



# 56th Annual AOA Research Conference— Abstracts, 2012

This issue of JAOA—The Journal of the American Osteopathic Association features abstracts from the posters that will be presented at the 56th Annual American Osteopathic Association (AOA) Research Conference. These posters represent the most recent work of numerous osteopathic medical clinicians, researchers, educators, and students.

This year's abstracts are organized into 5 groups:

- series F—fellowships (see below)
- series P—osteopathic manipulative medicine/osteopathic principles and practice (see page 530)
- series C—clinical studies (see page 535)
- series B—basic sciences (see page 551)
- series ME—medical education (see page 558)

To enhance the readability of this special feature to the JAOA, the abstracts have been edited for grammar and basic JAOA style. The

content of these abstracts has not been modified; neither the AOA Council on Research nor THE JOURNAL assumes responsibility for the abstracts' content.

This year's AOA Research Conference, "Premier OMM Relevant Research and Charting a Collaborative Way Forward," will take place in San Diego, California, from Sunday, October 7, to Thursday, October 11, during the AOA's 2012 Osteopathic Medical Conference & Exposition (OMED 2012), "Maximize Today, Prepare for Tomorrow."

For more information on the AOA Research Conference or other programs taking place during OMED 2012, access the conference's Web site at <http://www.osteopathic.org/omed>. The AOA Research Conference program can be accessed at <http://www.osteopathic.org/inside-aoa/events/omed-2012/Pages/program.aspx>.

## AOA Research Fellowships

### F1

#### Burnout Among Osteopathic Otolaryngology Residents: Identification, Prevention, and Treatment During Formative Training Years

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**Hypothesis:** Osteopathic otolaryngology residents experience lower rates of burnout compared with previously published rates for Accreditation Council for Graduate Medical Education (ACGME) residents.

**Methods:** A cross-sectional, questionnaire-based study of US osteopathic otolaryngology residents was conducted. The questionnaire, adapted with permission from a published survey, was generated using Zoomerang survey software and e-mailed to all residents matriculated in US osteopathic otolaryngology residency programs. The 23 questions (6 requiring multiple responses) were divided into demographic information, professional stressors, personal and professional life satisfaction, a modified Maslach Burnout Inventory–Human Services Survey (MBI-HSS, used with permission) and mentor-resident interactions. Using the MBI-

HSS, burnout rates were measured by high emotional exhaustion (EE), high depersonalization (DP), and low personal accomplishment (PA). Results were compared with published results for ACGME residents. Osteopathic and ACGME residents were compared using  $\chi^2$  and *t* tests. Spearman correlations were used to test for associations between burnout scores and demographics, stressors, satisfaction, and mentor interaction.

**Results:** Of the 102 residents contacted, 48 (47%) responded. Burnout rates were low, moderate, and high for 23%, 66%, and 11%, respectively, for osteopathic residents, compared with rates of 14%, 76%, and 10%, respectively, for ACGME residents ( $P=.18$ ). Rates of EE and DP were not statistically different between osteopathic residents and ACGME residents, but PA scores were higher in osteopathic residents ( $P=.03$ ). Differences in sleep hours (6.6 vs 6.2,  $P=.04$ ) and work hours (62 vs 71,  $P<.001$ ) were not statistically significant. Increased EE was associated with decreased hours of sleep ( $r=-0.42$ ,  $P=.003$ ). No correlations were found between sleep and DP or PA. Increased influence from a mentor was associated with decreased burnout rate for all 3 components: EE ( $r=-0.54$ ,  $P=.002$ ), DP ( $r=-0.59$ ,  $P=.0006$ ), and PA ( $r=0.44$ ,  $P=.02$ ).

**Conclusion:** To our knowledge, the current study is the first to quantify burnout among osteopathic residents. Our results suggest that osteopathic residents have lower rates of burnout compared with ACGME residents. Osteopathic residents reported lower rates of low PA, increased hours of sleep and decreased overall work hours. The study was limited by a small sample size and moderate response rate.

**Acknowledgment:** Funded by an American Osteopathic Association Research Fellowship.

### ◆F2

#### Effects of Nonaerobic Maximal Effort Exercise on Fatigue and Health-Related Quality of Life in Deconditioned Patients With Multiple Sclerosis

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**Background:** Multiple sclerosis (MS) is a chronic, progressive neurodegenerative disease characterized by mental, emotional, and physical fatigue, each negatively impacting physical and mental functions in addition to Health-Related Quality of Life (HRQL). Assessing HRQL may be achieved with the MS Quality of Life (MSQL) survey, which includes Modified Fatigue Impact Scale (MFIS) for physical, cognitive and psychomotor perceptual subsets. The Multiple Sclerosis Functional Composite (MSFC) score—combining the timed 25-foot walk, timed upper extremity coordination (9-hole pegboard) test and cognitively influenced 3-minute Paced Auditory Serial Addition Test (PASAT)—provides a more global assessment of actual function.

**Hypothesis:** Patients with MS with documented functional improvement on MSFC and a physical exercise protocol will perceive lower physical and mental fatigue impact (MFIS subscales) and lower pain impact as reflected in better HRQL measures.

**Methods:** We obtained institutional review board approval to re-examine data from our prior multicenter study, investigating a 10-week nonaerobic maximal effort exercise (MEE) with follow-up measures after 6 weeks and 12 weeks. Customized equipment (IsoPUMP; Neuromuscular Engineering,

Nashville, Tennessee) was selected to control and document isometric and eccentric MEE leg press and total body lunge repetitions (every 4 seconds with Valsalva maneuver; increasing during 10 weeks from 3 repetitions to 5 repetitions). Fifty-five patients could be analyzed for MSFC scores; 51 for most MSQL measures.

**Results:** Subscores for MFIS showed significantly reduced perceived fatigue impact on HRQL at end of exercise regimen and at 3 months later (cognitive  $P<.003$ , physical  $P<.003$ , and total  $P<.002$ ). A significant decrease was also seen in MSQL pain effect scores.

**Conclusion:** Integrating a nonfatiguing MEE protocol achieved a statistically significant reduction of the perception of negative impact by pain, physical fatigue, and cognitive fatigue on a number of HRQL measures in patients with MS. Correlations between perception and function were noted in several areas compared with prior reports of improvements in strength, gait speed, and PASAT in this same group.

**Acknowledgment:** This study was supported by a joint Civilian-Veterans Affairs project grant.

## Osteopathic Manipulative Medicine/Osteopathic Principles and Practice

### P1

#### Neonatology-Osteopathy (NE-O) Study: A Randomized Controlled Trial on the Effect of Osteopathic Manipulative Treatment on Length of Stay

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**Background:** The use of osteopathic manipulative treatment (OMT) in preterm infants has been documented and results from previous studies suggest an association between OMT and length of stay (LOS) reduction, as well as significant improvement in several clinical outcomes.

**Objective:** To show the effect of OMT on LOS in a sample of premature infants.

**Methods:** A double-blinded, randomized controlled trial was conducted on preterm newborns admitted in a single neonatal intensive care unit between 2010 and 2011. Patients (N=51) free of medical complications with gestational age between 28 weeks and 38 weeks were enrolled and randomized in 2 groups: study group (n=21) and control group (n=30). All patients received routine pediatric care and OMT was performed on the study group for the entire period of hospital-

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ization. Endpoints of the study included differences in LOS and daily weight gain.

**Results:** Results showed a significant association between OMT and LOS reduction, as seen in the differences between the study group and control group (mean difference, -1.787; 95% confidence interval, -3.555 to -0.0015;  $P < .05$ ). Osteopathic manipulative treatment was not associated to any change in daily weight gain.

**Conclusion:** The present study confirmed that OMT could play an important role in the care of preterm infants in the hospital setting.

## ◆P2

### Comparison of Traditional Chinese Medicine Tui-Na and OMM Treatment: Common Fundamental Principles

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**Context:** Previous observational research of Tui-Na, a manual therapy in traditional Chinese medicine (TCM), described similarities to osteopathic manipulative medicine (OMM) soft tissue and articulatory treatment techniques.<sup>1</sup> Some Tui-Na diagnostic methodology relied on tissue texture abnormality, asymmetry, restriction of motion, or tenderness (ie, TART findings)—not qi flow along acupuncture meridians—and used a tensegrity model approach to diagnosis and treatment.<sup>2</sup> Despite these similarities to OMM diagnosis and treatment, there is currently limited research comparing their fundamental principles.

**Hypothesis:** We hypothesized that this form of Tui-Na, which utilizes TART findings and a tensegrity-based diagnostic and treatment process that is visually analogous to OMM, uses similar treatment principles as those found in OMM.

**Methods:** During the Touro University California, College of Osteopathic Medicine (TUCOM) Global Health Program Summer Clerkship at Taipei Hospital, Taiwan, first-year osteopathic medical students video-recorded, with institutional review board approval, 2 Tui-Na treatments by a TCM physician (Y.H.). Patient consent was obtained, no identifying information was recorded, and patient faces were censored for privacy. Osteopathic manipulative medicine faculty at TUCOM analyzed the videos while the students provided English-language translation.

**Results:** Tui-Na has techniques that use myofascial continuity lines similar to those described in *Anatomy Trains*<sup>3</sup> for both diagnosis and treatment. The treatments observed demonstrated long lever approaches that used (a) direct recoil

by means of the upper extremity, with combined articulatory principles, a principle used in some OMM techniques, including visceral manipulation,<sup>4</sup> and (b) oscillatory vibrational force created by rhythmic dropping of the lower extremity (converting potential energy to kinetic), which travels along fascial continuity to target the dysfunctional tissue. The rhythmic nature of (b) is akin to how Robert Fulford, DO, used the percussion hammer and how Zachary Comeaux, DO, used manual oscillation in facilitated oscillatory release.<sup>5</sup>

**Conclusion:** Tui-Na techniques were developed independently from OMM techniques, yet certain commonalities suggest shared fundamental principles and therefore mechanisms of action (MOA) that underscore the therapeutic effectiveness of these methods. Providing method of action of a therapy can provide validation to the scientific and medical communities that outcome studies alone do not, which may facilitate future funding and research.

## References

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## ◆P3

### Correlating Chapman Tender Points With Diagnostic Studies in Patients Presenting to the Emergency Department With Chest Pain

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**Hypothesis:** The presence of Chapman tender points will correlate with laboratory diagnosis and clinical presentation of patients presenting to the emergency department with chest pain.

**Overview:** This research project correlated palpatory findings of specific Chapman tender points with laboratory tests and chief complaint in patients presenting to the emergency

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department. The presence of specific tender points was assessed using a pressure algometer and patient ratings for tenderness using the visual analog scale (VAS). These findings were then correlated with the final diagnosis and other clinical studies.

**Methods:** Participants included adults ( $\geq 18$  years) in an urban level 1 trauma center with an emergency medicine residency in place. All participants were voluntary and medically stable. Participants were grouped according to the primary or secondary complaint of “chest pain” or “other,” and the researcher was blinded to the participants’ chief complaint. A pressure algometer was used to standardize applied pressure. Participants were palpated for tenderness at a control point, 3 bilateral anterior and 3 bilateral points corresponding to Chapman points for myocardium and lung. Diagnostic studies and final diagnosis were collected for all participants. Descriptive statistics were calculated for all variables. This research project was approved by hospital and university institutional review boards.

**Results:** A total of 70 participants, 29 in the study group and 41 in the control group, were recruited. Numerous points showed statistical significance ( $P \leq .05$ ) for tenderness, defined as  $\geq 10$  mm difference from the control point on the VAS. These included 4 of the 12 points in patients presenting with the chief complaint of “chest pain” and 6 of the 12 points in patients presenting with a lung complaint. The left anterior lung ( $P = .013$ ) and left posterior lung ( $P = .007$ ) points in the combined group of patients with diagnostic examinations showing heart or lung pathology were statistically significant.

**Conclusion:** Differences at numerous points were statistically significant. Although no 1 Chapman tender point was statistically significant in greatest frequency, 11 of the 12 points were statistically significant in at least 1 participant group. Further exploration of this topic using a larger study group would be of great interest.

### P4

#### Classification of Musculoskeletal Disorders in Medically Underserved Regions in South America

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**Context:** Understanding and elucidation of acute and chronic musculoskeletal somatic dysfunction in medically underserved areas of South America has yet to be achieved and

remains a priority for the World Health Organization. Existing literature for this area poorly characterizes musculoskeletal conditions, specific to body region and type of pain.

**Hypothesis:** Anecdotal data indicate that poor and underserved South Americans are experiencing increases in work-related musculoskeletal disorders, and that there is an expanding need for interventions that target improved health and management of somatic dysfunction.

**Methods:** To evaluate acute and chronic musculoskeletal dysfunctions in underserved communities in 456 patients aged 18 to 86 years (mean [standard deviation], 44.7 [17.23] years) receiving medical care during outreach trips to Ecuador, Peru, and Argentina. Patients were invited to complete an anonymous 1-page questionnaire that ascertained generalized and specific musculoskeletal acute (past 7 days) and chronic (past year) pain. Survey items also included age, sex, height, weight, occupation, general health, number of physician visits in the past year, pain in the past year and pain in the past 7 days. The survey was offered in Spanish and took approximately 10 minutes to complete. Data were analyzed using SPSS (version 20; SPSS Inc, Chicago, Illinois).

**Results:** The sample ( $N=456$ ) consisted of women (72%) and men (28%). Fifteen percent had not seen a physician in the past year, 14.9% saw a physician once, 11.8% saw a physician twice, and 10.3% saw a physician 3 times. Forty percent reported their health status to be “poor/not too bad.” Acute and chronic lower back pain was reported by more women than men (67.3% vs 32.7% and 69% vs 31%, respectively). Acute and chronic pain in each body region was statistically significantly associated with older age. Reports of acute pain for all respondents were associated with chronic pain for each corresponding body region. Regarding occupation, homemakers and agricultural/trade workers experienced more wrist/hand pain and ankle/foot pain than professional trades or the unemployed.

**Conclusion:** Data from this study help to determine which treatment modalities, including osteopathic principles and procedures, will be most beneficial when developing targeted health care services, and thus, generate guidance protocols specific to age, occupation, and sex for future medical providers practicing in this region.

### ◆P5

#### Effect of Counterstrain Treatment on Contralateral Satellite Tender Points

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**Background:** It follows from the osteopathic tenet of body unity that treating somatic dysfunction on 1 side of the spine

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would diminish pain experienced on the other, and we have observed this to be true in patients complaining of bilateral muscle pain.

**Objective:** To determine whether treating an active posterior shoulder tender point (TP) with counterstrain (CS) would similarly influence the contralateral anatomic site.

**Methods:** In our mixed-model, randomized controlled trial, 51 adult volunteer participants were randomized to either the CS or sham arm. A brief osteopathic structural examination was performed, followed by an assessment of the trapezius and levator scapulae muscles for TPs. When an “active” TP was palpated, the site was marked, and a symmetric “quiescent” TP was found and marked on the contralateral side. A blinded researcher then applied a pressure algometer (JTech Medical, Salt Lake City, Utah) to assess the pressure pain thresholds (PPT) of both points. The treatment group received standard CS treatment at the active TP, and the sham group received a simulated treatment over the area. After the CS or sham intervention, the active and quiescent points were both remeasured with the algometer.

**Results:** Participants in the CS arm (n=25) had a mean (standard deviation [SD]) PPT of 4.09 (1.55) in the active TP pretreatment, which significantly increased to 5.41 (1.90) post-treatment. This corresponds to a mean (SD) PPT of 5.95 (1.94) in the quiescent TP pretreatment, which increased to 5.99 (2.14) after treating the active site, but this was not statistically significant. Participants in the sham arm (n=26) had a mean PPT of 5.04 (1.81) in the active TP preintervention, which significantly increased to 5.93 (1.93) after intervention. The quiescent side had a preintervention mean (SD) PPT of 6.44 (2.04), with a postintervention mean (SD) of 6.42 (1.66), however, this does not represent a statistically significant change.

**Conclusion:** Counterstrain treatment of an active TP on 1 side of the body did not have an appreciable effect on the contralateral anatomic site in the population we studied. Interestingly, both the CS and sham arms showed a significantly increased PPT following intervention, which could be due to placebo effect or simply the inherent therapeutic value of human touch.

**Acknowledgment:** This study (ATSU AZ IRB approval #2010-35) was financed by the F. Herbert Fields DO Memorial Research Fund.

#### ◆P6

### Lymphatic Pump Technique Enhances Pulmonary Immunity and Facilitates the Clearance of Respiratory Infection With *Streptococcus pneumoniae*

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**Background:** Lymphatic pump technique (LPT) is thought to aid in the removal of built-up metabolic wastes, toxins, exudates, and cellular debris that occur during infection or edema. Furthermore, LPT has been reported to enhance immune function. *Streptococcus pneumoniae* is known to be a common cause of otitis media, meningitis, and respiratory infections. In addition, it is a major cause of pneumonia in older adults and infants. Clinical trials have shown LPT effective at decreasing hospital length of stay, decreasing the length of intravenous antibiotics, and lowering incidence of death when compared to only conventional care when treating patients with pneumonia. Few studies have explored the underlying mechanisms that exhibit the protective mechanism previously shown in clinical trials.

**Objective:** To determine if LPT would enhance the clearance of *S pneumoniae* respiratory infection in a rat model, and explore the mechanisms associated with such clearance.

**Methods:** Rats were nasally infected with  $\sim 1 \times 10^8$  *S pneumoniae* CFUs. Rats were divided into control, sham, or LPT treatment groups. Rats then received (1) a daily sham treatment consisting of intravenous administration of 10 mg/kg propofol anesthesia followed by 4 minutes of light touch, (2) 4 minutes of LPT daily under anesthesia, or (3) no treatment or anesthesia (control). At different time points, lungs were collected and measured for *S pneumoniae* bacteria and the number of pulmonary leukocytes. In addition, blood and spleens were collected to measure the extrapulmonary immune response. Further, bronchoalveolar lavage fluid was collected at different time points and analyzed for inflammatory mediators. In vitro studies using isolated alveolar macrophages and in vivo depletion studies on alveolar macrophages were also performed.

**Results:** Animals treated with LPT showed a statistically significant ( $P < .05$ ) decrease in total CFUs/lung postinfection. In vitro studies showed an increase in macrophage nitric oxide production in animals treated with LPT, suggesting a pulmonary macrophage polarization effect towards the M1 phenotype. Analysis of bronchoalveolar lavage fluid showed a difference in the concentrations of pulmonary associated protein D and IL-6. Furthermore, preliminary results show that depleting alveolar macrophages will result in the loss of protective function, suggesting macrophages as major players in LPT-induced protection.

**Conclusion:** We have shown that LPT enhances the clearance of pneumococcal bacteria in the lungs and have shown results, which suggest a mechanism for such a clearance. Our initial findings support the clinical use of LPT to treat patients with pneumonia.

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### P7

#### Acute Effects of Osteopathic Manipulative Treatment on Persistent Hindlimb Flexion

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**Hypothesis:** Persistent hindlimb flexion (PHF) that lasts for weeks is induced by noxious electrical stimulation to the mid-thigh in the anesthetized rat. It serves as an animal model for restricted range of motion associated with somatic dysfunction. In this study, we investigated the effects of osteopathic manipulative treatment (OMT) on PHF. Our null hypothesis was that OMT would not affect PHF.

**Methods:** First, we evaluated the effect of acute OMT on PHF. We induced PHF in anesthetized rats by delivering electrical stimulation (2 mA pulses, 7 ms, 100 Hz) across wound clips applied to the medial and lateral thigh for 1 hour. The initial PHF was measured by applying weight in grams (g) to the flexed limb until leg lengths were equal. Then, a single OMT session (eg, soft tissue, balanced ligamentous tension, facilitated positional release technique, stretching) was performed by 1 of 2 practitioners for 7 minutes and PHF was remeasured. During sham treatment (SHAM) the practitioners' hands rested lightly on the caudal half of the rat for 7 minutes. Second, we evaluated the effect of OMT delivered on day 0 and remeasured 3 days later. Third, we evaluated the effect of repeated OMT on consecutive days. Persistent hindlimb flexion was measured prior to and after a single OMT session on days 0, 1, and 2.

**Results:** A 2-way analysis of variance revealed a significant treatment effect (SHAM vs OMT,  $F_{1,12}=12.27$ ,  $P=.004$ ) but no practitioner ( $F_{1,12}=1.4$ ,  $P=.250$ ) or interaction effects ( $F_{1,12}=3.19$ ,  $P=.099$ ) on day 0. The OMT group experienced a larger reduction in PHF, as measured by mean (standard deviation) (7.4 g [1.13 g]), than the SHAM group (2.4 g [0.70 g]). A single initial OMT session did not affect PHF remeasured on day 3 ( $t$  test,  $P<.617$ ). Repeated OMT resulted in a trend toward acute effects on days 1 and 2, when reductions for the SHAM group ranged from -4.4 g to 4 g and reductions for the OMT group ranged from 0 g to 11 g.

**Conclusion:** A single, brief OMT session reduced PHF immediately after induction, and this effect was not dependent on the practitioner. The single OMT effect did not last when measured 3 days later. There was a trend toward acute OMT effects when administered on subsequent days. Future investigations will evaluate the effects of longer-duration OMT with and without increased frequency.

**Support:** Some of these data were presented at the 2011 Annual Meeting of the Society for Neuroscience. This study was approved by the Institutional Animal Care and Utilization Committee. We received a College of Osteopathic

Medicine Research Fellowship, and grants from the University of New England Center for Excellence in Neuroscience and University of New England Research VP Faculty.

### P8

#### Assessing Palpation Thresholds Using Static Lumbar Spine Models

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**Background:** Spinal diagnosis is taught at all colleges of osteopathic medicine.

**Objective:** In this observational study, static models of transverse processes were used to objectively assess students' ability to discern rotational asymmetry through palpation.

**Methods:** First-year osteopathic medical students completed 3 palpatory assessments that included foam-covered and uncovered static lumbar models. Block transverse process models simulated asymmetries of the transverse processes (range, 1-6 mm) using blocks of different heights. For the lumbar spine models, bronze vertebrae were secured to a wooden base; the magnitude of the asymmetry (range, 2-6 mm) was the difference in the heights of the right and left transverse processes. For all models, students were asked to determine whether the right side of the model was anterior or posterior relative to the left side. Using logistic regression, thresholds were defined as the magnitude of asymmetry where the predicted probability of correctly determining the direction of asymmetry exceeded a specified amount (.80, .90, or .95). The local institutional review board approved the study.

**Results:** A total of 346 students completed the assessments. In the uncovered block transverse process model (assessment 1), students correctly identified the direction of asymmetry with 89% probability at 1 mm (.80 threshold), 93% probability at 2 mm (.90 threshold), and 95% probability at 3 mm (.95 threshold). For the covered block transverse process model, students correctly identified the direction of asymmetry with 80% probability at 1 mm (.80 threshold), 92% probability at 2 mm (.90 threshold), and 98% probability at 3 mm (.95 threshold). In the uncovered lumbar spine model (assessment 2), students correctly identified the direction of asymmetry with 93% probability at 2 mm (.80 and .90 threshold) and 95% probability at 3 mm (.95 threshold). In the covered lumbar spine model (assessments 2 and 3), students correctly identified the direction of asymmetry with 87% probability at 4 mm (.80 threshold); the .90 and .95 thresholds were not defined with the range of asymmetries tested.

**Conclusion:** Most first-year osteopathic medical students were able to discern the direction of rotational asymmetry

on static models of transverse processes. Future studies should evaluate whether accuracy when palpating lumbar spine models translates to accuracy when palpating humans.

**Acknowledgment:** This study was funded by a Kirksville Osteopathic Alumni Association grant and an endowment from the Osteopathic Heritage Foundation.

## P9

### Three-Dimensional Analysis of OMT in the Post-Total Arthroplasty Knee

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**Background:** Total knee arthroplasty is one of the most successful operations performed in the United States. According to the Agency for Healthcare Research and Quality, more than 600,000 knee replacements are performed each year in the United States. Most patients begin exercising their knee the day after surgery. Typically, a physical therapist will provide patients with specific exercises to strengthen and restore knee movement to allow walking and other normal daily activities soon after surgery. The use of osteopathic medicine in the perioperative period is well documented in the literature. However, the use of osteopathic manipulative treatment (OMT) techniques (articulatory, facilitated positional release, fascial ligamentous release, functional, myofascial/integrated neuromuscular release, and soft tissue) and the effect in the post-total knee arthroplasty patient is not clear.

**Objective:** To describe the benefit of OMT using 3-dimensional (3D) analysis. Our finite element model records 3D images of in vivo knee joint kinematics during OMT, determining impact of load and strain on soft tissue motion. Previous finite element knee models have described the mechanical forces generated by OMT and other forms of manual therapy, but no study has described the effect of OMT on the postarthroplasty knee using a 3D mathematical model.

**Methods:** Explicit dynamic finite element analyses have been used to efficiently predict total knee replacement kinematics and contact mechanics during dynamic loading conditions. A 3D, finite element model was created by the acquisition of a computed tomography (CT) scan of a total knee arthroplasty. The image data were imported into Mimics version 8.1.1 for editing and 3D reconstruction. For this project, a CT scan with an XY resolution of 512×512 pixels was used, with a resulting pixel size of 0.391 mm and the helical scan was retro-reconstructed into 1-mm slices. The total number of slices in the scan was 217, and the scan was performed using 0° gantry tilt. A 3D voxel model of the bone under study was made. We found an appropriate threshold range that could best capture the relevant information contained in the knee joint. Using this threshold value, all pixels within this range were processed to a color mask. Once loaded into the software,

the color mask acted as the input to the 3D reconstruction process, with all images properly registered and aligned for orientation. The computer-aided design (CAD) model was calibrated with other CAD-based software to analyze dynamic force. Using known data on the contact pressure distribution at the patient-physician contact region during osteopathic manipulation, the model was subjected to known load, stress, and strain values.

**Results:** Osteopathic manipulation did not significantly affect the contact behavior of the arthroplasty components in all degrees of freedom. In addition, no compression of the fascia was observed, resulting in less stress on the polymer insert.

**Conclusion:** The authors have explored the benefit of OMT utilizing the application of 3D rendering and CAD. The model demonstrated the relationship between the mechanical forces and fascial deformations produced in OMT, which may stimulate fascial mechanoreceptors. This approach can aid in the development of improved OMT techniques, which would be reconstructed from CT or magnetic resonance imaging.

## Clinical Studies

### ◆C1

#### Method for Peel Force and Subjective Discomfort During Removal of Adhesive Barriers

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**Hypothesis:** Adhesive barriers secure medical devices to skin and are used in wound care, tube fasteners, and ostomy products. Current laboratory adhesion models do not translate on humans. The aims of this study were to develop methodology to measure barrier peel force in vivo; and determine if there were any relationships between barrier formulation, barrier width, participant discomfort during barrier removal, and substrates.

**Methods:** Three hydrocolloid barrier formulations A, B, and C (Hollister Inc, Libertyville, Illinois) measuring 0.5 in × 2.5 in, 1.0 in × 2.5 in, and 1.5 in × 2.5 in were adhered to EMA tape control and Vitro-Skin synthetic skin substrates for 30 minutes. Peel force was measured with a MTS Insight Instron and a cyberDERM Inc Mini Peel Tester. Normalized peel force (peel force per barrier width, in inches) was derived. We obtained approval from institutional review board to use similar materials and methods on 18 normal volunteers who provided informed consent. Participants additionally reported their discomfort on a 5-point Likert scale. Data were ana-

◆ Indicates posters entered in the AOA Council on Research's Student Poster Competition, a judged event that takes place during the poster session at the AOA Research Conference.

lyzed using analysis of variance with a Student-Neuman-Keuls test for multiple comparisons.

**Results:** Peel force on EMA tape between devices were highly correlated, validating the Mini Peel Tester. On EMA tape and Vitro-Skin, B barrier formulations' peel force were greater than C. In contrast, on skin, all formulations' peel force and discomfort were not different. However, data were suggestive of a weak direct relationship between peel force on skin and discomfort. Normalized peel force was the same for all barrier widths on Vitro-Skin, while data on EMA tape indicated an effect of width on normalized peel force. On skin, normalized peel force was greatest and least in the 0.5-in and 1.5-in barriers, respectively. The 1.5-in barriers always had the least precise peel force. Peel force on EMA Tape and human skin had a strong positive relationship, and Vitro-Skin did not predict in vivo adhesion.

**Conclusion:** These data could help develop an ideal barrier that has sustained robust adhesion and produces minimal discomfort upon removal. Our validated methodology could be used in future barrier peel-force studies on target skin. Adhesion on skin is complicated, and further investigation is required until final conclusions can be made about these barriers.

## C2

### Negative Pressure Vacuum Therapy, an Alternate Approach in Managing a Post-Cesarean Section Pelvic Infection

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**Context:** Cesarean section is the most common major surgical procedure on women in the United States. Wound infection occurs in 2% to 16% of all women who have cesarean sections. Endometritis accounts for nearly half of these infections. Conventionally, endometritis is treated with intravenous (IV) antibiotics, while the traditional management of wound infections has been wound debridement and wet-to-dry dressing changes. In refractory cases, surgical intervention is the preferred method. The use of negative-pressure open-abdominal vacuum therapy has not yet been reported for treatment of postoperative endometritis. For the unfortunate woman diagnosed with postoperative endometritis unresponsive to antibiotic therapy, hysterectomy may be the only option.

**Objective:** To present a case of post-cesarean-section wound and endometrial infection that was successfully managed with negative-pressure, open-abdominal and wound vacuum therapy.

**Case:** An 18-year-old woman (G2 P0010) presented with prolonged rupture of membranes, resulting in the development of chorioamnionitis. Because of concerns about fetal heart rate pattern remote from delivery, the patient underwent a cesarean section. The patient returned on postoperative day

7 with endometritis and a wound infection, which both proved to be refractory to IV antibiotic therapy as recommended by the Centers for Disease Control and Prevention. The patient underwent surgical exploration and, as a result of the infectious process, fascial and uterine defects were revealed. Rather than proceeding with a definitive surgical procedure, a negative-pressure, open-abdominal vacuum was used. The patient avoided hysterectomy, and was discharged to home in stable condition with no signs of remaining infection.

**Conclusion:** Negative-pressure, open-abdominal vacuum therapy may be a viable alternative treatment for patients with postoperative endometritis refractory to IV antibiotics. Hysterectomy and loss of fertility is the standard therapy for patients with severe post-cesarean section uterine infections that are unresponsive to antibiotics. Open-abdominal management of severe intra-abdominal infection has been used when a single surgical procedure is unlikely to be effective in controlling the infection. This method of wound care has proven to be effective in multiple clinical settings but is novel for obstetrical uterine infections. Treatment with IV antibiotics and negative-pressure, open-abdominal vacuum and wound vacuum devices proved to be curative for our patient with a postpartum infection. A further benefit is that now, an 18-year-old woman may conceive and carry a pregnancy, whereas previously, hysterectomy would have been the therapeutic option of choice. We believe that this treatment option should be considered for infected uteri that do not respond to standard antibiotic therapy after cesarean section. Whether this uterus will tolerate a subsequent pregnancy has yet to be determined. The patient has been counseled to undergo a repeat cesarean section at term if she does become pregnant in the future.

## C4

### Problematic Perceptions and Functional Deficits Among Parents With Bipolar Disorder

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**Introduction:** Previous research has identified the substantial personal, financial, psychological, and societal costs due to bipolar spectrum disorder. Patients diagnosed with bipolar disorder routinely experience problematic occupational and social outcomes.

**Objective:** To expand the investigation of costs related to bipolar disorder, particularly for individuals with parenting roles.

**Hypothesis:** It was hypothesized that parents diagnosed with bipolar disorder would show problematic attitudes, perceptions, behaviors, and emotions in the context of their parenting role.



**Methods:** The participants in this study were men and women with a diagnosis of bipolar disorder who were parenting at least 1 child and a control group of parents without any psychiatric diagnosis. A structured interview—which comprised 70 questions about various aspects of parenting behaviors and attitudes—was administered to the participants, who responded using a 5-point Likert scale. The Midwestern University institutional review board approved the project.

**Results:** Factor analysis produced 7 components with eigenvalues greater than one that explained 83.2% of the total variance. The factors were: parenting effectiveness, relational functioning, emotional recognition, intergenerational influences, occupational functioning, coping with anger, and social compliance. Independent samples *t* test indicated that parents with bipolar disorder had greater dysfunction in parenting effectiveness ( $t=3.93$ ,  $P=.001$ ), relational functioning ( $t=3.78$ ,  $P=.000$ ) and occupational functioning ( $t=-2.41$ ,  $P=.019$ ). Chi-square analysis indicated that parents with bipolar disorder had greater difficulty coping with anger ( $\chi^2=20.67$ ,  $P=.000$ ) and with social compliance ( $\chi^2=7.06$ ,  $P=.008$ ).

**Conclusion:** Parents with bipolar disorder showed significantly diminished parenting effectiveness, relational functioning, occupational functioning, difficulties coping with anger, and poor social compliance, compared with parents in the control group. Results suggest a need for parenting support services and programs to promote effective parenting and relational functioning among persons with bipolar disorder.

#### ◆C5

### Hypothyroidism and Its Effects on the Biomarker Translation Test (BT Test) for Breast Cancer Screening: How Undiagnosed and/or Untreated Hypothyroidism Can Cause a False Positive Test

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The Biomarker Translation Test (BT Test) is a blood-based screening tool that uses a specific multiprotein biomarker analysis for the early detection of breast cancer. The BT Test is designed to screen generally healthy women, identifying breast cancer in its early stages before it is easily detectable by 2D mammography. The BT Test is also used by practitioners for patients with abnormal mammograms to help distinguish between invasive and benign breast neoplasms. In clinical studies, the BT Test has identified existing breast cancers with an accuracy of 97% in women aged 49 years or younger and 86% in women aged 50 years or older. A controversial link remains between the relationship of hypothyroidism and breast cancer, although it has been well established that both conditions are associated with an increased inflammatory state. The present study examines the role thyroid function

plays on the positive predictive value of the BT Test and therefore the number of false-positive test results. The protein biomarkers included in the BT Test may also be elevated in the presence of undiagnosed and therefore untreated hypothyroidism. This study identified a higher false-positive rate in BT Tests among women with untreated hypothyroidism compared with women who are euthyroid or are in treatment for hypothyroid. Seventy women without any contraindications conflicting with their eligibility for the test were screened for breast cancer using the BT Test. Untreated hypothyroidism was present in 90.9% of the patients with a positive BT Test and in 10.2% of the patients with a negative BT Test. Data suggest a correlation among hypothyroidism, positive screening, and cancer in the clinical setting. These findings strongly suggest that physicians should screen their patients for hypothyroidism prior to ordering the BT Test to decrease false-positive results and subsequently decrease time, stress, and patient costs.

#### C6

### Efficacy of Group Visits in Outpatient Management of Diabetes

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**Introduction:** The world of primary care has caught the eye of the nation with a reinvented model of health care termed the Patient Centered Medical Home (PCMH). As part of the PCMH, the American Academy of Family Physicians has identified group medical visits as a tool to improve critical health parameters, such as diabetic goals, patient behavior, and self-efficacy in disease management.

**Objective:** To determine if the group visit model, facilitated by family medicine residents, improves diabetes mellitus (DM) metabolic parameters and patient knowledge of DM.

**Methods:** The study was composed of 2 groups of patients. One group participated in the study from January 2010 to June 2010 and the other from July 2010 to December 2010. During the 6 months, participants attended a monthly workshop on a pertinent topic. At every session, vital signs were recorded. Levels for HbA<sub>1c</sub> were recorded at the first visit and 6 months later. All participants filled out a patient satisfaction survey at study completion. Primary outcomes were HbA<sub>1c</sub> levels and the scores on a 23-question DM knowledge test developed by the University of Michigan.

**Results:** A total of 19 participants completed their 6-month block, including both the pre- and postintervention knowledge

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examinations. All of the participants studied had DM. At the conclusion of the study, HbA<sub>1c</sub> decreased from 8.8% to 8.1% ( $P=.026$ ). Scores on the DM knowledge test increased from 13.8 to 16.4 questions correct ( $P=.001$ ). The average weight decreased from 228.3 lb at baseline to 221.2 lb ( $P=.044$ ). Systolic blood pressure decreased from 133.9 mm Hg to 121.1 mm Hg ( $P=.005$ ). Patient satisfaction surveys demonstrated high satisfaction, scoring a 5 out of 5 possible points.

**Conclusion:** Patients who obtain their DM care in a group visit, through interaction with family medicine residents, show improvement in values of HbA<sub>1c</sub>, weight, and systolic blood pressure. Patients also improve in DM knowledge. Patient satisfaction with the group visit model is rated as high. Lastly, these gains were realized in a well-established DM patient population previously considered to be under good control without medication adjustments. Family medicine residency programs are encouraged to add group visits to the community medicine rotation.

### ♦C7

#### Therapeutic Effects of Massage and Music Therapy on Neural Activity

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**Background:** Considerable research has been geared toward finding ways to alleviate pain and improve the comfort of patients. Music and massages have been found to lower blood pressure and cortisol levels, and activate dopamine neurotransmitters and endorphin molecules to induce relaxation. Moreover, electroencephalogram readings show a beneficial balance in the 2 brain hemispheres after music and massage sessions, which offset pain with pleasurable effect and may also have some important implications in treating depression.

**Objective:** To compare the analgesic effects of massage and music therapy in order to evaluate which method was more effective for achieving the maximum level of pain tolerance for people undergoing painful stimuli.

**Hypothesized:** It was hypothesized that a combination of both therapies would produce increased pain tolerance and therapeutic effect for the patients compared with patients not experiencing therapy while exposed to stressful stimuli.

**Methods:** Fifty-four participants were split into 3 experimental groups—music only, massage only, and massage plus music—and a control group of neither. Baseline physiologic measures of heart rate, blood pressure, and frontal lobe brain waves were collected for 3 minutes before stressful stimuli were applied. Participants submerged 1 hand in a bath of

cold water (pain stimulus) while being timed. The physiologic measures continued to be collected throughout the procedure. When the participant could no longer stand the painful stimuli, the hand was withdrawn, and heart rate, blood pressure, and frontal lobe brain waves were collected for an additional 3 minutes.

**Results:** The blood pressure and heart rates of participants in the 3 experimental groups significantly decreased compared with the control group. Additionally, the submersion times of the massage plus music group showed increased pain tolerance by an average of 3 minutes. The combined therapy of massage plus music also produced increased left-side brain wave response from more than 70% of participants, revealing a positive effect.

**Conclusion:** The present study demonstrated that a combination of music and massage therapy produced improved pain tolerance and pleasurable effect. These findings have implications in the clinical setting for pain management or as combination therapy in conjunction with modern medicine.

### C8

#### Circulating Soluble Receptor for Advanced Glycation End Products Is Inversely Correlated to Oxidized Low-Density Lipoproteins in Healthy Participants

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**Background:** There is mounting evidence that circulating soluble receptor for advanced glycation end products (sRAGE) exert anti-atherogenic effects by acting as decoys abolishing the RAGE signaling. A recent experimental study has revealed that oxidized low-density lipoprotein (oxLDL) can be one of the RAGE ligands. Thus, sRAGE are considered emerging important markers in atherogenesis and CVD. The interaction of oxLDL with RAGE is of great interest. However, there are no clinical data to show whether there is an association between circulating sRAGE and oxLDL levels.

**Objective:** To investigate the correlation between sRAGE and malondialdehyde-low-density lipoprotein (MDA-LDL), as an oxLDL marker, in asymptomatic participants.

**Methods:** Clinical data—including the conventional atherosclerotic risk factors, serum sRAGE and MDA-LDL—were measured in 33 asymptomatic participants (15 male, 18 female; mean age, 65 years). The serum MDA-LDL was measured by an enzyme-linked immunosorbent assay (Sekisui Co Ltd, Tokyo, Japan) with intra- and interassay coefficients of variation of 6.5% and 9.0%, respectively. The serum sRAGE was measured by an enzyme-linked immunosorbent assay (R&D Systems Inc, Minneapolis, Minnesota).

♦ Indicates posters entered in the AOA Council on Research's Student Poster Competition, a judged event that takes place during the poster session at the AOA Research Conference.

**Results:** The mean (standard deviation) levels of sRAGE and MDA-LDL were 1101 (250) ng/L and 70 (13) U/L, respectively. A simple linear regression analysis showed that there was a significant inverse correlation between sRAGE and MDA-LDL levels ( $r=-0.36$ ,  $P<.05$ ). A stepwise multiple linear regression analysis also identified MDA-LDL to be a variable correlated independently, significantly, and inversely with sRAGE ( $\beta=-0.36$ ,  $P<.05$ ).

**Conclusion:** The inverse correlation between circulating sRAGE on oxLDL levels suggests that part of the anti-atherosclerotic effects of sRAGE may be related to oxLDL quenching. Further studies are required to confirm the observed relationship.

## C9

### Paraoxonase-1 and Ischemia-Modified Albumin Excursions After a Cerebrovascular Accident: A Pilot Study

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**Background:** In cerebrovascular disease, the nervous system is exposed to ischemic conditions due to the lesion proper, respiratory disorders and vascular spasms. In ischemic and other strokes, the necrotic core is surrounded by an area of inflammation, in which tardy cell death exacerbates the early insult and oxidative stress. Paraoxonase-1 (PON1) is an esterase enzyme carried by high-density lipoprotein which exerts protective effects against oxidative damage. Ischemia-modified albumin (IMA) is a biomarker for cardiac and other tissue ischemia.

**Hypothesis:** We hypothesized that, as a consequence of the necrosis, inflammation, and oxidative stress induced by a stroke, PON1 activity decreases after a stroke while IMA increases. Because serial serum PON1 and IMA measurements in stroke have not been reported, we conducted this pilot study to explore their excursions after a stroke.

**Methods:** Patients (N=20) from the Neurosurgery Department of Showa University Northern Yokohama Hospital were enrolled. Consecutive blood samples during admission were obtained for 13 patients (5 with ischemic stroke, 5 with hemorrhagic stroke, 3 with acute brain diseases of other etiologies). Sera were obtained on admission within 48 hours after the onset and compared with those obtained after admission for up to 30 days. Sera from healthy adult volunteers were obtained from Showa University Northern Yokohama Hospital workers (15 males, 15 females; mean [standard deviation] age, 33.1 [11.4] years). As controls, individual day-to-day variation of IMA and PON1 was measured in healthy participants for up to 2 weeks. Paraoxonase-1 activity was determined using paraoxon, dihydrocoumarin, and phenylacetate

as substrates. Ischemia-modified albumin was measured in serum by the decrease in cobalt 2+ binding.

**Results:** Activity of PON showed a consistent decrease in levels (from -10% to -40%) below onset levels during the first days, returning to previous values in a week mirroring recovery ( $P<.01$ ). Those changes were paralleled by opposite excursions in IMA (from 20% to 60%) above onset levels ( $P<.01$ ). Both ischemic and hemorrhagic strokes displayed a similar pattern. The biologic variation of either PON1 or IMA shows a CV of only 8% to 16%. Patients with acute brain illness but no stroke showed trends but no significant changes. In 2 patients with longer follow-up, recovery to normal values and reinfarction, IMA and PON1 changes reflected the events.

**Conclusion:** Our data show for the first time that IMA increases after stroke in humans, in a pattern compatible with onset of cell death and free radical damage, while PON1 activity decreases suggesting that both markers together could be selected for further studies addressing the predictive value of a ratio delta IMA/delta PON1. Changes in PON1 may be due to acute phase changes in HDL, to free radical damage to PON1, to PON1 dissociation, or to all of these factors combined. These issues will be the participant of further studies.

## C10

### Soluble Receptor for Advanced Glycation End Correlates Negatively With BMI in Patients With End-Stage Renal Disease Undergoing Hemodialysis: A Mechanism for the Obesity Paradox?

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**Background:** Advanced glycation end products (AGEs) are a heterogeneous group of adducts formed on proteins, lipids, and nucleotides by oxidative and carbonyl stress, and linked with inflammation. These products accumulate in the serum of patients with a variety of disorders and are particularly high in end-stage renal disease (ESRD). Earlier studies of patients with ESRD on hemodialysis (HD) demonstrated that circulating soluble receptor for AGEs (sRAGE) levels are increased and that low levels of sRAGE are predictors of future cardiovascular mortality among these patients.

**Objective:** To investigate the correlation between sRAGE and clinical parameters, such as body mass index (BMI) and lipids, among patients with ESRD on HD.

**Methods:** We studied 33 patients with ESRD on HD (12 male, 18 female; mean age, 64 years; median duration of HD, 5 years). Clinical parameters were measured after an overnight fast pre-HD. In addition to BMI, serum lipid panels such as total cholesterol, triglycerides, and high-density lipoprotein

cholesterol were measured using enzymatic methods. Serum sRAGE was measured by an enzyme-linked immunosorbent assay using the Quantikine Human RAGE Immunoassay (R&D Systems Inc, Minneapolis, Minnesota).

**Results:** The univariate correlation analysis showed that sRAGE was significantly and inversely correlated with BMI and triglycerides. A subsequent stepwise multiple regression analysis for sRAGE revealed an independent, significant, and inverse correlation between sRAGE and BMI only ( $\beta=-0.42$ ,  $P<.01$ ).

**Conclusion:** We show an independent, significant and inverse correlation between circulating sRAGE and BMI during the pre-HD period in patients with ESRD on HD. It may be wise to follow this inverse association between sRAGE and BMI over time, because of the debate regarding the obesity paradox (ie, better chance of survival reported for some series dialysis patients with higher BMIs vs patients with lower BMIs). Is it because they have less inflammatory sRAGEs? A significant increase of circulating sRAGE levels in patients with ESRD on HD has been previously reported and this was confirmed in the present study. It remains unclear whether the increase of sRAGE is caused by the up-regulation of RAGE to prevent cell/tissue damage by inflammatory and oxidative molecules such as AGEs or whether the increase is simply based on the decline in renal clearance. Future studies are warranted to elucidate the biologic mechanisms of the association between sRAGE and BMI.

### C11

#### Circulating Soluble Receptor for Advanced Glycation End Products Increase After a Cerebrovascular Accident and May Be a Marker for Cerebral Inflammation: A Follow-Up Pilot Study

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**Background:** Circulating levels of soluble receptor for advanced glycation end products (sRAGE) have been proposed as biomarkers of cardiovascular disease (CVD). In the brain, RAGE is present on neurons, glia, and endothelial cells. In ischemic and other strokes, the necrotic core is surrounded by an area of inflammation, in which tardy cell death exacerbates the early insult. The RAGE ligand high-mobility group box 1 (HMGB-1) was shown to be elevated in serum of stroke patients and released from ischemic brain tissue in a mouse model of cerebral ischemia. No follow-up study of sRAGE excursions after cerebrovascular accidents has been reported so far.

**Hypothesis:** We tested the hypothesis that sRAGE levels

increase after a cerebrovascular episode in humans and thus be a marker of brain inflammation.

**Methods:** Twenty patients from the Neurosurgery Department of Showa University Northern Yokohama Hospital were enrolled. Among them, consecutive blood samples during admission were obtained for 13 patients (5 with ischemic stroke, 5 with hemorrhagic stroke, and 3 with acute brain diseases of other etiologies). Sera were obtained on admission within 48 hours after onset, and were compared with those obtained after admission for up to 30 days. Sera from a control group of healthy adult volunteers (N=30) were obtained from Showa University Northern Yokohama Hospital workers (15 males, 15 females; mean [standard deviation] age, 33.1 [11.4] years). For the control group, individual day-to-day variation of sRAGE was measured for up to 2 weeks. Soluble RAGEs were measured in serum samples by an enzyme-linked immunosorbent assay (R&D Systems Inc, Minneapolis, Minnesota). The intra- and interassay coefficients of variation were 2.6% and 7.6%, respectively.

**Results:** At onset, the mean (standard deviation) levels of sRAGE were 1101 (502) ng/mL and not significantly different than the control population. Levels of sRAGE showed a consistent concentration increase (from 150% to 200% above onset levels) after the first week, with a peak in the second week. Both ischemic and hemorrhagic strokes displayed a similar pattern. The biologic variation of sRAGE shows a CV of only 11%. Patients with acute brain illness but without stroke showed no significant changes.

**Conclusion:** We provide evidence for the first time that sRAGE increases after stroke in humans, in a pattern compatible with onset of necrotic cell death and suggestive of a contribution of RAGE to inflammation and ischemic brain damage. In stroke, soluble mediators from the necrotic core area may diffuse to the contiguous penumbra and elicit a deferred inflammatory response that plays a role in secondary neuronal necrosis. If confirmed in larger series, the HMGB-1-RAGE mechanism linking necrosis with macrophage activation may provide a target for anti-inflammatory therapy in stroke.

### C13

#### Utilizing Exercise as Medicine to Improve the Health of America's Truckers

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**Background:** Long-haul commercial truck drivers have a variety of health problems, some of which are due to their

work environments. Paradoxically, truckers often have sedentary lifestyles, leading to increased rates of obesity, hypertension, and sleep disorders. Improvements to truckers' health also have the potential to improve public safety on the highways.

**Objective:** A self-administered, facilitated survey was conducted to determine trucker sentiment toward increasing exercise while on the road.

**Hypothesis:** Truckers will exercise at on-site truck stop gyms if suitable facilities are available.

**Methods:** We conducted a 14-question survey at truck stops in Arizona, New Mexico, California, Kansas, and Oklahoma. Truckers were approached by investigators, who obtained consent and either facilitated completion of the survey or provided instruction for self-completion. The 14 questions documented age, sex, height, weight, waist size, smoking habits, hypertension, diabetes mellitus, high cholesterol, sleep apnea, seeing a doctor regularly, exercising regularly, exercising more if given the opportunity, and, lastly, if participants were willing to use a truck stop gym for a nominal fee. Each answer was self-reported.

**Results:** A total of 100 truckers answered the survey. Forty-two percent reported regular exercise, and 70% said they would exercise more if they had the opportunity. Interestingly, this rate was increased by nearly one-third to 93% who indicated they would exercise regularly at on-site facilities if they were made available for a nominal fee. Additionally, our study supports other research showing higher rates of smoking in truckers than in the general population (49% vs 18%). Diabetes mellitus is higher in truckers as well (13% vs 8.7%). Responding truckers had poor access to primary care compared with the general population (42% vs 80%). Surprisingly, only 8% of truckers reported sleep apnea, contrary to the 28% reported by the Federal Motor Carrier Safety Administration.

**Conclusion:** It is well known that exercise can lower all-cause morbidities. We found in this survey that 93% of the truckers would work out at an on-site truck stop facility if available and would do so for a nominal fee. This is a 23% higher rate than if given only the opportunity (eg, had more time) to work out. These findings reveal a potential for improvement in truckers' health and public safety and warrant further study.

## C14

### Is the Placebo Effect Revealable in Newborns? Results From a Randomized Controlled Trial in Osteopathy

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**Background:** Placebo effect has been largely studied and debated in medicine. Interestingly, the majority of studies have focused on children and adults but not on newborns. In the field of osteopathic medicine, few studies documented this effect using sham therapy. A previous study showed the association between osteopathic manipulative treatment and length of stay (LOS) in newborns. However, no research has been conducted on the placebo effect on newborns treated with osteopathic medicine.

**Objective:** To detect the association between placebo treatment and change in clinical outcome in newborns.

**Methods:** A double-blinded randomized control trial was carried out on 250 preterm newborns without medical complications (gestational age, 29-37 weeks). After enrollment, all participants were randomly assigned to study (n=107) or control groups (n=143). All preterm newborns received routine pediatric care and osteopathic sham therapy was administered to the study group for the entire period of hospitalization. Primary outcome was to evaluate the effectiveness of sham therapy in reducing LOS.

**Results:** At entry, univariate statistical analysis showed no differences between groups. At the end of the study, after adjusting for all potential confounders, generalized linear model analysis showed no difference in the primary outcome (mean difference, 2.444; 95% confidence interval, 0.447-5.337;  $P=.09$ ).

**Conclusion:** This study is the first in the field showing no effect of placebo treatment using sham therapy on newborns, raising questions about the age when placebo effect starts.

## C15

### Acceptability of Fluzone Intradermal Vaccine to Patients and Vaccine Administrators in the United States

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**Context:** This study was designed to evaluate the acceptability of Fluzone Intradermal influenza vaccine in clinical practice in the United States amongst patients and vaccine administrators, and to compare the intradermal (ID) and intramuscular (IM) influenza vaccines in terms of patient preference, vaccine selection in future years, and postinjection pain and anxiety.

**Methods:** This was a postlicensure study of Fluzone ID involving 249 vaccine recipients and 8 vaccine administrators. Fluzone ID was licensed in the United States in May 2011 and uses a novel microinjection device with a 1.5-mm 30-gauge needle that delivers a smaller volume and antigen load than the IM vaccine. Study participants and vaccine admin-

istrators were surveyed at the time of injection concerning vaccine acceptability, vaccine preference, and postinjection pain and anxiety. A subgroup (74.3% of participants) that had received the IM influenza vaccine within the past 3 years was asked to compare the ID vaccine with their prior IM vaccine experience. Participants were then surveyed 7 days later.

**Results:** Participants were offered 3 vaccines: Fluzone ID, Fluzone IM, and Flumist (Medimmune). Of the 367 individuals immunized, 67.8% chose the ID vaccine and 31.9% chose the IM vaccine. Overall satisfaction immediately after vaccination with the ID vaccine was high (99.6%). Satisfaction in the ID vaccine subgroup that had received the IM vaccine in the past 3 years was 99.4%, and this group reported a preference for the ID vaccine over the IM vaccine, in addition to less postinjection pain and anxiety compared with the IM vaccine both immediately and 7 days after vaccination. All vaccine administrators reported satisfaction with the ID vaccine.

**Conclusions:** The present study demonstrates the overall acceptability of the Fluzone ID vaccine in clinical practice in the United States by both patients and vaccine administrators. Additionally, our study is the first to document a patient preference for ID influenza vaccine over IM vaccine. We believe that as the medical community and their patients become more familiar with the ID vaccine mode of delivery, its popularity and usage will grow.

### C17

#### Use of Prealbumin Levels to Assess Adequacy of Nutritional Support of Critically Ill Patients in the Pediatric Intensive Care Unit Setting

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**Background:** Assessing the nutritional needs of critically ill children is difficult because of substantial shortcomings in the methods traditionally used to estimate energy requirements. The most accurate method is indirect calorimetric measurement, but this method is not practical.

**Objective:** To examine the relationship between prealbumin as an indicator of nutritional support and Resting Energy Expenditure, measured by indirect calorimetric method (mREE), among critically ill children. This study was approved by the Advocate Health Care institutional review board.

**Methods:** We studied 10 critically ill children who were intubated and required mechanical ventilation at the Pediatric Intensive Care Unit at Advocate Hope Children's Hospital. They were evaluated for inclusion-exclusion criteria. The first measurement was done within the first 24 hours of nutrition being started. The measurements were obtained at least 20 minutes after a steady state was reached. The total energy

intake was calculated from the content of enteral/parenteral feedings. Levels of mREE were measured by indirect calorimetric method. The mREE levels and total energy intake were measured daily and the prealbumin and C-reactive protein (CRP) levels were measured every other day for 3 days or until the patients were extubated.

**Results:** All 10 critically ill children in the Pediatric Intensive Care Unit completed the study. C-reactive protein level correlated with mREE and prealbumin levels and was considered a confounder. Partial correlation between prealbumin and mREE levels adjusting for CRP for day 1 was 0.223 ( $t=0.56$ ,  $P=.595$ ), day 2 was 0.559 ( $t=0.67$ ,  $P=.622$ ) and day 3 was 0.887 ( $t=3.34$ ,  $P=.045$ ). Improvement in least squares mean of the prealbumin level for day 1 was 9.4 kcal, day 2 was 10.3 kcal, and 9.9 kcal after adjusting for CRP ( $F=0.94$ ,  $P=.418$ ). There was an improvement in least squares mean of the mREE level for day 1 (53.9 kcal/d), day 2 (62 kcal/d), and day 3 (56.9 kcal/d) after adjusting for the CRP ( $F=0.67$ ,  $P=.529$ ). There was a significant improvement in least squares mean of total intake for day 1 (20.6 kcal/d), day 2 (49.3 kcal/d), and day 3 (48.7 kcal/d) after adjusting for the CRP ( $F=11.03$ ,  $P=.002$ ).

**Conclusion:** There were positive correlations between prealbumin and mREE levels adjusted for CRP for all investigated days. We concluded that prealbumin measurement is a good indicator of nutritional support in critically ill children.

### C18

#### Impact of Buprenorphine Transdermal System 5 g/h (BTDS 5) and 20 g/h (BTDS 20) on Quality of Life in Opioid-Experienced Patients With Moderate to Severe Chronic Low Back Pain

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**Objective:** To compare the health-related quality of life among opioid-experienced patients with moderate to severe chronic low back pain who were treated for 12 weeks with Buprenorphine Transdermal System 5  $\mu\text{g}/\text{h}$  (BTDS 5) or Buprenorphine Transdermal System 20  $\mu\text{g}/\text{h}$  (BTDS 20), and to describe health-related quality of life in patients who used BTDS 20 continuously for 1 year.

**Methods:** Data were from a multicenter, enriched, double-blind, randomized trial comparing BTDS 20 with BTDS 5 for relief of pain. The core study consisted of a screening period, a 21-day run-in period to establish patients' sensitivity and tolerability to BTDS 20, and a 12-week randomized double-blind phase. A subsequent 52-week, open-label extension phase provided further treatment with the buprenorphine transdermal system to volunteers from any treatment arm in the core study. The Short Form Health Survey, version 2 (SF-36v2), a 36-item health outcomes survey that measures 8

quality of life and physical and mental outcomes, was administered to patients at the start and end of the run-in period, at weeks 4, 8, and 12 of the double-blind phase, and at 7 visits throughout the extension phase. All analyses were post hoc. Analysis of covariance models compared SF-36v2 scores between BTDS 5 and BTDS 20 treatment arms at week 12 of the double-blind phase, controlling for scores at screening and end of run-in. Repeated measures mixed-effects models examined treatment differences across double-blind phase visits. Mixed-effects models also examined scores across visits of the extension phase for participants who were consistently treated with BTDS 20.

**Results:** At 12 weeks, BTDS 20 produced statistically greater improvements than BTDS 5 in bodily pain, role limitations due to physical health and overall physical well-being ( $P < .01$ ). Treatment arm differences in overall physical well-being emerged by 4 weeks and were sustained throughout the double-blind phase. Improvements in overall physical quality of life were maintained throughout the course of the extension phase by patients consistently treated with BTDS 20.

**Conclusion:** These data suggest that opioid-experienced patients with chronic low back pain who received 12 weeks of BTDS 20 experienced less pain, better physical functioning, and better well-being than those receiving BTDS 5. Differences in overall physical well-being emerged within 4 weeks of treatment, and improvements were maintained for a full year with consistent BTDS 20 treatment.

### ◆C19

#### Effects of Utilizing Yoga Nidra on Reducing Symptoms of Depression and Anxiety in a Psychiatric Population

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In a 12-month period, more than 28 million Americans suffer from depression and more than 56 million from anxiety. Antidepressants were the third most commonly used prescription medicine in the US from 2005 to 2008. There are several pilot studies that have shown evidence for the benefit of using Yoga as an intervention for depression and anxiety. Yoga Nidra, a specific practice of Yoga, is the practice in which the individual begins to mentally scan his or her physical body, to explore emotions and physical sensations, and to develop a sense of awareness of various symptoms that may be associated with good or ill feelings. We hypothesized that Yoga Nidra exercises would improve self-reported depression and anxiety symptoms. The study used a naturalistic clinical outcomes design. Participants enrolled in the study received Amy Weintrub's Yoga Nidra instructions as part of a clinical management by their psychologist, distributed as 20- and 40-minute instruction tracks on an MP3 player or CD. Participants completed the Beck Depression Inventory (BDI),

Beck Anxiety Inventory (BAI), and a Yoga usage log at each of 3 study visits at approximately 2-week intervals. A total of 12 participants were enrolled, of whom 10 were women. The median BDI score decreased from 30 at baseline to 16 at the final study visit, representing a change in level of depression from moderate depression to mild mood disturbance. Similarly, the BAI decreased from a median of 27 to 13, indicating a change in anxiety from moderate to very low. Most participants chose to use the same track length throughout the study. Most women used the 40-minute track, whereas all men used the 20-minute track. These data suggest track preference based on sex; however, our study population was too small for this finding to be definitive. We found a marked improvement in participants' self-reported depression and anxiety. Future studies should focus on clinical correlation of Yoga Nidra practice and prescription medication for depression and anxiety.

### C20

#### Effect of Oxycodone Drug-Drug Interactions on Success of Rotating Oxycodone-Experienced Patients With Chronic Low Back Pain to Oxymorphone Extended Release

Matthew Wieman, MD; Qinfang Xiang, PhD

Endo Pharmaceuticals Inc, Chadds Ford, Pennsylvania

**Background:** In clinical practice, waning effectiveness or poor tolerability typically motivates rotation from one opioid to another, but in randomized clinical trials, the protocol may demand opioid rotation regardless of patient satisfaction with their present treatment.

**Hypothesis:** We hypothesized that the presence of an oxycodone drug-drug interaction (DDI) may increase the likelihood of a patient successfully rotating from oxycodone to oxymorphone extended release (ER) compared with a patient who had no oxycodone DDI.

**Methods:** The present study was a post hoc analysis of a population of 79 oxycodone-experienced patients with chronic low back pain who were required to rotate to oxymorphone ER in a randomized clinical trial. Our analysis revealed that 24 of these patients entered the trial taking oxycodone concurrently with  $\geq 1$  medication known to have a DDI with oxycodone. Patients discontinued oxycodone and were titrated for  $\leq 1$  month to a stabilized oxymorphone ER dose that reduced pain to  $\leq 40$  mm on a 100-mm Visual Analog Scale with  $\leq 2$  doses per day of rescue medication. These DDIs could potentially affect effectiveness or tolerability but data on clinical effects of the DDIs were not available for post hoc analysis. Informed consent and institutional review board approval were obtained.

◆ Indicates posters entered in the AOA Council on Research's Student Poster Competition, a judged event that takes place during the poster session at the AOA Research Conference.

**Results:** Overall, 36 oxycodone-experienced patients (46%) were successfully rotated to oxymorphone ER. Successful rotation was achieved with 24 of 57 patients with  $\geq 1$  oxycodone DDI (42%) and with 12 of 22 patients with no oxycodone DDI (55%;  $P=.55$ ).

**Conclusion:** Patients who entered the study taking oxycodone concurrently with a medication known to have a DDI with oxycodone were no more likely to rotate successfully to oxymorphone ER than patients with no oxycodone DDI. Limitations of this analysis included small sample size and absence of data on the clinical significance of the DDIs identified from medication records.

**Support:** This project was supported by Endo Pharmaceuticals Inc, Chadds Ford, Pennsylvania.

### C21

#### Oxymorphone Extended Release for Treatment of Patients With Chronic Pain: A Pooled Analysis of Safety at Dosages Equivalent to Morphine $\geq 180$ mg/d

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**Context:** The safety of high doses of opioids for the treatment of patients with chronic pain has not been well studied. A post hoc analysis was conducted to characterize the safety profile of oxymorphone extended release (ER) at dosages  $\geq 180$  mg/d of morphine equivalents.

**Methods:** Patients ( $N=422$ ) with chronic pain who participated in 10 clinical trials of oxymorphone ER were included in a pooled safety analysis. The incidences of different observed adverse events were categorized as they occurred within 3 oxymorphone ER dosage regimens:  $\geq 60$  to  $< 80$  mg/d,  $\geq 80$  to  $< 120$  mg/d, and  $\geq 120$  mg/d (respectively equivalent to morphine  $\geq 180$  to  $< 240$  mg/d,  $\geq 240$  to  $< 360$  mg/d, and  $\geq 360$  mg/d).

**Results:** Across all studies, 140 patients received oxymorphone ER  $\geq 60$  to  $< 80$  mg/d, 239 patients received oxymorphone ER  $\geq 80$  to  $< 120$  mg/d, and 180 patients received oxymorphone ER  $\geq 120$  mg/d. The dose of oxymorphone ER was unrelated to the incidence of several types of adverse events whose incidence is typically dose-related with other opioids (constipation, nausea, vomiting, abdominal pain, upper abdominal pain, depression, fatigue, sedation, somnolence, dizziness, falls, and drug withdrawal syndrome). The incidence of some adverse events not typically associated with opioids was greater with the higher oxymorphone ER dosages than with the lower dosages (eg, pyrexia, upper respiratory tract infection, urinary tract infection, viral gastroenteritis, anxiety, muscle spasms, and anemia).

**Conclusion:** Higher dosages of oxymorphone ER (60 to  $\geq 120$  mg/d; equivalent to 180 to  $\geq 360$  mg/d morphine) did not increase typical opioid-related adverse events in patients with

chronic pain, but were associated with an increased rate of some adverse events not usually observed with opioids. These findings are only valid for oxymorphone ER and should not be used to draw conclusions regarding the safety and tolerability of other opioid analgesics at high dosages.

**Funding:** The present study was supported by Endo Pharmaceuticals Inc, Chadds Ford, Pennsylvania.

### C22

#### Effect of Age, Race, and Sex on the Pharmacokinetics and Metabolism of Oxymorphone Extended-Release Tablets

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**Background:** The effects of age, race, and sex on the metabolism of oxymorphone extended release (ER) tablets have not been investigated.

**Methods:** This was a post hoc analysis of studies in healthy male and female volunteers measuring pharmacokinetics of oxymorphone ER in populations amenable to comparison: (study 1) young (aged 18-40 years) and older (aged  $\geq 65$  years) patients and (study 2) white and black patients. In study 1, participants received oxymorphone ER 20 mg once daily for 6 days. In study 2, participants received 2 single doses of oxymorphone ER 40 mg on 2 occasions separated by 7 days. Plasma concentrations for oxymorphone and its 6-OH-oxymorphone and oxymorphone-3-glucuronide metabolites were analyzed. In both studies, naltrexone was administered to minimize opioid effects and institutional review board approval and participant informed consent were obtained.

**Results:** Study 1 comprised 48 participants: 24 men and 24 women, 24 young and 24 older participants. Study 2 comprised 31 participants: 13 men and 18 women, 24 white and 7 black participants. Pharmacokinetic analyses in the 2 studies revealed that age-based differences were significant only after controlling for body weight. Geometric least squares mean steady-state area under the curve ( $\text{ng}\cdot\text{h}/\text{mL}$ ) in older participants (27.6) compared with younger participants (19.7) was significantly higher (ratio, 1.40; 90% confidence interval [CI], 1.2-1.6), and geometric least squares mean maximum concentration ( $\text{ng}/\text{mL}$ ) in older participants (3.5) compared with younger participants (2.6) was significantly higher (ratio, 1.33; 90% CI, 1.2-1.5). Similar results were observed for oxymorphone metabolites.

**Conclusion:** No sex or race differences were observed in the pharmacokinetics of oxymorphone ER; however, small sample sizes limit the sensitivity of this post hoc analysis. Mean and maximum concentrations of oxymorphone and its metabolites were 35% to 40% higher in older participants. Initiating oxymorphone ER at a lower dose in older patients is advisable to minimize adverse events.



**Funding:** The present study was supported by Endo Pharmaceuticals Inc, Chadds Ford, Pennsylvania.

### C23

#### Exhaled Nitric Oxide in the Management of Asthma in Children and Young Adults

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**Background:** The current methods of determining airway inflammation are imprecise and are often difficult for young patients to perform. Yet, the cornerstone for the treatment of patients with asthma is directed to the control of airway inflammation. The National Asthma Education and Prevention Program's guidelines recommend inhaled corticosteroids as a cornerstone of treatment, but at the lowest dose to control inflammation because of potential adverse effects of corticosteroids in children. Without a practical and accurate method of measuring airway inflammation, it is difficult to determine the safest dose. The use of a noninvasive simple measurement of airway inflammation will improve diagnostic accuracy and therapeutic intervention. The recent development of a method to measure exhaled nitric oxide (eNO), a noninvasive marker of airway inflammation, has made it possible to diagnose airway inflammation, the hallmark of asthma, and to monitor therapy.

**Objective:** To determine whether the use of an eNO measurement will help to more accurately prescribe and monitor inhaled corticosteroid therapy in patients with asthma.

**Methods:** Two groups of study participants (aged 8-18 years) were recruited from the University of Oklahoma clinic population. Of the 54 participants in the final sample, 40 already had a diagnosis of asthma, whereas 14 comprised a nonasthmatic control group. The sample was primarily male (n=36) and white (n=45). Mean (standard deviation) age was 11.69 (2.79) years, with 29 participants younger than 12 years. Institutional review board approval was obtained for the study. All 54 participants were evaluated by the principal investigator, who recorded clinical history and performed a cardiopulmonary physical examination, followed by pulmonary function testing and eNO measurements. At the initial visit, participants with asthma were given a medication-use log for home use and were scored for asthma symptom severity according to the National Asthma Education and Prevention Program guidelines. Asthma control was assessed from 2 different measures to accommodate participants of different ages. Participants aged 12 years or older were administered the Asthma Control Test, whereas participants younger than 12 years were administered the Childhood Asthma Control Test.

For every day of the study, participants with asthma recorded their symptom scores (cough, wheeze, and dyspnea) on diary cards daily, along with medication use and peak expiratory flow measurements. All participants with asthma measured peak flow with the TRU ZONE Peak Flow Meter (Monaghan

Medical Corporation, Plattsburgh, New York). They returned to the clinic for 4 follow-up visits at 4, 8, 12, and 24 weeks after initial evaluation. Spirometry and eNO values were repeated during each visit. The results from each visit were then faxed to the referring physician to use in the care of the participant with asthma. Nonasthmatic controls underwent only baseline testing. Exhaled nitric oxide measurements were performed prior to spirometry. Single breath on-line measurement were performed following American Thoracic Society and European Respiratory Society recommendations using the NIOX 3124 Nitric Oxide Monitoring System (Aerocrine AB, Stockholm, Sweden). The participants inhaled air scrubbed of eNO to total lung capacity. They then exhaled at a rate of 50 mL/sec against a fixed resistance and maintained a constant expiratory pressure. This prevented nasal nitric oxide contamination and provided a fixed, controllable exhalation rate. The participant exhaled until the eNO reached a plateau. This procedure was repeated until 3 samples with less than a 10% difference were collected. The eNO value was taken as the mean of 3 acceptable samples. Spirometry was performed using a MicroLab Spirometer ML 3500 in accordance with standard guidelines of the American Thoracic Society.

**Results:** No significant differences were found in baseline spirometric values between participants with asthma and participants without asthma. However, mean baseline eNO values were 62% higher in participants with asthma compared with participants without asthma (24.10 ppb vs 14.96 ppb). During the study, eNO was negatively correlated with asthma control and baseline eNO appeared to be a marker of predicted improvement over time.

**Conclusion:** Although the customary measures of pulmonary function—forced vital capacity, forced expiratory volume in 1 second, and forced expiratory volume/forced vital capacity ratio—are frequently within predicted normal ranges, participants with asthma often demonstrate significant symptoms when asthma control questionnaires are administered. Although the clinical examination is normal and spirometry within normal predicted ranges, airway inflammation may still be present and account for symptoms. Thus, eNO appears to be a critical variable for explaining changes in asthma control. The measurement of eNO is useful in enhancing diagnostic accuracy of asthma and in aiding the clinician to determine appropriate corticosteroid dosage to control airway inflammation.

### ◆C24

#### NEXUS C-Spine Criteria: Compliance Review

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◆ Indicates posters entered in the AOA Council on Research's Student Poster Competition, a judged event that takes place during the poster session at the AOA Research Conference.

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**Hypothesis:** The implementation of a standardized charting system for the National Emergency X-Radiography Utilization Study (NEXUS) cervical spine criteria will improve charting compliance and better assist the physician in diagnosing cervical spine injury.

**Methods:** We conducted a retrospective analysis of emergency room patients from July 2010 to September 2010. The list of patients was narrowed down using a filtering system built into the charting program. Patients were selected on the basis of age ( $\geq 18$  years) and the manner in which they arrived at the emergency department (by means of ambulance on a backboard and in a cervical immobilization collar). We reviewed charts for compliance with the NEXUS criteria and the adequate charting of the results. The data were reviewed for statistical relevance with Microsoft Excel (Microsoft Corporation, Redmond, Washington). A charting template was then implemented into the standardized charting system beginning on July 1, 2011. A compilation of patient information was obtained for July 2011 through September 2011 using the same selection criteria as the initial review. The charts were again reviewed for compliance with the NEXUS criteria and data were analyzed with Microsoft Excel. A comparative analysis of the pre- and posttemplate charting was performed.

**Results:** The current study revealed that the implementation of a standardized charting template for the NEXUS cervical-spine criteria improved charting compliance by more than tenfold (6% before implantation to 81% after implementation).

**Conclusion:** Future research into the use of a standardized template for the NEXUS criteria may include a close look at the use of radiographic studies and the implication that the use of the criteria has on the overall time and cost of an emergency room visit.

### C25

#### Analysis of Functional Status in Multiple Sclerosis Patients After Progressive Nonaerobic High-Intensity Maximal Effort Exercise (MEE)

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**Background:** Multiple sclerosis (MS) is a disease with a wide-

ranging impact on functional status, often quantified using the Multiple Sclerosis Functional Composite Score (MSFCS). The MSFCS includes the standardized *z* scores of 3 functional tests: the Paced Auditory Serial Addition Test (PASAT-3'') for cognitive function, 9-Hole Peg Test (9-HPT) for arm function, and timed 25-foot walk (25-TW) for leg function. One of the most common symptoms experienced by MS patients is severe fatigue brought on by aerobic exercise. Nonaerobic maximal effort exercise (MEE) is thought to increase strength without increasing fatigue. The IsoPUMP (Neuromuscular Engineering; Nashville, Tennessee) is a stationary exercise device designed for patients to safely perform isometric and eccentric MEE leg presses and whole-body lunges.

**Hypothesis:** That 10 weeks of MEE will improve participants' individual functional tests and MSFCS.

**Methods:** A total of 68 participants (55 with complete data) enrolled in this intent-to-treat study. At baseline, participants completed questionnaires and performed functional tests. A progressive MEE protocol was implemented biweekly for 10 weeks with follow-up measurements at weeks 16 and 22. Participants performed a Valsalva maneuver with each isometric or eccentric MEE on the IsoPUMP (4 seconds per repetition, repeated 3-5 times with short rest periods as needed in between). Effect size was determined to assess statistical significance of any improved functional component.

**Results:** Significant improvements in the cognitive function (effect size, 0.64;  $P < .001$ ), leg function (effect size, 0.39;  $P = .001$ ) and overall MSFC (effect size, 0.32;  $P < .001$ ) were noted at 12 weeks after treatment. However, the changes in arm function were not statistically significant.

**Conclusion:** When comparing MS participant's functional status with baseline, it was noted that the participants showed significant improvements in cognition and leg function, with prolonged effects observed after treatment. Although changes in the upper extremity function measures were not statistically significant, an improvement in overall function was observed. Whereas the obtained functional improvement was mild, such a result is impressive for this patient population because the underlying disease process usually predisposes patients to functional deterioration over time.

**Acknowledgment:** This study was supported by a joint Civilian-Veterans Affairs project grant.

### C26

#### Reliability of Pressure Pain Thresholds in the Supraspinatous Muscle—Palpation and Algometry

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**Objective:** To assess the intraexaminer and interexaminer reliability of pressure pain thresholds (PPTs) as determined by manual palpation and pressure algometry in the supraspinatus muscle, as well as the agreement between palpatory- and algometric-determined PPTs.

**Methods:** Three physicians palpated the supraspinatus muscles of 10 asymptomatic adults in a blinded fashion. Each physician identified 2 points they predicted to be tender and 2 predicted control (less tender) points bilaterally. The PPTs were measured by applying a force through a flexible pressure sensor pad overlying the points until pain was elicited. Each point was tested 3 times by manual palpation and then 3 times by pressure algometry. Intraclass correlation coefficients (ICCs) were used to measure the intraexaminer and interexaminer reliability for both palpatory- and algometric-determined PPTs, as well as agreement between palpation and algometry. The PPTs from the 3 repetitions were used for calculation of the intraexaminer ICC and averaged for the other ICCs. For the interexaminer ICC, only the 38 points that were identified by at least 2 physicians were included.

**Results:** The overall intraexaminer reliability was almost perfect for PPTs determined by palpation (ICC, .91; 95% confidence interval [CI], .90-.93; n=240) and substantial for PPTs determined by algometry (ICC, .71; 95% CI, .65-.76; n=240). The ICCs for individual examiners ranged from .86 to .94 for PPTs determined by palpation. The interexaminer reliability was fair for PPTs determined by palpation (ICC, .33; 95% CI, .05-.61; n=38) and by algometry (ICC, .41; 95% CI, .12-.70; n=33). The agreement of palpation with algometry was fair (ICC, .27; 95% CI, .14-.41; n=189). The ICC (95% CI) for predicted tender points was .43 (.31-.56) and control points was .49 (.37-.61), indicating moderate agreement for both.

**Conclusion:** Intraexaminer reliability for determining PPTs was very high for both palpation and algometry. However, the interexaminer reliability among palpating examiners and agreement between palpation and algometry was only fair. Future research needs to be conducted to determine reasons for this variability and to refine methodologies to improve interexaminer reliability and consistency between palpation and algometry.

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## C27

### Pain Pressure Thresholds of Predicted Tender Points by

### Algometry and Palpation

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**Hypothesis:** Both manual palpation and pressure algometry were hypothesized to have lower pain pressure thresholds (PPTs) for points in the supraspinatus muscle that were predicted to be tender by palpation when compared to physician-predicted control (less tender) points. Additionally, palpation was expected to better discriminate physician-predicted tender points from control points compared with algometry.

**Methods:** Three physicians palpated the supraspinatus muscles of 10 asymptomatic adults in a blinded fashion, each identifying 2 points they predicted to be tender and 2 predicted control points bilaterally. The PPT at each point was measured by applying force through a flexible pressure sensor pad overlying the points until pain was elicited. Each point was tested 3 times by manual palpation and then 3 times by pressure algometry. A Cox proportional hazards model with a random effect for participant was used to compare predicted tender and control points on PPTs determined by palpation and by algometry. Nonparametric discriminate analyses were used to estimate the false-positive (predicted tender points with high PPTs), false-negative (predicted control points with low PPTs), and overall error rates of using PPT to discriminate between predicted tender and control points.

**Results:** Levels of PPTs for all 3 physicians (n=1365) were lower for predicted tender points than predicted control points ( $P<.003$ ). The physicians had significantly different PPTs for tender points ( $P=.0001$ ) but not control points ( $P=.65$ ). Additionally, PPTs from palpation were higher than PPTs from algometry for all 3 physicians ( $P<.0001$ ). The overall error rate of PPT in discriminating tender and control points was comparable for palpation (263/717 [37%]) and algometry (281/648 [43%]). The false-positive rate was lower for palpation (32%) than algometry (54%). The converse was true for the false-negative rate (42% for palpation vs 32% for algometry).

**Conclusion:** Both palpation and algometry had lower PPTs for predicted tender points than control points. The PPTs from palpation were better at classifying predicted control points, whereas PPTs from algometry were better at classifying predicted tender points. These data indicate that manual palpation and pressure algometry may be useful in combination.

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## C28

**Prospective, Randomized Comparison of Continuous Nebulized Racemic-Albuterol With Levalbuterol in Pediatric Patients**

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**Background:** Levalbuterol, an R-isomer of albuterol, has been used in the management of bronchospasm, and has been shown in some studies to have a favorable profile compared to racemic albuterol. However, few data exist regarding the safety and efficacy of levalbuterol in a continuously nebulized mist.

**Method:** We conducted a prospective, randomized, double-blind controlled clinical study. The study population was 85 patients (birth to 18 years) who were admitted to the Pediatric Intensive Care Unit (PICU) in status asthmaticus or severe bronchospasm necessitating continuous bronchodilator nebulization. Patients were randomly assigned to receive nebulized racemic albuterol or nebulized levalbuterol at different dosages: (1) racemic albuterol 15 mg/h, (2) racemic albuterol 10 mg/h (3) levalbuterol 7.5 mg/h, (4) levalbuterol 5 mg/h and (5) levalbuterol 2.5 mg/h. All patients were continuously monitored for changes in mental status, respiratory and heart rate, oxygen saturation, and blood pressure. Respiratory distress score, pulmonary function tests including peak expiratory flow rate, forced expiratory volume at 1 second, and forced vital capacity (FVC) were obtained when feasible at baseline, 1 and 2 hours after treatment, and every 4 hours for 24 hours. Hours of hospital and PICU stays were collected as the primary outcomes.

**Results:** Forty patients weighing more than 20 kg completed the study; dosages 1 to 5 were administered to 10, 6, 8, 7, and 9 patients, respectively. Average length of hospital stay in hours for dosages 1 to 5 were 33.8±19.7, 35±12.4, 41.7±28.3, 31.2±22.8, and 58.3±23.2, respectively ( $F=2.6$ ;  $P=.044$ ). Average length of PICU stay in hours for dosages 1 to 5 were 37.8±17.9, 47.6±47.8, 53.6±46.4, 40.4±16, and 34.6±15.3 respectively ( $F=1.12$ ;  $P=.37$ ). Levels of FVC significantly increased for dosage 2 at 4 hours ( $P=.0212$ ) and for dose 4 at 8 hours after drug administration ( $P=.029$ ). Oxygen saturation decreased for dose 1 at 4 and 8 hours. Systolic blood pressure increased for dose 5 at 2, 4, 8, and 12 hours. Heart rate increased among patients who received dose 5 after 4 hours ( $P=.049$ ). Comparison of other variables was not statistically significant.

**Conclusion:** Patients who received dosage 5 (ie, levalbuterol 2.5 mg/h) underwent the longest hospital stay. The difference in length of stay in PICU was not statistically significant among the 5 different groups. Therefore, levalbuterol at different doses did not show any superiority to the conventional

racemic albuterol. A larger sample study is needed to confirm our findings.

## C29

**Comparisons of Adverse Events Reported After Receiving Seasonal and H1N1 Influenza Vaccines Via Injection and Nasal Spray**

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**Background:** The influenza vaccine is generally considered to be safe with low levels of adverse events (AEs). The current study reviewed neurologic, cardiovascular, urinary, general, and dermatologic AEs reported in 2010 after receiving seasonal and H1N1 flu vaccines and recorded in the Vaccine Adverse Event Reporting System (VAERS), administered by the US Centers for Disease Control and Prevention and US Food and Drug Administration.

**Objective:** To compare AEs among people who received vaccines for seasonal flu shot (SFS), and seasonal flu nasal spray (SNS), H1N1 flu shot (H1N1FS), and H1N1 flu nasal spray (H1N1NS), with results stratified by sex. The AEs that followed the vaccination ranged from mild to severe, progressing to death in some cases. Many AEs were reported to the VAERS and were categorized on the basis of primary body system affected. We focused on outcomes associated with events in such areas as cardiopulmonary (CP) (eg, arrhythmias), neurologic (NE) (eg, sensory deficits), urogenital (U) (eg, proteinuria), dermatologic (D) (eg, rash), and generalized (G) (eg, muscle aches).

**Hypothesis:** That there are statistically significant differences in the AEs between women and men for different flu vaccines and for different ways in which the vaccine was administered (ie, intravenously or nasally).

**Results:** A total of 14,827 AEs were reported to the VAERS. Women reported 9653 AEs and men reported 5174. Among women, numbers of AEs and deaths for SFS, SNS, H1N1FS and H1N1NS were 5897 (39.8%) and 7 deaths, 2691 (18.1%) and 3 deaths, 445 (3%) and no deaths, and 620 (4.2%) and 1 death, respectively; among men, numbers were 2780 (18.7%) and 9 deaths, 1625 (11%) and 2 deaths, 339 (2.3%) and no deaths, and 430 (2.9%) and 12 deaths, respectively. For SFS group, women experienced more AEs in NE category by 1470 cases ( $P<.0001$ ). For SNS group, there were no statistically significant differences between sexes in number of cases of CP, D, G, and NE categories. For H1N1FS group, women reported a higher number of CP by 131 cases, D by 67 cases, G by 139 cases, and NE by 183 cases ( $P<0.0001$ ). For H1N1NS group, women reported a higher number cases in D by 21 cases ( $P=.002$ ) and in NE by 22 cases ( $P=.028$ ). No statistically sig-

nificant difference was observed in number of cases for other factors.

**Conclusion:** Women report a significantly higher number of AEs in CP, D, G, and NE cases compared with men for SFS, H1N1NS, and H1N1FS, but not SNS.

### ◆C30

#### Patient-Physician Communication in Rural Appalachia: A Preliminary Study in Participatory Methods

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**Hypothesis:** Communication is an essential ingredient in patient-physician interactions and is pivotal in determining patient adherence to physician instructions, which have with the ultimate goal of enhancing patient outcomes. Little research has focused on understanding the dynamics of the patient-physician relationship and the quality of communication on patient satisfaction and health outcomes in rural southeast Ohio.

**Objective:** To identify gaps in patient-physician communication in rural southeast Ohio and to explore participant engagement in focus groups.

**Methods:** Three focus groups were conducted to gauge participants' perceptions of communication during their recent interactions with their physicians. One focus group was facilitated by a "cultural insider," another by a "cultural outsider," and the third cofacilitated by both. The focus groups involved semistructured and open discussions. The open discussions afforded the participants an opportunity to freely articulate their personal experiences.

**Results:** Transcripts were developed from these focus groups and the transcribed data coded inductively as well as deductively. The research team highlighted key data points and grouped raw data into analytic themes. Selected emerging themes included better engagement from physicians, more time spent listening earnestly, and a holistic approach to medicine.

**Conclusion:** These findings provided, and may continue to provide, a unique foundation to further explore the impact that culture has on patient-physician communication. By gleaning higher-quality information related to patient-physician communication problems and gaps, we will gain a better understanding of how to improve patient-physician relationships and health outcomes for the people of southeast Ohio.

### C31

#### Cholera Outbreaks on Hispaniola: Effects of Distance and Disease From the Epicenter

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**Context:** Natural disasters are responsible for many epidemics worldwide. In 2010, an earthquake on the island of Hispaniola, comprising Haiti and the Dominican Republic, resulted in one of the largest cholera outbreaks in modern history. Of the 42 provinces affected, none was hit harder than Port-au-Prince, Haiti.

**Objective:** To evaluate the association between the outbreaks of cholera in Port-au-Prince and provinces of various distances from the epicenter on the island of Hispaniola.

**Hypothesis:** That residents from areas further from the epicenter are less likely to develop cholera.

**Methods:** A cross-sectional study of all residents of the island of Hispaniola evaluates the odds ratio (OR) of cases of cholera that occurred at the epicenter of the 2010 earthquake compared with other provinces at various distances from the epicenter. We defined distance as the driving distance between the capital of each province to the epicenter. Odds ratios for each province were calculated compared with Port-au-Prince. We also looked at the effect of population density on the OR of contracting cholera.

**Results:** Compared with the average of the residents on the island, residents in Port-au-Prince are found to be 2.09 times more likely to develop cholera (OR, 2.09; 95% confidence interval [CI], 2.06–2.13;  $\chi^2$  test= 6716.9; df=1;  $P<.0001$ ). The furthest province from the epicenter was Samana in the Dominican Republic. We found that Samana residents were 27 times less likely to be affected by the Cholera outbreak compared with residents near the epicenter (OR, 0.037; 95% CI, 0.030–0.045;  $\chi^2$  test=2484.822, df=1,  $P<.0001$ ). Odd ratios for all 42 provinces were calculated and reported in a Table.

**Conclusion:** Odds ratios were found to decrease as distances from the epicenter increased. This was found to be closely related to previous literature. On the basis of our findings, population density also affected ORs.

**Editor's Note:** Table not pictured.

### C32

#### Physician Attitudes About Providing Care to Patients Receiving Long-Term Opioid Therapy

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◆ Indicates posters entered in the AOA Council on Research's Student Poster Competition, a judged event that takes place during the poster session at the AOA Research Conference.

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**Hypothesis:** Approximately 76 million US citizens have chronic pain and over 25% of visits to primary care physicians involve a pain complaint. Physicians struggle with issues such as increases in opioid prescribing to relieve suffering, unintentional opioid overdose deaths, and regulatory oversight of physician practice. A structured office visit for long-term opioid use improves physician comfort, organization, and outcomes in treating chronic pain.

**Methods:** Family medicine physicians completed a survey about opioid prescribing and experiences with practice redesign to standardize care for patients receiving long-term opioid therapy (LTOT). Responses were dichotomized from a 5-point Likert scale (ie, strongly disagree, disagree, unsure, agree, strongly agree) into agree (somewhat or strongly agree) or disagree (unsure, disagree, or strongly disagree).

**Results:** A total of 26 physicians, 12 faculty and 14 of 16 PGY2-3 residents, completed the survey. A majority of respondents (77%) had completed 4 LTOT visits. Respondents reported that they (42%) or a family member (27%) had received an opioid prescription in the past. Physicians agreed that the LTOT visit (a) improved their comfort with chronic pain management (69%), (b) improved their knowledge (77%), or (c) helped identify opioid misuse (77%). Paradoxically, many respondents agreed that the LTOT visit was organized (100%), efficient (100%) and adequately staffed (68%), but 58% reported an increase in appointment time. Similarly, 81% agreed that LTOT visits involve a stressful conflict between provider and patient, but also agreed that LTOT visits improve the patient-physician relationship (50%), and improve patient satisfaction with pain control (46%).

**Conclusion:** Family medicine physicians have a high level of endorsement for planned LTOT visits, but they continue to feel that visits for LTOT patients involve a level of conflict between provider and patient.

### C33

#### Prevalence of Childhood Obesity in Rural vs Urban Areas

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**Objective:** To compare the prevalence rates of obese children aged 10 to 17 years living in urban and rural areas of Virginia, Georgia, and New York.

**Methods:** Our cross-sectional study used available data from the *National Survey of Children Health 2007*, from the Center for Child and Adolescent Health. Data from the 3 states were analyzed using a 2×2  $\chi^2$  test.

**Hypothesis:** That children living in rural areas have a higher prevalence of obesity compared with urban areas.

**Results:** We compared the obesity rate among 3 states: Virginia (118/811 [14.5%]), Georgia (121/795 [15.2%]), and New York (138/870 [15.9%]). Children living in Georgia had greater risk of being obese compared with children living in Virginia (odds ratio [OR], 1.054). Children living in New York have greater risk of being obese compared with children living in Virginia (OR, 1.107). We also compared the obesity rate between urban and rural areas and in all states, finding that children were more likely to be obese in urban areas: New York (OR, 1.255;  $\chi^2=0.498$ ;  $df=1$ ; 95% confidence interval [CI], 0.667-2.364;  $P=.48$ ); Virginia (OR, 1.394;  $\chi^2=1.813$ ;  $df=1$ ; 95% CI, 0.858-2.27;  $P=.178$ ); Georgia (OR, 2.127;  $\chi^2=11.05$ ;  $df=1$ ; 95% CI, 1.353-3.345;  $P<.001$ )

**Conclusion:** Georgia shows greater significance of rural vs urban areas in childhood obesity.

**Data Source:** <http://www.childhealthdata.org/browse/survey>

### C34

#### Localizing Pelvic Bony Landmarks: A Methodology for Determining Consistency

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**Hypothesis:** The consistency of osteopathic medical students' finger placements during palpation of anatomic landmarks will display minimal variability because of several factors, including the particular landmark being palpated and the side of the body being palpated.

**Methods:** Four osteopathic medical students palpated 5 pelvic landmarks: anterior superior iliac spine (ASIS), pubic tubercle (PT), iliac crest (IC), posterior superior iliac spine (PSIS), and ischial tuberosity (IT) of 59 volunteer participants from the local community. Landmarks were palpated in a rotating order by the student examiners in a blinded fashion. After an examiner assessed whether the right landmark was superior or inferior, the location of the examiner's finger placement on the landmark of the participant in 3-dimensional (3D) space was captured using the Vicon 3D motion capturing system. For each combination of landmark, participant, and side of the body being palpated, a cluster of 4 3D locations corresponding to each of the 4 examiners resulted. The measure of consistency of the localization of the landmark was calculated as the mean of the 4 Euclidean distances between each observation and its cluster center—interpretable as the size of the radius (in millimeters) of a sphere capturing the examiners' finger placements. A mixed models approach was used to test for differ-

ences between landmarks and between sides of the body. Tests between different landmarks used a Tukey-Kramer adjustment to control type 1 error rate.

**Results:** There was a significant difference between landmarks ( $P < .0001$ ). The ASIS had the most consistent localization (5.1 mm), followed by PT (7.2 mm), IC (10.8 mm), PSIS (11.2 mm), and IT (12.2 mm). The differences seen between IC vs PSIS, IT vs PSIS, and IC vs IT were not statistically significant. However, all other pairwise differences were statistically significant. The IT landmark exhibited more precision for landmarks on the participant's right side than the left. The difference was 2.7 mm (95% confidence interval, 2.1-3.4;  $P < .0001$ ). All other landmarks were not significantly different between left and right sides ( $P > .25$ ).

**Conclusion:** The current study attempted to objectively quantify the consistency among medical students in localizing anatomic landmarks by palpation. Using this methodology, it may be possible with further research to assess the degree of consistency and source of variation in students' palpation techniques.

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## Basic Science

### ◆B1

#### Corticotropin-Releasing Hormone-Immunoreactive Axon Varicosities Innervate Growth Hormone-Releasing Hormone-Immunoreactive Neurons in the Human Hypothalamus

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It is a general consensus that stress is one of the major factors that suppresses growth. Previous studies revealed that the catecholaminergic and neuropeptide Y (NPY) system influences growth hormone (GH)-release by means of modulating GH-releasing hormone (GHRH)-secretion. Indeed, catecholaminergic and NPY-immunoreactive axon varicosities abut on the surface of the GHRH neurons forming contacts. These juxtapositions appear to be real synapses and may represent the morphologic substrate of the impact of stress on growth. However, the role of corticotropin-releasing hormone (CRH), a major stress hormone, in the stress-suppressed growth has not been elucidated yet. In the present study, we examined the possibility that CRH influences GH secretion via modulating GHRH release by a direct synaptic mechanism. Since the verification of these synapses by electron microscopy is problematic in humans because of a long postmortem time, to reveal the putative CRH-GHRH juxtapositions, double-label immunohistochemistry was used. In the infundibular nucleus, numerous GHRH perikarya received abutting CRH fiber varicosities forming multiple contacts while passing by.

No gaps appeared between the contacting elements. The morphology of these CRH-GHRH juxtapositions suggests that, among other neurotransmitters/neuromodulators, CRH influences growth by modulating the hypothalamic GHRH secretion by means of direct synaptic mechanisms.

### B2

#### Low-Magnitude, Long-Duration Myofascial Release Enhances Wound Healing Responses of In Vitro Bioengineered Tendons

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**Background:** Previously, we investigated dose response myofascial release (MFR) on bioengineered tendons (BET) and its effect on normal human dermal fibroblasts (NHDF) cytokine secretion, hyperplasia, and hypertrophy. Results suggest that changes to these cellular parameters are highly dependent on MFR time- and magnitude-dosing. In this study, we investigated MFR treatment dosing and its potential role in modifying bioengineered tendons' wound healing response. These data will serve to augment the evidence base describing MFR clinical efficacies on soft tissue injuries.

**Hypothesis:** We hypothesized that treating wounded BETs with varying magnitude- and time-dosed MFR would result in different wound healing times.

**Methods:** The NHDFs were seeded in collagen gel matrices, each attached at 2 nylon mesh anchor points allowing constructs to be freely suspended from the elastomeric well bottom. Bioengineered tendons were allowed to acclimate for 48 hours, at which point a puncture wound was applied to the construct using a 0.75-mm Harris Uni-Core apparatus. Tissue constructs were strained with 1 of the following strain regimens: (1) nonstrain; (2) 90-second MFR stretching at 3%, 6%, 9%, or 12% beyond resting length; or (3) 6% MFR held for 1-, 2-, 3-, 4-, or 5-minute durations. Wound images were captured prior to strain (time 0) and at 3, 18, 24, and 48 hours after strain ( $n=4-9$  per group). Change in wound size was measured using CellProfiler and Adobe Photoshop. Data were analyzed by 1-way analysis of variance with post hoc Dunnett test;  $P$  values less than .05 were considered statistically significant.

**Results:** Nonstrain BETs showed steady decreases in wound size over time. At 48 hours, we measured a significant decrease in wound area when compared to time 0. Regarding duration dosing, the 1- and 2-minute MFR treatment was not different from nonstrain. Myofascial release durations of 3 and 4 minutes yielded earlier significant decreases in wound size at 18

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hours, and 5 minutes of MFR showed the earliest decrease in wound size at 3 hours. For magnitude dosing, wound closure was not observed in 12% and 9% MFR groups. The 6% MFR resulted in significant decreases in wound size at 48 hours, and the 3% MFR resulted in significant decreases in wound size at 18 hours.

**Conclusion:** Results indicated that low-magnitude, long-duration MFR may enhance wound healing rates. These studies provide evidence for a time- and magnitude-dependent MFR dose response, potentially useful in refining manual therapy treatment.

**Funding:** American Osteopathic Association, Arizona Biomedical Research Collaborative.

### ◆B3

#### Investigation of the tcdE Holin Protein as a Potential Chemotherapeutic Target for Treatment of the Disease Caused by *Clostridium difficile*

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Because of the 300 daily fatalities, an approximate 25% annual increase since 2000, the seemingly incurable *Clostridium difficile* has been at the forefront of ongoing development. We hypothesized that the tcdE protein is the mechanism by which the *C difficile* transmits the toxins that cause colitis. Predication of the hypothesis tcdE induces permeability though the holin protein was on the basis of the discovery of Rood, confirming that toxin B causes the symptoms of the disease. Our hypothesis integrates Rood's discovery that toxin B causes the symptoms of the along with principles established by Tan, Wee, and Song in their tcdE holin protein experiment with *Escherichia coli*. Initially, we chose a strain of *C difficile* containing the tcdE gene, which codes for the holin protein, which increases permeability. Then, the most difficult and time-consuming part was choosing a vector (pDGORIT) that can correctly insert the tcdE gene into a well-known and sequenced bacterial cell (*E coli* DH5 $\alpha$ ). After this part was successfully done, the orientation must be confirmed *C difficile* (4 different primers tcdENOL, tcdECoS, tcdEHinS, and TcdEHinL). After completion, an in vitro transcription and translation may be done. Further pursuit of the pDG148-STU plasmid will be accomplished because of the recent creation of an *E coli* DH5 $\alpha$  with the tcdE insert oriented correctly for promotion by SP6. In the current study, the toxic effect of the tcdE gene was a notable roadblock that had to be overcome. Selecting a different plasmid was an excellent way around it, but in the end it was the slight variations on the pDG148STU. Before this experiment is complete, an in vitro transcription and transla-

tion must successfully be carried out. The real proof that the tcdE sequence codes for a protein that increases the permeability of *C difficile* may be established with subsequent electrophysiology studies.

### B4

#### Maternal High-Fat Diet Influence on IL-6 Cytokine Expression and Birth Outcomes

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**Background:** It is believed that maternal diet can permanently impact the health of offspring by means of irreversible alteration of signaling pathways of growth and development. Interleukin-6 (IL-6) is a pro-inflammatory cytokine that is associated with metabolic and cardiovascular disease.

**Objective:** To determine how a high-fat diet (HFD) during pregnancy and lactation influences IL-6 expression and tissue morphology in offspring.

**Hypothesis:** It was predicted that offspring of female mice consuming high-fat diets would have increased levels of IL-6 and histologic changes in the placenta, leading to poor pregnancy outcomes.

**Methods:** The C57BL/6 female mice were separated into 4 groups: (1) high-sugar diet (HSD), a standard rodent diet supplemented with 18% protein, 62% carbohydrate, and tap water; (2) ethanol (EtOH), standard rodent diet and 5% ethanol in tap water; (3) HFD, standard rodent diet supplemented with 20% protein, 60% fat, and tap water; and (4) control, standard rodent diet and tap water. One month after these diets were implemented, mice were bred and pups were collected at postnatal days (PNDs) 1, 21 (weaning stage), and 42 (at sexual maturity). Hearts and livers of offspring were collected for IL-6 quantification by enzyme-linked immunosorbent assay. Additionally, hearts, livers, and placentas were collected for histopathologic analysis. Crown-to-rump lengths were measured at PNDs 1, 21, and 42. Offspring bone morphology was also analyzed by means of light microscopy and microCT (x-ray microtomography).

**Results:** Levels of IL-6 were elevated in HFD offspring at PNDs 21 and 42. At PND 42, hearts of HFD offspring demonstrated notable valvular mucoid degeneration. Histopathologic examination of placentas of HFD mothers showed thrombosis and necrosis. Crown-to-rump lengths of HFD offspring were consistently shorter than age-matched controls, reaching statistical significance at PND 21 ( $P < .01$ ). Compared with the control group, the HFD group had smaller litter sizes ( $P < .05$ ) and higher postnatal mortality ( $P < .01$ ).

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**Conclusion:** Maternal consumption of HFD during pregnancy and lactation leads to early mortality, growth restriction, and increased IL-6 levels in offspring. Proposed mechanisms include placental oxidative damage, necrosis, decreased oxygen and nutrient delivery to the fetus, and prolonged inflammation in the maturing offspring. The current study emphasizes the importance of maternal diet to birth outcomes and lifelong health of the offspring.

#### ◆B5

##### Exogenous Lipoxin A4 Reduces Inflammatory Gene Expression Profile in Neutrophils: One Possible Mechanism for the Improved Survival Outcome in Sepsis

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**Background:** Sepsis is an important cause of human mortality. The pathogenesis of sepsis is mediated in part by an overwhelming rise in acute inflammatory cytokines leading to end organ damage. Lipoxin A4 (LX) is a class of eicosanoid molecule that decreases systemic inflammation. In vitro studies of lipopolysaccharide-induced sepsis have shown that LX decreases neutrophil (NEU) migration to site of infection. During acute inflammation, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) is upregulated in macrophages and NEUs. High levels of circulating TNF- $\alpha$  have been shown to increase mortality and morbidity in septic patients. Systemic release of TNF- $\alpha$  can damage the mitochondrial electron transport chain and lead to release of free radicals. Oxidative stress from free radicals will lead to further organ dysfunction and damage commonly seen in sepsis. Previous work in the laboratory has shown that exogenous LX increased the survival of rats in a clinically relevant cecal ligation and puncture (CLP) model of sepsis. The effect of exogenous LX on NEU during CLP-sepsis has not, to our knowledge, been investigated in vivo. The present study examines TNF- $\alpha$  gene expression from NEU in the peritoneum of septic rats with and without LX treatment.

**Hypothesis:** That LX increases NEU migration and decreases TNF- $\alpha$  gene expression.

**Methods:** Sprague-Dawley rats were divided into 3 experimental groups: sham surgery, CLP+vehicle saline and CLP+LX (1.8  $\mu$ g LX injected intravenously 1 hour after CLP). All rats were sacrificed 24 hours after CLP. Ficoll density gradient isolated NEUs from the peritoneum. Cytospin and Diff-Quik staining were used to visualize purity of NEU isolation. Extraction of RNA and clonal DNA were made before TNF- $\alpha$  was analyzed by real-time quantitative polymerase chain reaction.

**Results:** Ficoll density gradient gave an overall yield of >92% NEU in each group. Neutrophil counts were significantly higher ( $P=.035$ ) in CLP+LX ( $10 \times 10^6$ ) vs CLP+saline groups ( $5 \times 10^6$ ). Compared with CLP+LX group, the CLP group had

significantly increased TNF- $\alpha$  gene expression in NEUs, as expected ( $P=.04$ ).

**Conclusion:** These results suggest that exogenous LX may improve survival in CLP sepsis by promoting increased recruitment of NEUs that also have decreased TNF- $\alpha$  gene expression. The mechanism and implications of increased NEU migration in CLP+LX group will be studied in future work. In addition, the laboratory needs to confirm the presence of an increase in CLP and decrease in CLP+LX TNF- $\alpha$  levels in the blood.

#### ◆B6

##### Effects of Lipoxin A4 on Alveolar Macrophages in Response to Peritoneal Sepsis

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**Background:** Sepsis is a life-threatening condition that kills more than 100,000 Americans each year. It is marked by excessive systemic inflammation followed by a paradoxical immunoparalysis. Subsequently, the patient is vulnerable to bacterial overgrowth and multiorgan failure. To date, there is no specific treatment approved for patients with sepsis. Lipoxin (LXA4) is an anti-inflammatory arachidonic acid metabolite that facilitates the resolution of inflammation, promotes bacterial clearance, and boosts the innate immune system without causing hyperreactivity. Lipopolysaccharide (LPS), a gram-negative bacterial endotoxin, was used to trigger an immune reaction under septic conditions while IL-6, an inflammatory marker, approximated immune function and response.

**Hypothesis:** Our hypothesis was LXA4 treatment in sepsis would improve immune function at sites distal to the nidus while causing a reduction in systemic inflammation.

**Methods:** Rats were divided into 3 groups. The sham group received only open laparotomy. The second group received open laparotomy with cecal ligation and puncture (CLP) and was treated with intravenous saline (as a vehicle control) 1 hour after surgery. The therapy group received open laparotomy and CLP but was treated with intravenous LXA4 (1.8  $\mu$ g per rat) 1 hour after surgery. At 24 hours after surgery, blood was taken from the inferior vena cava and plasma was isolated. Bronchioalveolar lavage samples were also collected. Alveolar macrophages ( $1 \times 10^6$  cells/well) were cultured overnight in DMEM $\pm$ LPS (*Escherichia coli* LPS; 500 ng/mL). Supernatants were then taken and stored at -80°C for enzyme-linked immunosorbent assay later.

◆ Indicates posters entered in the AOA Council on Research's Student Poster Competition, a judged event that takes place during the poster session at the AOA Research Conference.

**Results:** Plasma IL-6 was lower in CLP rats treated with LXA4 compared with CLP rats given vehicle saline. Plasma IL-10, an anti-inflammatory cytokine, was reduced with LXA4 treatment, although these differences were not statistically significant. Alveolar macrophage production of IL-6 without LPS did not differ between CLP groups. Incubation of LPS caused an increase in IL-6 production in macrophages taken from LXA4 treated rats (n=8). Conversely, LPS caused a decrease in IL-6 production in macrophages taken from CLP rats given vehicle saline (n=7,  $P<.05$ ).

**Conclusion:** Alveolar macrophages taken from CLP rats given only saline showed immunoparalysis as evidenced by an inability to produce IL-6 on LPS stimulation. Administration of LXA4 improved the ability of alveolar macrophages to secrete IL-6 in response to LPS. Combined with the results demonstrating LXA4 decreased plasma IL-6, the data suggest that LXA4 can reduce systemic inflammation and reverse immunoparalysis during sepsis.

### ◆B7

#### Effect of Insulin on *Escherichia coli* Catheter-Associated Biofilm Formation

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**Overview:** Biofilm formation is essential for contraction of *Escherichia coli* catheter-associated urinary tract infections. Insulin, a quorum-signaling compound for *E coli*, is excreted with glucose in the urine and thus may affect biofilm development.

**Hypothesis:** Insulin enhances formation of *E coli* catheter-associated biofilms in diabetic individuals.

**Methods:** Rubber (lubricious-coated) and silicon-coated catheter segments (5 mm; n=6) were incubated (18 hours, 37°C) in artificial urine (AU) alone (control) or with glucose (0.1%) and/or insulin (40  $\mu$ U/mL) containing 105 CFU/mL *E coli* ATCC25922. After incubation, segments were washed (4 $\times$ , PBS) and either immediately stained (crystal violet) or re-incubated (30 minutes, 37°C) in PBS alone and with insulin, then re-washed prior to staining. Eluted stain levels (ethanol, 3 mL) were quantified spectrophotometrically (Abs590 nm). Statistical analysis was done by analysis of variance (InStat, GraphPad) with post hoc analysis (Tukey).

**Results:** The level of *E coli* adhering to rubber catheters was significantly higher (12.2-fold;  $P<.01$ ) than that measured for silicon catheters (maximum biofilm levels of 0.53 and 0.043, respectively) regardless of condition tested. Neither glucose nor insulin affected adherence to the rubber catheters. How-

ever, for silicon catheters glucose and insulin significantly ( $P<.01$ ) increased the biofilm levels compared with AU alone, AU+insulin or AU+glucose (8.9%, 8.7%, and 6.3% increase, respectively). None of the conditions tested significantly enhanced biofilm release.

**Conclusion:** Catheter composition significantly affects *E coli* biofilm formation in a simulated diabetic urinary environment. Thus, health care providers may need to factor in an individual's metabolic profile when choosing the type of Foley catheter to use.

### ◆B8

#### Direct Synaptic Communication Between the Somatostatinergic and Growth Hormone-Releasing Hormone (GHRH)-Immunoreactive(IR) Neurons in the Human Hypothalamus

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Somatostatin is a 14-28 amino acid peptide that is located not only in the gastrointestinal system but also in multiple sites of the human brain. The inhibitory effect of somatostatin on growth hormone (GH) secretion from the pituitary gland is a well-known phenomenon. There is a general consensus that somatostatin is released into the hypophysial portal blood and modulates GH secretion by hormonal action. In the present study, we explored the possibility that, in addition to the hormonal route, somatostatin may also influence GH secretion via influencing the release of GHRH by direct synaptic contacts. In turn, GHRH modulates GH secretion by means of the classic portal route. Because the verification of these synapses by electron microscopy is virtually impossible in humans because of the long postmortem time, to reveal the putative somatostatinergic-GHRH juxtapositions, double-label immunohistochemistry was used. By examining the slides with high magnification, we observed that the large majority of the GHRH perikarya received contacting somatostatinergic axonal varicosities in the arcuate nucleus. The morphology and the abundance of these juxtapositions indicate that these associations are functional synapses, and they represent, at least partially, the morphological substrate of the somatostatin-influenced GHRH secretion. Thus, in addition to influencing the GH secretion directly by means of the hypophysial portal system, somatostatin may also modulate GH release from the anterior pituitary by regulating the hypothalamic GHRH secretion by means of direct synaptic contacts.

### ◆B9

#### Cytokine Response to Lymphatic Pump Treatment in AIA Rats

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◆ Indicates posters entered in the AOA Council on Research's Student Poster Competition, a judged event that takes place during the poster session at the AOA Research Conference.

**Hypothesis:** Rheumatoid arthritis (RA) is an autoimmune disease with an unknown etiology. However, the development of RA is thought to involve chronic inflammatory cytokines, antibodies, and structurally damaging enzymes. Clinically, lymphatic pump treatment (LPT) can be used to intentionally increase lymphatic return and reduce edema.

**Objective:** To show that LPT can alter cytokine expression in ankles of rats with adjuvant-induced arthritis (AIA) and to quantify that difference in cytokine expression between non-treated control and LPT ankles.

**Methods:** Twelve female Lewis rats received a 1-time injection of complete Freund adjuvant. The Lewis rats were randomly placed into two groups and allowed to develop AIA. After onset of arthritis, LPT was performed on 1 group of animals 6 times over 11 days. Lymphatic pump treatment was performed by rhythmically pressing below the rib cage 30 to 40 times over a 30-second period. The control or sham group was held for 30 seconds. Arthritis was assessed by measuring ankle circumferences and by articular index scoring through the study. The ankles of rats in the sham and LPT groups were homogenized to generate lysates. Rat cytokine antibody arrays were used to identify and compare the expression profiles of multiple cytokines present in the LPT and sham ankle lysates. Array results were quantified by enzyme-linked immunosorbent assay (ELISA).

**Results:** Rats who received LPT showed decreased swelling in ankles and also showed a decrease in articular index scores compared with the sham group. Cytokines elevated in AIA rats that were identified by the array to be markedly decreased by LPT included IL-2, CINC-1, and CINC-2. Specific cytokine ELISAs showed the average concentration of each cytokine (IL-2, CINC-1, CINC-2) was reduced by LPT when compared with the sham ankles.

**Conclusion:** Our findings suggest that using LPT results in a reduction of inflammatory cytokines, ankle edema, and articular index score.

#### ◆B10

##### Effects of Cadmium on the Urinary Excretion and Tissue Localization of Cystatin C in Rat Kidney

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**Background:** Chronic cadmium (Cd) exposure results in proximal tubule injury characterized by polyuria and proteinuria. As a result of the extensive dissemination of Cd in the environment, there has been considerable interest in the identification of early biomarkers of Cd-induced kidney injury. Cys-

tatin C is a low molecular-weight protein that has been proposed as a biomarker for renal injury. Cystatin C is normally filtered at the glomerulus and then metabolized by the proximal tubule epithelium.

**Objective:** To determine if cystatin C might be an early biomarker of Cd nephrotoxicity.

**Methods:** Male Sprague-Dawley rats were given daily subcutaneous injections of Cd (0.6 mg/kg, 5 d/wk). At 6, 9, and 12 weeks, 24-hour urine samples were collected and analyzed for levels of cystatin C, total protein, creatinine, and kidney injury molecule-1 (Kim-1). Representative animals were euthanized and their kidneys were processed for histopathologic analyses and immunohistochemical visualization of cystatin C and other molecules of interest. The animal treatment protocols were in compliance with the National Institutes of Health guidelines and were approved by Midwestern University's Animal Care Committee.

**Results:** Cadmium caused a 1- to 2-fold increase in urinary excretion of cystatin C that was evident at all 3 time points. Urinary Kim-1 showed even more pronounced elevations at the same time points. No change in urinary protein was evident until 12 weeks, whereas urinary creatinine was not affected by Cd. Histologic analyses revealed proximal tubule injury (separation and retraction of cells). Immunolabeling studies revealed that Cd altered the pattern of cystatin C distribution in the proximal tubule. Control samples revealed speckled labeling beneath the apical cell surface. By contrast, the samples from Cd-treated animals exhibited diffuse cystatin labeling in the cytoplasm and on the cell surface. Both the pattern of labeling and the Cd-induced changes for cystatin C paralleled those of the brush border transport protein megalin, which has been implicated as a mediator of cystatin C uptake in the proximal tubule.

**Conclusion:** Cadmium increases the urinary excretion of cystatin C and this effect may involve disruption of megalin-mediated uptake of cystatin C by epithelial cells of the proximal tubule.

**Funding:** The present study was supported by Midwestern University and National Institutes of Health grant number ROI006478.

#### ◆B11

##### Effects of TNF- $\alpha$ on GM3-synthase Levels and Its Subsequent Activation of the Insulin Receptor in C2C12 Myocytes

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Both TNF- $\alpha$  and nonesterified fatty acids have been proposed

◆ Indicates posters entered in the AOA Council on Research's Student Poster Competition, a judged event that takes place during the poster session at the AOA Research Conference.

as crucial factors in the development of the insulin-resistant state. The increased secretion of TNF- $\alpha$  contributes to altered systemic as well as adipose tissue lipolysis, leading to elevated levels of circulating free fatty acids that might potentially increase sphingolipids and gangliosides. Because skeletal muscle is a key metabolic tissue, defects in insulin signaling in this tissue are central to the pathogenesis of type 2 diabetes mellitus. Caveolae are specialized plasma membrane microdomains that are thought to serve as signaling platforms for several receptors including the insulin receptor (IR) and glucose transporters (eg, Glut-1, Glut-4) by means of interaction with caveolin-1 and caveolin-3 proteins. Recent research has shown that TNF- $\alpha$  has an effect on the insulin signaling pathway by upregulating the production of GM3-synthase, the enzyme responsible for producing ganglioside-GM3. We hypothesized that exposure of C2C12 cells to TNF- $\alpha$  will result in deregulation of the insulin signaling cascade and affect the pattern of IR localization to the plasma membrane by promoting a shift of IR from caveolae to other membrane domains enriched in ganglioside-GM3 expression. In the present study, C2C12 mouse myocytes were differentiated into skeletal myotubes and treated with TNF- $\alpha$ , insulin, and a TNF- $\alpha$  antagonist, individually and in combination. The treated cells were subjected to SDS-polyacrilamide gel electrophoresis and Western blot analysis with antibodies against insulin receptor- $\beta$ , phosphorylated insulin receptor, GM3-synthase (GM3-S) and actin (loading control). Immunofluorescence analysis using the same antibodies and the caveolin proteins was also done. Immunofluorescence microscopy demonstrated higher levels of GM3-S in cells treated with TNF- $\alpha$ , which was reversed by treatment with the antagonist. These results suggest that TNF- $\alpha$  antagonists could be used as therapeutic agents in order to decrease GM3-synthase levels and increase the level of insulin receptor phosphorylation. These data could provide information relevant to the treatment of type 2 diabetes mellitus.

### ◆B12

#### **Insulin Signaling and Caveolae: Role of Saturated Fatty Acids in the Development of Insulin Resistance in 3T3-L1 Adipocytes**

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Caveolae are microdomains recently recognized as critical for proper compartmentation of insulin signaling; however, their role in the pathogenesis of insulin resistance is not fully understood. Caveolae are particularly abundant in adipocytes and especially critical for insulin signaling transduction.

Research demonstrated that the inhibition of insulin signaling and the elimination of insulin receptors from the caveolae were associated with an accumulation of glycosphingolipids such as ganglioside GM3. A growing body of evidence suggests that saturated fatty acids, such as palmitate and ceramide, play a role in the pathogenesis of insulin resistance. Both palmitate and ceramide are precursors to ganglioside GM3. Here we determined the effect of palmitate and ceramide on the total protein expression and the cellular protein distribution of caveolin-1, insulin receptor, phosphorylated insulin receptor, and Glut4 in 3T3-L1 adipocytes. We measured protein expression by Western blot analysis and protein distribution by immunofluorescence microscopy. Our results indicated no significant changes in total protein expression of Glut4, insulin receptor, phosphorylated insulin receptor or caveolin-1 in the presence of palmitate or ceramide. We provide evidence for disregulation of insulin signaling due to altered colocalization of Glut4 to the caveolae and a possible significant change in the ability of insulin receptor to be activated after treatment with palmitate, but not with ceramide. No other significant changes were observed in 3T3-L1 adipocytes other than the increase in activated insulin receptor in the presence of increased insulin in the control groups as to be expected.

### ◆B13

#### **Analysis of *Chlamydia pneumoniae* and Alzheimer Disease-like Pathology in the Brains of BALB/c Mice Following Direct Intracranial Infection With *Chlamydia pneumoniae***

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**Objective:** To measure the location and degree of burden of *C pneumoniae*, amyloid deposition, and glial cell activation in the CNS following direct intracranial injection and to compare this data with results obtained from previous studies in this laboratory.

**Hypothesis:** We hypothesized that *Chlamydia pneumoniae* antigen and activated inflammatory cells will be observed in the infected mouse brains following direct intracranial injection and A $\beta$  deposition will be observed in areas where inflammation occurs.

**Methods:** In the current study, BALB/c mice were infected by means of direct intracranial injection, with a respiratory isolate (AR-39) of *C pneumoniae*. Brains were analyzed at 7 and 14 days after infection, by means of immunohistochemistry, for the presence of *C pneumoniae*, amyloid deposits, and activated glial cells.

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**Results:** The presence of *C pneumoniae*, amyloid deposits, and activated glial cells was detected in the brains following direct intracranial infection with *C pneumoniae*. At 7 days after infection, the average number of *C pneumoniae*-specific immunoreactive sites was  $68 \pm 51.06$  for the infected mice and at 14 days after infection, the average was  $60 \pm 43.79$  for the infected mice. Within 0.84 mm of Bregma, the location of the injection, 166 of 203 total *C pneumoniae*-specific immunoreactive sites (82%) and 26 of 27 (96%) total amyloid deposits were detected at 7 days after infection. At 14 days after infection, 126 of 179 (70%) total *C pneumoniae*-specific immunoreactive sites and 13 of 32 (41%) total amyloid deposits were detected in this area of the brain (within 0.84 mm of Bregma). From 7 to 14 days after infection, the *C pneumoniae* and amyloid deposits located near the injection site, within 0.84 mm of Bregma, spread distally from this location to other regions of the brain.

**Conclusion:** These data confirm that *C pneumoniae* is capable of establishing an infection in the central nervous system. Although deposits were observed, the lack of a substantial amount of amyloid deposits suggested that deposits may require longer than 14 days to generate following infection with *C pneumoniae*. As early as 7 days after infection, inflammation was observed in response to the presence of *C pneumoniae* or soluble amyloid in the CNS and the contribution of both infection with *C pneumoniae* and the presence of soluble amyloid elicit the inflammatory response that presumably precedes and contributes to amyloid deposition.

#### ◆B15

##### Autoantibody-Induced Endocytosis Contributes to Neuronal Functional Loss and Amyloid Deposition in Alzheimer Disease Brains

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**Background:** Our previous studies reported abundant immunoglobulin G (IgG) bound to neurons in the brains of patients with Alzheimer disease (AD), an observation indicative of blood-brain barrier (BBB) breakdown. The ubiquitous presence of brain-reactive autoantibodies in the blood have suggested that a defective BBB in brains of patients with AD allows autoantibodies to leak into the brain, bind to neurons, and enhance the brain deposition of amyloid-beta (A $\beta$ ) peptide, especially A $\beta$ 42.

**Hypothesis:** We hypothesized that binding of autoantibodies to neurons induces chronic endocytosis in these cells, leading to 3 pathologic consequences: (1) neuronal functional deficits due to constant stripping of key proteins from cell surfaces, (2) a continual deposition of exogenous A $\beta$ 42 from the blood into the lysosomal compartments of neurons, and (3) hyper-

trophy of the neuronal lysosomal compartment to accommodate the increased influx of endocytic vesicles.

**Methods:** To test this, we carried out an immunohistochemical study on human brain with AD. We also used an aged mouse model, which received tail vein injections of A $\beta$ 42 peptide for 3 months while under conditions of constant BBB permeability induced by Pertussis toxin.

**Results:** Immunohistochemistry (IHC) revealed abundant IgG-positive neurons in human brain regions showing typical pathology of AD as well as in the brains of mice with a permeable BBB. Antibodies to neuronal receptors (eg, alpha7 nicotinic acetylcholine receptors, NMDA receptors and glutamate R2 receptors) showed that, in regions of AD pathology, these receptors were localized to cell surfaces, but were also in endocytic vesicles and the lysosomal compartment. Localizing cathepsins B and D, enzymes confined to lysosomes, IHC consistently showed great expansion of the lysosomal compartment of neurons in areas of pathology.

**Conclusion:** Results suggest that chronic BBB breakdown triggers a pathologic cascade in brains with AD in which brain-reactive autoantibodies and A $\beta$ 42 in the blood leak into the brain tissue, bind to neurons and induce chronic endocytosis. The endocytosis drives the neuronal deposition of A $\beta$ 42 and receptor stripping from the surface membrane, leading to neuronal functional deficits. These findings emphasize the need to maintain the structural and functional integrity of the BBB and point to the BBB as a key therapeutic target for preventing initiation of AD and blocking progression of AD.

**Support:** The present study was funded by the Osteopathic Heritage Foundation.

#### ◆B16

##### Quantitative Analysis of Structural Changes of Growth Cone Central Domain (C) in *Xenopus laevis* Retinotectal Axonal Navigation

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**Background:** Appropriate motor and sensory development relies on axonal elongation through diverse tissues to reach synaptic partners located throughout the developing body. This embryonic axonal navigation is accomplished by the motile structure at the distal tip of an elongating neuronal axon called the growth cone, a dynamic, actin-supported extension of a developing axon seeking its synaptic target. The growth cone is described in terms of 3 regions: the peripheral domain, the transitional domain, and the central domain. Previous studies showed that the central domain is primarily

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composed of a microtubule-based cytoskeleton, is generally thicker, and contains many organelles and vesicles of numerous sizes. Here we will focus on mathematical analysis of the shape of the central domain and their relationship to axonal navigation in the optic tract of *Xenopus laevis*.

**Hypothesis:** We hypothesized that there will be structural changes in central domain growth cone in axonal navigation through the optic tract of *Xenopus laevis*.

**Methods:** The width and length of the central domain growth cone of 2 retinotectal axons were measured from an in vivo time-lapse video of *Xenopus laevis* embryo recorded by Sonia Witte of Cambridge University. Using Image J, growth cone central domains were demarcated based on higher intensity of membrane GFP expression (likely due to greater curvature of the central domain). The length and width of the central region of the growth cones were then measured from these markings.

**Results:** The fine-scale structure of the central domain of the growth cone in axons of the optic tract is variable. The measurements demonstrated no clear correlation between central domain length and width to axonal navigation. Changes in width of the central domain of the growth cone were less significant than changes in the length of the central domain of the growth cone. There is a sudden decrease in the length of the central domain growth cone immediately before the axon reaches its destination at the tectum.

**Conclusion:** The shape of the central domain of the growth cone reflects its function. The greater length allows axonal guidance and navigation through the optic tract. Once the axon reaches its destination at the tectum, axonal navigation is no longer necessary and the growth cone disappears as axons prepare to arborize at their destination. Understanding of structural changes in axonal growth cone in the optic tract of *Xenopus laevis* allows comparison of wild-type growth cone with abnormal embryonic growth cone.

### ◆B17

#### Expression of Prophage Genes in *Salmonella enterica* Serovar Typhimurium Under Environmental Stressors

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**Background:** Bacteriophages, or phages, are viruses that infect bacteria. A temperate phage has the ability to insert its genome into the bacterial chromosome and reside in a dormant stage (ie, prophage stage). Reactivation, or induction, of a prophage leads to the expression of its genes, activation of the lytic cycle, and search for a new host. Phages often carry virulence

genes, and they play an important role in evolution of bacteria and infectious diseases.

**Objective:** To evaluate expression levels of prophage genes during normal growth of the host and exposure to various stressors through the use of *Salmonella enterica* serovar Typhimurium LT2, a pathogen that has 4 prophages, all of which are known to carry virulence genes.

**Hypothesis:** Our hypothesis was that environmental stress can lead to prophage induction, and thus can make the bacteria host more virulent.

**Methods:** S Typhimurium was grown in the presence of various stressors: temperature (30°C, 37°C, 43°C), media composition (minimal salts, nutrient rich, tryptone rich), competition (cocultured with *Escherichia coli*), growth phase (exponential, stationary, starvation), pH, and oxidative stress. For each condition, the cultures were harvested for RNA extraction. Prophage RNA was then quantified using real-time PCR. Results are presented as fold difference compared with normal growth conditions.

**Results:** Preliminary results show that (1) without environmental stressors, there is a spontaneous expression of prophage genes, and (2) this basic level of gene expression can be dramatically increased depending on the environment the host is exposed to (eg, a 4.5-fold increase in nutrient-rich media, a 3.3-fold increase in the presence of oxidative stress, a 2.2-fold increase when the host is cultured with another Enterobacteriaceae).

**Conclusion:** The stressors tested in this study mimic conditions a bacterial pathogen is most likely to encounter during infection. Therefore, our data strongly support our hypothesis that prophage induction related to environmental changes or factors can be of major importance in bacterial virulence. This type of study should help us better understand the pathogenesis of diseases caused by a prophage carrier bacterium.

## Medical Education

### ME1

#### Pregnancy, Parenthood, and the Effect on the Residency Program

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**Context:** The most recent Accreditation Council of Graduate Medical Education data, for the academic year 2009-2010, show that of the 4869 obstetrics and gynecology (OB/GYN) residents in training, 3830 (79%) are women, clearly representing the largest proportion of women in residency training.

**Objective:** In early 2010, we completed a pilot survey of OB/GYN program coordinators to ascertain the prevalence of pregnancy during residency, the duration of the post-

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partum leave, and the amount of additional training time required to graduate.

**Methods:** An anonymous survey was sent to program coordinators of the 247 OB/GYN programs in the United States. They were queried about the total number of residents in their program, the number of female residents in their program, the number of women in their program who had been pregnant during the past 4 years (2007-2010), the time pregnant women in their program missed from training and makeup time these women required to complete their residency training, the number of residents whose partner had been pregnant or was pregnant at the time of the study, and residents who had not been pregnant or whose partner had not been pregnant.

**Results:** Throughout the 4 years we surveyed, 24% of the female residents in training were pregnant, and 28% were required to extend their residency training. On the basis of these data, we initiated a follow-up survey of current residents in training that were or are currently pregnant during their residency, residents whose partner were or are currently pregnant, and residents who have not been pregnant or whose partners have not been pregnant. We received 259 completed surveys. Of these respondents, 21% were pregnant and 4.2% had a partner who was pregnant. More than 80% of the pregnancies were planned. Among the population of female residents, 36% missed time training during their pregnancy. Of the new mothers, 85% admitted to interrupted sleep patterns and less studying at home after their delivery. Of those whose partner had delivered, 89% felt that their sleep was interrupted, and 100% felt that they were studying less at home. Women who had not been pregnant or whose partners had not been pregnant (45%), felt they had to work harder because a coresident was affected by a pregnancy, whereas 17% were resentful that a coresident was adversely affecting their own residency experience. Finally, 40% felt that the residents who were out because of a newborn should be required to make up the time.

**Conclusion:** These data offer insight as to how pregnancy affects the pregnant resident, her partner, and her colleagues. Clearly, pregnancy decreased the ability of pregnant residents and partners to study at home, and the interrupted sleep may have affected daytime learning potential. Programs may consider offering the postpartum residents the opportunity to study in the hospital or perhaps designing a reading curriculum that may be completed upon the resident's return. Residents who had not been pregnant or whose partners had not been pregnant felt the burden of work to be more difficult and harbored resentment of fellow residents, a fact that may encourage programs to initiate interventions to alleviate these feelings. Further studies might monitor Council on Resident Education in Obstetrics and Gynecology scores and written boards pass rates correlating to pregnancy in residency training.

## ME2

### Communicating About Osteopathic Medicine: An Analysis of Osteopathic Residents' Responses to the Question "What's the Difference Between a DO and an MD?"

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**Background:** As the number of practicing osteopathic physicians (ie, DOs) increases, more patients will find themselves being treated by physicians who wear the letters DO on their white coats. Many will have had no prior experience with osteopathic medicine. Our challenge in osteopathic medical education is to enable our students and residents to communicate effectively about osteopathic medicine, ensuring that they can professionally present and accurately promote their profession.

**Objective:** To generate themes from osteopathic residents' descriptions of the difference between DOs and allopathic physicians (ie, MDs) and to compare the generated themes and responses to a statement on the Web site of the American Osteopathic Association (AOA).

**Methods:** During the 2010 and 2011 Nova Southeastern University College of Osteopathic Medicine Resident Objective Structured Clinical Examinations (ROSCE), the following question was asked by the standardized patient: "I see you have DO behind your name. What's the difference between a DO and an MD?" Resident responses were digitally recorded, transcribed, and distributed to residency program directors as part of their core competency assessment. After the ROSCE reporting was completed and upon approval from the institutional review board, the 362 archived resident responses were deidentified and qualitatively analyzed.

**Results:** The following 7 themes emerged: (1) DOs use osteopathic manipulative treatment, (2) DOs and MDs have similar licensing, prescribing rights, and practice opportunities, (3) DOs have a more holistic philosophy, (4) DOs have additional musculoskeletal training, (5) DO and MD medical schooling is the same, (6) DOs have an "extra tool in their bag," and (7) DOs focus on the body's interconnectedness. Six of these themes closely match concepts in the AOA statement. However, 1 theme (DO and MD medical schooling is the same) is not in the AOA statement. Further review revealed that 2 concepts in the AOA statement—"preventing illness through healthy lifestyle" and "help the body heal itself"—were only mentioned by 1% and 7% of the residents, respectively.

**Conclusion:** Given that only 2 generated themes were mentioned by more than 50% of the residents, the resident responses were incomplete. Although the ROSCE time limit may have impacted some residents' ability to fully answer the question, the author recommends examining curricula to determine whether current instruction and assessment is this type of patient communication is adequate and whether the

concepts of prevention, wellness, and helping the body heal itself are being sufficiently taught.

### ME3

#### Significance of Medical School Elective Rotations on Residents Who Have Successfully Matched

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**Context:** Osteopathic medical students applying for residencies have dealt with a more competitive match than in the past. Factors surrounding this competition have sometimes been discussed in light of elective choices.

**Objective:** To determine whether students who have matched have any correlation with elective rotations. This information may provide direction for future students pursuing those specialties.

**Methods:** A retrospective chart review of anonymous students who attended Midwestern University/Chicago College of Osteopathic Medicine. Data were collected from 2007 to 2011 and organized by the elective rotations that students chose. We chose to compare a primary care specialty, family medicine (FM), with a specialty, emergency medicine (EM), looking for differences and similarities. There were 127 students who eventually matched into FM and 90 who matched into EM.

**Results:** Students who matched into EM took 27.9% of their electives in EM, followed by 13.6% in radiology, 5% in FM, and 4.1% in toxicology (Figure 1). Students matching into FM took 27.5% of their electives in FM, followed by 8.8% in radiology, 3.8% in dermatology, and 2.5% in EM (Figure 2). Students who matched into EM took 2 or more rotations in EM 65.3% of the time (Figure 3). Students matching into FM took 2 or more rotations in FM 48.8% of the time (Figure 3). Lastly, students matching into FM chose Accreditation Council for Graduate Medical Education (ACGME) residencies 41.7% (Figure 4) of the time compared with EM with 30% of the time (Figure 5).

**Conclusion:** Students matching into EM or FM commit a significant proportion of their elective rotations on a select few specialties, using the majority of electives on the specialty they wish to match (Figure 3). The remaining electives are spent on applicable skills for that residency. Using this strategy, the students in the current study matched the majority of the time into AOA residencies, though still competitive for ACGME residencies (Figure 4 and Figure 5). We believe that this gives appropriate guidance for students pursuing EM and FM on how to wisely use elective rotations.

**Editor's Note:** Figures not pictured.

### ME4

#### Folic Acid Is an Important Factor in Preventing Neural Tube Defects

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**Background:** Consumption of a folic acid supplementation before and after conception lowers the risk of giving birth to a child with a neural tube defect (NTD). Publicly available data and results from published articles were used to compare and to reevaluate the effect of folic acid.

**Hypothesis:** Mothers who take folic acid before and after conception have lower odds of giving birth to a child with NTD compared with mothers who never take folic acid. A mother with an education level of greater than 13 years has lower odds of having a child with NTD compared with a mother with an education level of less than 9 years.

**Method:** A retrospective cohort study used published findings from De Marco et al (2011) to determine the NTD rate in comparison with folic acid supplementation, as well as the mother's education level. De Marco's data were interpreted using a different reference point. A 2008 study from the March of Dimes Foundation interviewed 2003 women of child-bearing years. Of the 1682 (84%) that were aware of folic acid, only 185 (11%) of these women knew that folic acid is supposed to be taken before conception. This study also explained that those women of any level of college education showed a higher awareness of folic acid compared with women of a lower level of education. We combined data from the 2 studies to come up with an overall conclusion. Primary and secondary outcomes are, respectively, the number of NTDs and the awareness of NTDs.

**Results:** After reanalyzing the data from De Marco et al, we found that a mother who takes folic acid before and after conception has a 0.037 times significantly lower chance of giving birth to a child with an NTD compared with a mother who never takes folic acid ( $\chi^2$  test=60.56; df=1;  $P<.0001$ ; 95% confidence interval [CI], 0.013-0.107). A mother with an education level of greater than 13 years has a 0.205 times lower odds to have a child with a NTD compared with mother with an education level of less than 9 years ( $\chi^2$  test=20.528; df=1;  $P<.0001$ ; 95% CI, 0.100-0.419).

**Conclusion:** There is significant evidence to support that those women who consume folic acid before and after conception have a significantly lower chance of having a child with a NTD. Women with a higher level of education also have a greater awareness of folic acid when compared with women of a lower level of education. This finding supports the notion that mothers with a higher level of education have



a lower prevalence of giving birth to children with NTDs.

#### ◆ME5

### Reducing the Stigma of Mental Illness Among Medical Students

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**Context:** The American Osteopathic Association House of Delegates Resolution 205 (A/2011—"Depression Awareness in Medical Schools") recommends "increased awareness of depression amongst U.S. medical students" because of the increasing body of research describing the rise of depression, burnout, and suicidal ideation among medical students. There is consequently a need to understand mental health issues as a component of professional development.

**Hypothesis:** A student-led symposium addressing mental and emotional health topics relevant to medical students would reduce the stigma associated with mental illness.

**Methods:** A 2-hour, student-run Patient Perspective symposium was held during the second-year neuroscience block at an osteopathic medical school in the northeastern United States. One week before the program, a student-developed, online wellness survey measured prevalence of mental illness, common feelings during medical school, coping mechanisms used for stress, and use of mental health resources. Immediately before and after the program, students were asked to report their familiarity with mental illness and their feelings regarding a vignette about a mentally ill woman, using "Mental Illness Among Us" (provided by the University of California, San Francisco School of Medicine and adapted for the event) for the pre- and postsurveys. During the program, data from the online survey were shared, student organizers discussed emotional wellness and positive coping mechanisms in the context of the profession, and student panelists shared their experiences with mental health issues. A faculty psychiatrist spoke about mental health resources and attendees received pamphlets listing these resources. The event concluded with student-led breakout sessions at which stress during medical school and strategies for promoting positive coping mechanisms were discussed, followed by the postsurvey.

**Results:** One hundred thirteen students completed the presurvey, 89 of whom completed the postsurvey. For these 89, differences between pre- and postsurvey responses were universally in the direction of increasing acceptance and decreasing stigma of those with mental illness. All differences were statistically significant. The largest shift regarded students' reluctance to disclose their own theoretical mental illness to colleagues.

**Conclusion:** Incorporating an emotional health symposium into medical students' training may increase understanding and acceptance of those who may have mental illness and reduce stigma associated with mental illness.

#### ME6

### Consumer Attitudes Toward Purchasing Organic Food

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**Background:** The relationship between consumer attitude and awareness about perceived benefit of organic food may further our understanding of consumer purchase.

**Objective:** The current study evaluated the perceptions and knowledge of organic food content and governing laws among consumers and which factors compelled these consumers to continue purchasing organic foods.

**Hypothesis:** Women are more interested in organic food than men.

**Methods:** A cross-sectional study using the Organic Food Consumption (OFC) survey was developed to allow for better understanding of the general population's knowledge of organic products and purchase habits. Each survey consisted of 20 general questions consisting of lifestyle, knowledge of organic products, food preference, and concern for the environment. Surveys were distributed to 44 students in the Edward Via College of Osteopathic Medicine–Virginia Campus postbaccalaureate class. Main outcome measures were knowledge of organic products, total consumption of organic products, perception of organic products, and general health and welfare.

**Results:** Thirty-six students completed the survey, 25 women and 11 men ranging from ages in the early twenties to mid-thirties. Of these 36 students, 21 ranked produce as the organic product that they are most likely to purchase, with beverages being the product that they are least likely to purchase. Students were most concerned with food safety or lack of additives when purchasing organic products. Women also showed much more interest in learning more about organic products ( $P=.0081$ ).

**Conclusion:** Participant responses suggest that the following areas could benefit from future research: (1) health benefits of organic food, (2) safety of organic food, (3) production of organic produce, and (4) production of organic drinks and bev-

◆ Indicates posters entered in the AOA Council on Research's Student Poster Competition, a judged event that takes place during the poster session at the AOA Research Conference.

erages. Understanding the consumer's general perception toward organic food is vital in determining areas of interest and disinterest, thereby revising organic food education in a competent, reasonable manner.

### ME7

#### What We Know About Chronic Disease in Central Appalachia: A Meta-Analysis

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Appalachia encompasses more than 420 counties, including West Virginia and parts of 12 other states. The Virginia Diabetes Plan 2008-2017 reports that Appalachian coal-dependent counties in southwest Virginia experience a 63% increase in the prevalence of diabetes compared with the non-Appalachian counties. Thus, regional inequalities persist despite previous programmatic efforts to alleviate health disparities. The objective of this study was to compare rates of chronic diseases in central Appalachia reported by agencies with those reported by original investigators. A meta-analysis of literature on the health effects of coal mining on residents in central Appalachia was systematically conducted. More than 40 relevant articles were identified with the search terms “Appalachian,” “coal mine,” and “health.” Most studies addressed the major chronic diseases (ie, heart disease, cancer, hypertension, diabetes, and obesity). Comparing published results from data collected for

different levels is problematic. For example, agency data on average annual cervical incidence cancer rates are reported to differ (13%) between non-Appalachia and Appalachia Virginia (Appalachia Community Cancer Network, National Cancer Institute). However, findings cannot be fairly discussed and compared with an epidemiological, original peer-reviewed study that obtains region-specific data. Although both confirm higher cancer rates in Appalachia compared with the state average, other studies have not been able to confirm significant differences in the number of chronic diseases per person by place of residence (McGarvey et al, 2011). Although national data provide a big picture, peer-reviewed studies are often too region-specific to be applied to state policies and programs. Although the health problems of Appalachia are unique compared with the rest of the United States, they are not homogenous within the region. By combining rich quantitative data, such as those collected by national agencies, with detailed qualitative surveys used in original research, creative methods can be designed for health intervention programs. Our analysis confirms the need for further research to more specifically define the target areas affected by disproportionate rates of chronic conditions. Identifying and characterizing specific areas will provide the direction needed to refine methods of intervention focused on readily modifiable factors to improve human health in central Appalachia.

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