt for allopathic students are significantly lower than the average osteopathic student's debt at graduation; in 2016, the difference between osteopathic and allopathic student debt was greater than \$50,000. Since osteopathic tuition rates are increasing at an average of 4.3% per year, it is expected that the debt burden of osteopathic medical students will continue to increase accordingly. With a predicted physician shortage in the United States, particularly in

primary care, and current national legislative debate on the future of loan repayment programs, identifying the impact of medical student debt on the career choice of osteopathic medical students is particularly urgent. The decision to enter a primary care specialty is multifactorial, but osteopathic medical students have historically entered primary care specialties at rates meaningfully higher than allopathic medical students. Other characteristics such as marital status, intellectual content of the specialty, prestige in the medical field, and gross income play a role in specialty selection; however, the rising costs of medical graduate debt may play an increasingly large influence on specialty selection.

Methods: Data from the American Association of Colleges of Osteopathic Medicine's annual survey of graduating seniors were collected from graduation years 2014 (before SAS) through 2018 (2018 data were not available at the time the abstract was prepared, but will be included in the final poster.) Specifically, data on individual student self-reported debt level and self-reported predicted specialty training were collected from the study in a variable set that also included college of osteopathic medicine (COM), COM location (rural vs urban), COM structure (private vs public), and student self-reported undergraduate debt level. Because the survey was given to most graduating students after the residency match occurred, there is high correlation between projected specialty choice and residency specialty. Data were sub-grouped at 3 levels: rural vs urban COM location; private vs public COM structure; and student debt level. Medical school debt level was stratified into quartiles both including and excluding students with no debt. Specialty choice was sub-grouped into primary care vs non-primary care. Primary care was defined as family medicine, internal medicine, and pediatrics.

**Data Analysis:** A  $\chi^2$  analysis was performed predicting primary care specialty choice from medical school debt for all students, as well as only for students with debt. Additionally, a logit regression analysis predicting primary care specialty choice was conducted for all graduating students using the following variables: COM location (rural vs urban), COM structure, and total student debt.

Results: Of the 30,067 respondents for which any data were obtained by the survey during the period 2014 to 2017 (2018 data will be available for the poster but were not available for the abstract), 19,369 respondents (64.4%) quantified their total medical school debt. Of those respondents who quantified their debt, 12,511 (64.6%) reported no medical school debt. Of those with no debt, 7423 (32%) reported practicing in a primary care specialty (other choices were 15, 524 reporting a non-primary care career and 262 reporting an indefinite career). Of those with debt, 2240 of 6858 (32.7%) reported practicing in Primary Care (non-primary care = 4545; indefinite = 73). This difference was not statistically significant ( $\chi_2^2$ =1.257; P=.533). However, when grouped by debt quartile, the differences between the highest quartile of debt-holders, 30% of whom selected primary care, was statistically significantly different from the other groups ( $\chi_8^2=16.599$ ; P=.035). Among those graduates with debt, those in the top quartile of debtholders were again statistically significantly less likely to match primary care specialties at a rate of 30% vs 33.5% ( $\chi_6^2$ =16.561; P=.011). A logit regression analysis of all students predicting choice of primary care from total medical school loans, medical school structure (private vs public), desired practice location was statistically significant but explained only 10% of the variation in primary care specialty choice  $(F=217.49; r^2=0.10; P<.001).$ 

Conclusion: While many factors contribute to specialty choice, for osteopathic medical graduates, having the highest level of debt is currently associated with lower rates of selection of primary care specialties. The relationship between debt level and reduced preference for primary care residencies (and likely practice) is likely to be strengthened if currently available programs to reduce debt (and in some cases incentivize primary care practice) are de-funded, as is currently being discussed. With the addition to our study of 2018 data, when it becomes available from AACOM in August 2018, the impact of debt levels as most non-primary care residency programs move to the NRMP match under the single accreditation system, students with higher levels of debt may have trouble matching if they try to match into a non-primary care residency due to their debt. This study contradicts several other studies that have found no relationship between debt and specialty choice, generally in allopathic students. A recent analysis of debt level and practice location in osteopathic medical students indicates that debt may have some impact on desire to practice in a rural area. Likewise, this study shows that osteopathic graduates with the highest levels of debt are statistically significantly less likely to choose primary care than their less-indebted colleagues. Given increases in osteopathic medical school tuition and national policy under consideration that would de-fund loan repayment programs, including those specifically for primary care, these results indicate that current trends may exacerbate the shortage of primary care physicians.

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#### HS2—Osteopathic Philosophy

# Structure and Function in Medical Education: Trend Analysis of Osteopathic Medical Student Emotional Intelligence (EI) Suggests Curricular Modifications May Improve Functional Traits

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Background: A growing problem, physician burnout is linked to low EI, depression, anxiety, empathy, poor outcomes, suicide.1, 2 Research suggests it takes root in medical school,<sup>3</sup> giving educators a window to alter its course. Researchers have studied the risk factor empathy,4 an aspect of emotional intelligence (EI). EI encompasses empathy and other related traits.5 The authors sought to determine whether osteopathic medical students exhibit EI trends across matriculation, hypothesizing that if trends could be confirmed, solutions could be developed. Based on literature and initial analysis of the classes DO 2014-2016 suggesting declining EI, 2 key traits were identified for further analysis: empathy and self-regard. With grant support from the AOA, data collection continued to further assess these trends across DO 2014-2018. During the course of this longitudinal study, structural changes took place to the clinical curriculum for the classes of DO 2017-2018. These improvements served as an intervention, offering the opportunity to determine whether EI risk factors could be mitigated.

**Research Question:** Are there identifiable trends in osteopathic medical student EI linked to burnout? If so, can risk factors be positively impacted with educational interventions?

Significance/Osteopathic Relevance: With the first tenet of osteopathic medicine stating "the person is a unit of body, mind, and spirit," holistic development for osteopathic medical students is consistent with the osteopathic approach. EI offers a framework to facilitate and measure this. The third tenet recognizes that structure and function are inter-related. While this refers to patient care, the current study offers the ability to explore whether the same may be true for osteopathic medical education. If so, osteopathic medical educators may seek to better align education and practice.

Method: The Bar-On Emotional Intelligence Inventory/EQ-i 2.0 by MHS, Inc. was used. It has 133 self-report items and takes 15 minutes to complete online. It yields an overall EI score as well as scores in 5 domains and 15 subscales. It was offered to DO 2014-2018 at 3 junctures: in-coming, midway, and graduation. Students were emailed the link and provided a 2-week window for completion. Due to attrition, incentives were used for second and third admins in the form of enrollment in gift card drawings and extra credit. Changes took place to the clinical curriculum impacting DO 2017-2018 serving as an intervention. These included incorporation of adult learning models to increase student responsibility for their own development; improved communication channels for students and faculty/ preceptors; and a streamlined pathway between preclinical education, clinical education, and residency. The third/fourth-year Essentials of Clinical Medicine (ECM) course, a distance learning course that parallels rotations, was restructured to support the acquisition of Entrustable

Professional Activities (EPAs), mirroring the framework used in continuing medical education. Students were offered a variety of activities to choose from, giving them autonomy in directing their own learning. The rotations experience was enhanced. While this mainly impacted the third and fourth years, the Office of Clinical Education began interfacing with these classes during their first year. This included frequent contact with class representatives and a Facebook page, which helped give classroom learning context. Students logged their own experiential learning activities, further reinforcing self-responsibility.

**Data Analysis:** Of 1435 students from DO 2014-2018, 238 completed all 3 surveys, yielding a response rate of 17%. Statistical analyses were conducted to identify longitudinal trends using SAS software for Windows version 9.3 (Cary, North Carolina, USA). A time variable with 3 categories including baseline, mid-way, and graduation was created. Repeated measurement analysis of variance analyses were conducted. A plot of the average of the outcomes (y axis) against time periods (x axis) was used. Statistical analyses were 2-sided. *P*<.05 was considered significant.

Results: Per previous study of DO 2014-2016, overall EI, self-regard, and empathy declined across matriculation with a significant drop taking place mid-way. There were no significant upward trends. When overall EI was analyzed for DO 2017-2018 (n=94), the scores went up from 98.8 to 100.0 (average) mid-way, a non-significant increase (P=.2472), to 108.5 at graduation, a significant increase (P<.0001). Self-regard went from 97.8 to 98.0 (P=.9004) from first to second admin, then increased significantly between send and third with a final score of 103.0 (P<.0001). Empathy went from 104.1 to 103.7 mid-way (P=.7245), with a significant increase between second and third (P<.0001) and a final score of 109.3. With all classes combined, overall EI had a significant initial decrease from 99.6 to 97.7 midway (P=.0044) with a significant increase between second and third and a final score of 101.4 (P<.0001). Self-regard had a significant mid-way decrease from 98.3 to 96.6 (P=.0226), then went up significantly to 98.5 (P=.0063). Empathy had a significant mid-way decrease from 103.4 to 101.4 (P=.004) and a significant increase to 103.4 (P=.0079). Independence was found to have contributed most to the significant upward trend in overall EI in the clinical years, rising from 94.6 to 95.7 between first and second admins in a non-significant change (P=.1405), then to 99 (P<.0001) in a significant increase between second and third.

Conclusion: Results suggest structural changes to medical school curricula may improve EI traits linked to burnout in a subset of students. It is noteworthy that the biggest contributing factor to the increase in overall EI was independence, or "the ability to be self-directed; free from emotional dependency; decision-making, planning, daily tasks are completed autonomously.5" Future studies of burnout may wish to incorporate physician autonomy. Self-regard and empathy are also worth further study. The downward-upward trend suggests that given the right structure, osteopathic medical students can be resilient. The study has limitations. The small response rate makes generalizability difficult; the EI 2.0 is self-reported; participants self-selected; and given the longitudinal nature, other variables may have influenced results. Inter-institutional research is needed to determine whether these trends occur in the broader DO student population.

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#### ♦HS3—Osteopathic Philosophy

The Émigré Physicians' Experiences
Before, While, and After Attending an
American Osteopathic Medical
School: A Cross-Sectional, Mixed
Methods Study, Convergent Design
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Research Questions: We are investigating the reasons émigré physicians (EPs) leave their home countries and seek to practice medicine in the United States. We also sought to learn about their difficulties in obtaining licenses and residency matches when they arrive, their reasons for selecting the NYITCOM Émigré Physicians Program (EPP), their experiences at NYITCOM, and their abilities to match into residency programs. We are also interested in the EPs' perceptions of NYITCOM's EPP. The purpose of our study is to discover: (1) Why the EPs in NYITCOM's EPP left their home countries; (2) Why the EPs surveyed chose to enter NYITCOM's EPP; (3) The perceptions of the survey respondents as to how well NYITCOM's undergraduate medical education prepared them to be competitive applicants in the US residency match and for clinical practice in the US; (4) The EPs' perceptions of NYITCOM's EPP. Statement of Significance: More than 60,000 foreign-trained physicians living in the United States are not licensed in the United States.1

NYITCOM provides a unique path to residency in the United States by allowing these EPs to obtain a US osteopathic medicine degree after completing the 4-year medical school curriculum.<sup>2</sup> Many reasons influence EPs to leave their home countries and migrate to the United States to continue their medical careers. 1,3,4 However, the goal of getting licensed in the United States is inaccessible for many.4 EPs have difficulties obtaining US residencies. NYITCOM, through its EPP, provides a diverse group of students with a unique path to medical licensing and residency as osteopathic physicians. This endeavor is congruent with AACOM's efforts to increase diversity in medical schools by increasing the diversity in osteopathic medical schools and in practice. Research has identified that while the numbers of underrepresented minorities in US medical schools has increased, the racial and ethnic diversity between medical school graduates and the US population as a whole has decreased. In response, AACOM established a Diversity Committee in 2015 "with the goal of developing underrepresented minority interest in pursuing a career in osteopathic medicine, increasing the diversity of applicants to the nation's colleges of osteopathic medicine (COMs), and sharing resources to support prospective and current minority DO students as they navigate through medical school."5

Methods: Current and graduate EP students are being sent an online survey via email and Facebook requesting their participation. All non-EPP students are excluded. Three follow-up requests are being sent as needed to maximize response. Quantitative data are obtained through scaled items and qualitative data through comment sections. The researchers are offering a chance to win 1 of twenty \$25 gift cards as an incentive for completing the survey. As a study in progress, the 131 EPs who matriculated between 2014 and

2017 were contacted; 24 responded to date. We will be contacting over 600 EPs in total for this study. We anticipate the study will be completed and a poster prepared for OMED in October 2018. Data **Analysis:** Cross-sectional, methods study, convergent design. Quantitative: Demographic information and scaled data of respondents perspectives on how well NYITCOM prepared them for residency matches and clinical practice were analyzed by correlation and linear regression analysis using IBM SPSS Statistics 23. Statistical significance was determined by a P value of <.05. Qualitative: Textual data were obtained from survey participants' comments and organized on an Excel spreadsheet. Codes were derived from the text and used as an index to retrieve text. Categories were derived and themes were identified.

Results: Quantitative: The respondents' Match Prep scores were positively correlated with admission scores (r=0.49) and with Practice Prep scores (r=0.71). Admissions ( $\beta$ =0.40, P=0.041) and the Practice Prep ( $\beta$ =0.58, P=0.015) were the strongest predictors of Match Prep, based on the result of linear regression for the outcome variable of Match Prep and the predictor variables of English, Read, Admissions, Education, and Practice Prep. Qualitative: Text analysis revealed that: (1) EPs left their home countries in search of a better life/opportunities and for freedom/ asylum. Typical responses were, "Better life for my children, equal opportunities and freedoms," and "looking for a better future." (2) EPs chose NYITCOM because: It is the only program/ unique (mentioned in 6 responses), to follow dream/get residency/to practice medicine (mentioned in 11 responses), DO/holistic (mentioned in 3 responses), quality of the program (mentioned in 1 response), recommended/told about by a friend (mentioned in 2 responses), no MCAT required (mentioned in 3 responses). (3) The respondents generally had a positive perception

about their preparation for residency in terms of medical knowledge and cultural competence. Typical responses were, "Best experience of my life," "a very good program," and "good, challenging, and interesting." A common concern expressed by respondents was the need for more help in preparing them for the national board examinations, both COMLEX-USA and USMLE. Another common perception was that EP students should be better integrated into the NYITCOM student body. Suggestions included increasing communication about the EPP to faculty and non-EP students.

Conclusion: Perceptions of preparedness as competent practicing physicians was the strongest predictor of preparedness for residency match. EPs' perception of the admissions process was also a statistically significant predictor of preparedness for residency match. Regarding the results of the text analysis, the EPs moved to the US for a better life. They chose NYITCOM because the EPP is the only one of its kind and they heard about the quality of the program. The results of our preliminary survey of this small cohort of EPs showed the general perception was that the EPP was beneficial in preparing them for residency. AACOM researchers have identified a need for more diversity in osteopathic medical school graduates, and NYITCOM's EPP is a long-standing successful curriculum specifically tailored to the meet the medical education needs of the EPs, thereby increasing the diversity in osteopathic medical schools and in practice.

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#### ♦HS4—Osteopathic Philosophy

# Repair and Maintenance of the Cadaver Donor

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Research Question(s)/Hypotheses: Vital to the education of medical and health care professional students is a comprehensive understanding of human anatomy. One of the most effective resources to prepare these students for what they will see in their future clinical practice is the cadaver donor. These donors allow students to learn human anatomy away from the pages of a textbook or pictures in an atlas, as much is gained from the ability to palpate key structures and landmarks as well as the added benefits of studying anatomical variation, all of which are vital tasks and challenges that these students will one day face in their future careers. In a model in which multiple students learn from a single donor, damage is inevitable as these students develop their anatomical and palpation skills. However, in cases where multiple donors become damaged, key objectives for learning can become harder to localize and use, causing education to suffer as a result. It is also important to consider that each donor is a person and that it was their

wish that their body be used to educate future health care professionals. Because cadavers are a valuable education resource and the complex processes involved in securing donations, it becomes both physically and morally necessary to implement a proper care regimen. Including students in this maintenance and care protocol can have benefits for both the donors and the students. Properly maintained, the donors' ability to teach is preserved while students gain valuable repair, anatomical, and prosection knowledge. The aim of this research is to establish a model that will allow health care students to actively participate in the repair and maintenance of the cadaver donors. As osteopathic medical students, we are trained to consider a person from the perspective of mind, body, and spirit. At MSUCOM, we are also taught that our donors will act as both our teachers and our first patients. It becomes imperative to continue to look at our donors following the core tenants of osteopathy. In this sense, we can consider their body's function as educating future health care professionals, where appropriate structure equates to better education. This model allows us to help maintain that structure and further to show our respect for the mind and spirit of the individual who chose to be a teacher.

Methods: In this study, a multi-phase approach is currently being used to implement this model. In phase 1, a single student helped maintain donors in the laboratory primarily by prioritizing damage to the major vessels of the thoracic cavity sustained during embalming. The student also monitored for other damage sustained from student use of the donors. Additionally, to a minor extent this student assisted in the prosection laboratory in the repair of damaged objectives. In phase 2, the current phase of the study, a donor damage report list is in the process of being implemented. This allows for expanded surveillance and involvement as it affords the opportunity for students to report damage as it occurs or as it is

observed; it also functions to help better direct the student responsible for repairs to donors in need. Phase 3, currently in early discussion, is the involvement of the MSUCOM Student Osteopathic Surgical Association (SOSA) with the goal of forming a structured group of students who will be responsible for the maintenance and repair of donors in the laboratory. This would allow more student involvement and allow for an increase in the volume of repairs.

**Data Analysis:** While the repairs completed up to this point have been logged, currently no formal analysis has been completed. Looking further into this model's potential to increase the longevity of our donors and impact on teaching are avenues of future research.

**Results:** To date, more than 20 repairs have been completed by a single student. This number has the potential to be significantly increased as the plans for implementation of phase 3 become more finalized.

Conclusion: Through the use of a model where health care students take responsibility for the maintenance and repair of their cadaver donors, the overall well-being of the donor can be improved as well as the quality of education they provide. While further analysis into the longevity and impact on education still need to be analyzed and the model is currently in early stages of implementation, it lays the groundwork for applying core tenets of osteopathic medicine to the cadaver donor and the ability to create a lasting impact on health care education.

Acknowledgment/Funding Source: This research is currently being completed as part of an independent study project under the direction of Dr Loro L.L Kujjo. Student Doctor Meisel thanks Dr Kujjo for his support and mentorship up to this point and looks forward to working with him in the future.

#### ♦HS5—Osteopathic Philosophy

#### Teaching Technology: Assessing Telemedicine Education to Enhance Undergraduate Medical Training

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Introduction: There is a growing number of osteopathic and allopathic graduates each year; however, there is a discrepancy between the need and access to quality health care. One strategy to bridge the gap is the implementation of telemedicine (TM) to deliver health care to underserved and rural communities. A survey by the American Academy of Family Physicians found that 78% of respondents believe TM improves access to care, yet only 15% of those physicians themselves provided TM services within the past 12 months. The largest barrier to use is the lack of training. 1 We have conducted a literature review of published TM education plans to find functional modalities, assessments, and gaps in training. This information will help develop a TM curriculum for undergraduate medical students to be trained and improve future quality and access to care.

Research Question: What strategies are being used to teach the skills needed to operate TM devices and overcome patient-physician barriers in its use? What shortcomings have been found in educating users on the uses of TM modalities? Lastly, what methods have been used to test competency in taught skills involving TM?

Osteopathic Significance: There is an ongoing lack of access and need for quality health care. TM is a potential solution to bridge this gap. Undergraduate medical students will be members of the future health care force; thus, improving training through TM education will lead to

physicians trained in the use of TM modalities for future practice.

Methods: We carried out a systematic literature review of the PubMed database pertaining to published TM articles. PubMed was searched using the term "telemedicine" specifically within the abstract or title of the article and only with publications involving human subjects. Further Boolean operators and truncation were applied to include the terms "educate" and "training" in each article.<sup>2</sup> These words were chosen based on the emphasis of our project on TM, education of students, and training of TM technology. Pre-established inclusion and exclusion data were used to evaluate the articles for this study. Inclusion data pertained to studies of physicians or students trained and educated on TM devices and their use, and/or pitfalls in education, and/or methods of evaluation of taught skills. Exclusion criteria included the use of TM to train and educate a third party rather than physicians and patients. For example, "TM used to train nurses about mental health" would not be used because it does not focus on how TM was being taught for future use. Furthermore, searches limited to the past 5 years were used to emphasize the most current trends in TM education.<sup>2</sup> Search terms "learning," curriculum," and "teach" were bypassed to isolate articles solely about teaching the use of TM in the delivery of health care, not TM as a tool for delivering educational content. The initial phrase search yielded 117 articles, which were evaluated for inclusion and exclusion data. A total of 20 articles were identified for this study.

**Results:** The results were divided into 3 categories: modalities of teaching, areas of improvement, and suggestions for testing competency. Rollo et al<sup>3</sup> suggest a multi-level method of teaching, focusing on orientation to equipment, comparison of in-person and TM experiences, quality assessment of existing products, and exploring ethical, security, and privacy concerns. Other results iden-

tify creating an evidence-based curriculum and creating programming based on the needs of the clinical population at hand. Logistically, education can occur throughout training, with suggestions for a TM elective and digital-call in clinical years during more TM-friendly rotations. 4 Many products and devices are available for use, creating a concern in educating students. This leads to a need for teaching students how to evaluate TM devices and products and their potential clinical efficacy.<sup>5</sup> There must be an emphasis on teaching behaviors related to clinical care and not a memorization of steps and expected tasks.6 There are many methods to evaluate competency evaluation, emphasizing the importance of evaluating the technical aspects of device use, history taking, image capturing, physical examination capability, and communication skills. The United States Accreditation Council of Graduate Medical Education also establishes a framework of teaching and assessment, which is also suggested to be applied as a method of competency assessment.<sup>7</sup> Conclusions: The current generation of medical students has been described as "digital natives," well-versed in incorporating technology into social interaction. However, without formal training, this does not imply high-quality TM care delivery.4 Our data establish a baseline of the current literature, with results indicating the areas of need in TM education with ways to deliver content and assessment. Due to the limited number of TM education and training publications, our sample data remain small. However, this limitation further emphasizes the importance of research in this growing field of health care service. The literature reviewed suggests incorporation of skill development in all 4 years of medical education, as well an importance of social education in ethics, communication skills, and an ability to evaluate the quality of TM products. We hope to use these data to establish a true evidence-based curriculum for teaching and using TM during the first 2 years of medical training, with more clinically based application training for the third and fourth year. Further studies will also incorporate TM use in specific clinical conditions, such as diabetes management and mental health counseling, to create case-based learning as adjuncts to curriculum.

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