52nd Annual AOA Research Conference—Abstracts, 2008

This issue of JAOA—The Journal of the American Osteopathic Association *(August 2008) contains abstracts for poster presentations that will be given at the 52nd Annual American Osteopathic Association (AOA) Research Conference. Poster presentations will be provided by AOA research fellows (abstract series F), as well as osteopathic physicians, medical students and educators, clinicians, and researchers on the following general topics: osteopathic manipulative medicine and osteopathic principles and practice (series P), clinical studies (series C), basic sciences (series B), and medical education and health policy (series ME-HP).*

The 2008 AOA Research Conference will take place from Sunday, October 26, to Tuesday, October 28, during the American Osteopathic Association's (AOA) 113th Annual Convention and Scientific Seminar in Las Vegas, Nev. The theme of this year's conference is "Osteopathic Research: Advancing A.T. Still's Vision." For more information on the Annual Convention and Scientific Seminar, please see the DO-Online Web site (http://www.do-online.org).

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AOA Research Fellowships

♦F1

Osteopathic Manipulative Treatment for Postoperative Nausea and Vomiting

S.L. Schrick-Senasac, DO, MS[1], H.H. King, DO, PhD [2]
[1]University of North Texas Health Science Center, Fort Worth, TX,
[2]Osteopathic Research Center, Fort Worth, TX

Purpose: Postoperative nausea and vomiting (PONV) remains a concern despite medical advances; associated with potential mortality and morbidity, no therapy completely prevents its symptoms. This pilot study sought to evaluate the effect of osteopathic manipulative treatment (OMT) on the incidence and severity of PONV and to assess the feasibility of large-scale reproduction.

Methods: Individuals undergoing orthopedic surgery under general anesthesia were recruited as subjects and given informed consent based on the IRB-approved protocol. Seventeen subjects completed the study-eight receiving treatment, nine as non-treatment controls. The OMT maneuvers were from an approved list of non-aggressive techniques, including cranial manipulation. Subjects, amnestic from anesthesia, and the study coordinator were blind to the treatment group. Nausea and pain visual analog scale (VAS) scores as well as vital signs were collected at baseline and again at times following treatment. The Ambulatory Surgery-Rhodes Index for Nausea, Vomiting, and Retching was completed 1 day following treatment. Vital signs and VAS scores were analyzed as deviation from baseline, though significance could not be assessed with the sample size.

Results: Treatment and control groups were well matched with respect to demographics, risk factors for PONV, and baseline vital signs and VAS scores. There were no trends in reduction of incidence or severity of PONV; treatment group incidence of early emesis was reduced (0.37 v 0.89 episodes) as was 30-minute and peak nausea VAS scores and distress from nausea (0.5 v 1.9; 4 v 5.17; and 3.3 v 3.6, respectively). Additional analysis found pain VAS scores showing less elevation from baseline in treated subjects than controls (2 v 4.33 @ 30-minutes; 1.63 v 3.22 1-hour; and 1.1 v 3.8 post-discharge interview). This was accompanied by reduced mean utilization of pain medication in the post-anesthesia care unit (1.5 v 3.2 doses).

Conclusions: Incidence of PONV was low in both groups, likely because of prophylaxis with antiemetics. Future study should increase enrollment, include higher-risk subjects, and restrict prophylactic treatment of PONV. Reduction of pain and use of analgesic medication in the treatment group is congruous with recent research linking the effect of OMT to modulation of endorphin and endocannabinoid systems. This pilot study demonstrated proof-of-concept and feasibility, with minor alteration, for reproduction on a larger scale.

♦Indicates posters entered in the Student Prize Competition, a judged event that takes place during the Poster Session at the Research Conference.

Osteopathic Manipulative Medicine/Osteopathic Principles and Practice

♦P1

The Value of Osteopathy in Anesthesiology: A Survey

N.M. Johansson, OMS-IV[1], J. Yarmush, MD[2], A. Guirguis, PhD[3], M. Apergis, MA[2], A. Kalstein, DO[2]

[1]New York College of Osteopathic Medicine, Old Westbury, NY, [2]Department of Anesthesiology, New York Methodist Hospital, Brooklyn, NY, [3]Department of Statistics, New York Methodist Hospital, Brooklyn, NY

Hypothesis: Osteopathy plays a role in the acceptance into anesthesiology residency programs and practice as an attending.

Methods: A cover letter and 19 question survey, was mailed to all of the 558 osteopathic anesthesiologists in the 2007 membership directory of the American Osteopathic College of Anesthesiologists with a complete address. The survey asked about aspects of medical school, internship, residency, fellowship, and practice.

Results: There were 174 respondents (31.2%). One hundred forty two of the respondents (82%) completed an Osteopathic Rotating Internship. Fifty four of them (38%) followed their internship with residency at the same hospital. Forty five of 174 of the respondents (26%) did an anesthesia fellowship; of these, 25 (54%) specialized in pain management. Sixty eight of 174 (41%) respondents applied to only one anesthesiology program. One hundred twenty seven of 174 (76%) applied to a maximum of four programs. One hundred fifty of 174 respondents got their first choice of residency and of these 150, 51 went through the match and 99 did not. Ninety six of 174 respondents (56%) feel that they employ basic osteopathic principles into patient care, while 52 of 174 (30%) use osteopathic manipulative medicine (OMM) on their patients. The anesthesiologist surveyed felt that graduating from an osteopathic medical school helped 47 (27%), hindered 27 (16%), or was a neutral 100 (57%) factor in their acceptance into residency. OMM training and osteopathic principles helped 88 (51%), hindered 2 (1%), or was a neutral 84 (48%) factor in their anesthesiology careers.

Conclusions: The survey emphasizes that successful students (i.e., those students who were accepted into programs) felt confident in getting their choice of residency. This is illustrated by the large number of students who applied to between one and four residency programs. Osteopathic anesthesiologists who choose a fellowship most often choose pain management, which may be so because of a connection between pain management and osteopathic principles. Osteopathy has traditionally been associated with primary care medicine, but this survey shows that many anesthesiologists feel that OMM and osteopathic principles are helpful in their practice.

P2

Efficacy of Manipulative Treatment for Acute Low Back Pain in Active Duty Military Personnel

S.T. Stoll, DO, PhD[1], D. Maurer, DO, MS[2], K. Hensel, DO[1], D. Cruser, PhD, MPA[1]

[1]Department of Osteopathic Manipulative Medicine, UNTHSC-TCOM Osteopathic Research Center, Fort Worth, TX, [2]United States Army Medical Corps, Fort Worth, TX

This poster reports the findings of an efficacy study of manipulative treatment for acute low back pain (ALBP) in active duty military personnel. The Samueli Institute funded this study, conducted by the Osteopathic Research Center in 2006-07 at Fort Lewis Madigan Army Medical Center. Two primary outcome measures for this randomized, blinded, controlled clinical trial were pain (Visual Analog Scale), and functioning (Back Pain Functional Status Scale; Roland Morris Questionnaire [RMQ]). Other measures were patient expectation - treatment bias, restricted duty time, and medication use. ALBP was any acute event reported by a soldier, including a new episode (>30 day pain hiatus). We randomly assigned active duty male and female soldiers, ages 18-35, meeting inclusion/exclusion criteria, to a group receiving OMT plus routine care, or to a group receiving routine care-only. We evaluated all subjects on all measures at each of four once-a-week visits, and one month later. OMT was guided by somatic dysfunction (S/D) findings in: 1) Pelvic mobility and structural asymmetry, 2) Tenderpoint screening, 3) Lumbar segmental dysfunction. A standardized treatment protocol used ⩽ six techniques based on S/D findings. No physical therapy was included, only standard analgesics. All IRBs approved. One-third of 225 soldiers screened met all criteria. Of 73 enrolled, nine were deployed prior to randomization and one was deployed before the second visit. Final analysis included 63 subjects: 33 OMT (81.8% - four visits) and 30 routine-care-only subjects (90% - four visits). Intention to treat analysis used descriptive and inferential statistics. OMT subjects reported significant improvement in pain (p\sc65.05) and RMQ scores ($p<.05$) compared to routine-care-only. Analysis of between-group differences found that the groups were similar in restricted duty time and medications. Subjects in the non-OMT group reported a significantly stronger belief in routine care alone for improving pain compared to the OMT group. When controlling for patient expectation scores, there were no differences between the two groups on "pain now" or on RMQ scores at visit 4 or at 2 months. Military personnel miss time from duty for musculoskeletal injuries more than for any other health condition. The findings from this study provide important information about the efficacy and feasibility of using OMT to restore peak performance f in military personnel with ALBP.

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Editor's Note: Corrections to abstract P3 were published in the September 2008 issue of *JAOA—The Journal of the American Osteopathic Association* (2008;108:533). All corrections have been incorporated in this online version of the abstract, which was posted September 2008. An explanation of these changes is available at: http://www.jaoa.org/cgi/content/full/108/9/533.

♦P3

CV4 Alters Autonomic Balance During Paced Breathing

D.A. Ananyev, OMS-I[1], C. Rodriguez Jr., BS[1], R. Mercado[1], A. Bagla, OMS-II[1], M.A. Seffinger, DO, FAAFP[1], E.J. Wagner, PhD[2]
[1]Department of OMM, [2]Department of Basic Medical Sciences, WesternU/COMP, Pomona, Calif

Context: Compression of the fourth ventricle (CV4) has been shown to influence autonomic activity in several uncontrolled and non-randomized studies. It is unknown if the breathing rate influences these effects. This randomized controlled trial utilized paced breathing in the comparison of autonomic effects of CV4 OMT to sham (touch only).

Objective: To evaluate the effects of CV4 on autonomic balance in healthy subjects with standardized breathing rate.

Methods: Eighty healthy volunteer subjects (ages 20 to 65) gave informed consent to participate in the IRB approved study conducted in a temperature controlled room. Autonomic data was collected non-invasively from electrocardiogram (EKG) heart rate variability (HRV) and transcutaneous laser Doppler flowmeter (LDF) derived Traube-Hering (TH) wave measurements. LDF, EKG, and costal cage strain gauge respiratory rate measurements were collected while subjects lay supine on a padded table for three consecutive 7 minute periods: a resting baseline, an intervention (randomized CV4 or Sham, both provided by the same NMM/OMM specialist), and a post-intervention. Breathing was paced at .2 Hz (12 breaths per minute) via metronome to standardize the effects of respiration on heart rate and blood flow for all subjects. Data was analyzed with multivariate analysis and paired t-tests in SPSS.

Results: One tailed paired t-test analysis of LDF data showed that the CV4 ($p=.039$) vs. sham ($p=.175$) caused a significant decrease in TH signal power from pre to post-intervention. Once age was accounted for in the HRV data, multivariate analysis demonstrated significant differences ($p<.05$) in CV4 vs. sham. Paired t-test analysis of the HRV variables showed two-tailed significant differences ($p<.025$) in various HRV measures from CV4 but not sham interventions. Although from baseline to post-intervention both CV4 and sham indicated significant changes ($p<.025$) in average heart rate (HRave) and average time between consecutive R signals (RRave), only CV4 showed significant changes ($p<.025$) in standard deviation of the average of R to R intervals (SDANN), root means squared of successive differences between R-R intervals (RMSSD), number of R-R intervals greater than 50 milliseconds (NN50), and the number of NN50 divided by the total number of R-R intervals (pNN50).

Conclusion: The CV4 OMT procedure causes significant autonomic changes as measured by the LDF and EKG. These changes are unrelated to breathing rate or age.

P4

The Effect of Learning Strategies on Mastery of Palpation With the Virtual Haptic Back (VHB)

J.N. Howell, PhD[1], R.R. Conatser, MS[1], K. Bajaj, MS[1], D.C. Eland, DO[2], R.L. Williams, PhD[3]
[1]Institute for Neuromusculoskeletal Research, OUCOM, Athens, OH, [2]Department of Family Medicine, OUCOM, Athens, OH, [3]Department of Mechanical Engineering, Russ College of Engineering and Technology, Athens, OH

As part of their OMM course, two groups of medical students at the Ohio University College of Osteopathic Medicine were required to practice palpatory diagnosis on the VHB during the fall of 2006 and of 2007. The practice took place during the first 3 months of their medical training and consisted of 6 sessions, in which students identified regions of abnormal tissue texture on a haptically simulated virtual back. Details of the VHB have been published (*JAOA* 2008;108:29-39, *BMC Medical Education* 2008;8:14). The strategy used in 07 was different than that used in 06. In 06 students (N=89) were permitted to set the difficulty level in each trial. Some students proceeded voluntarily to the hardest levels, while others were content to restrict their attempts to easier levels. In 07 (N=104) the level of difficulty was automatically raised when the student had demonstrated mastery at any given level and was automatically lowered if, after 10 trials, the student had not achieved mastery. The criterion for mastery at any of the 10 difficulty levels was 3 correct identifications in a row or 6 correct out of 10 trials. We hypothesized that performance on the VHB might improve faster in 07 with the program pushing students to the limit of their performance ability. Performance profiles for the two years were similar, showing improved accuracy and speed in each of the 6 successive practice sessions. An overall trend toward better performance in 07 appeared, but only in the second session was the difference statistically significant ($P<.05$). The average level of precision achieved by the class at the end of the training sessions, represented by the Weber fraction (the smallest % difference in compliance successfully detected), was 14% in 06 and 13% in 07 (not significantly different), although a greater fraction (21%) of the 07 students were able to discriminate 7% differences than the 06 students (11.2%). The percentage of students rating the exercise as of definite value was 40% and 41%, and of possible value, 54% and 54%, in 06 and 07 respectively. The performance similarity between the two years suggests that the altered strategy of the program made little difference in improvement of palpatory performance or in student satisfaction. For most students the degree of mastery may not be strongly dependent upon their pushing themselves to the limit of their palpatory abilities throughout the practice sessions.

Acknowledgment: Sponsored by the Osteopathic Heritage Foundation.

♦Indicates posters entered in the Student Prize Competition, a judged event that takes place during the Poster Session at the Research Conference.

♦P5

The Use of Osteopathic Manipulation to Address Pulmonary Distress as Related to Asthma in Southwest Virginia

M. L. Latter, DO
VCOM, Blacksburg, VA

Background: Osteopathic Manipulative Therapy (OMT) is underutilized in addressing lung function and symptoms in asthma patients. The objective of this study is to determine if a single session of OMT can improve lung function and symptoms in patients suffering from asthma in order to develop a protocol by which physicians can use to apply OMT to address lung disease in patients. This was a randomized controlled quasi-experimental study which took place in family practice, pulmonology, and asthma specialist offices in southwest Virginia. Thirty-two participants aged 6 to 56 with asthma were recruited. The intervention was a 10 minute semi-individualized OMT protocol. Outcome measures were lung function and symptoms as displayed by spirometry, thoracic excursion, and a symptom rating scale.
Methods: Once IRB approval was obtained, variable baseline, within-subject study design was utilized allowing each person to serve as their own control. After informed consents were signed, pre and post test measurements include: participant spirometry FEV1, FVC, and PEF, and thoracic excursion upper and lower rib cage motion, and a five question survey with a rating scale to determine current asthma symptoms. A 10 minute OMT session included an individualized thoracic and rib screening and treatment with soft tissue, muscle energy, or facilitated positional release, suboccipital release, diaphragm release, and thoracic pump. Comparison between pre and post OMT lung function and symptoms portrayed change.
Results: Statistically significant ($p<.05$) improvements after initial OMT were documented for 8 out of 10 measurements. Only two spirometry values, FEV1 and PEF, did not significantly improve. However, many of the participants were in advanced treatment for asthma, thus higher spirometry values limited potential elevation values.
Conclusions: With a simple, easy to repeat, 10 minute semi-individualized OMT session, researchers demonstrated improved lung function and symptoms in this group of participants in Southwest Virginia. Future studies expanding on this pilot study should further explore this finding. In future studies, the researchers recommend using a larger patient population including patients with lower pre treatment spirometry values in order to accurately monitor potential for change.

♦P6

Osteopathic Manipulative Medicine in the Treatment of Acute Otitis Media Symptoms

J.W. Torres, OMS-II[1], D.C. Mason, DO, FACOFP[2], J. Kaari, DO[3]
[1]UMDNJ-SOM, Stratford, NJ, [2]Department of Osteopathic Manipulative Medicine, UMDNJ-SOM, Stratford, NJ, [3]Department of Pediatrics, UMDNJ-SOM, Stratford, NJ

Hypothesis: It is generally accepted that a primary cause of Otitis Media is dysfunction of the eustachian canal, with an effusion. The eustachian canal is lined with respiratory mucosa, and directly connects the middle ear to the nasopharynx. The intimate relationship between myofascial structures has already been demonstrated. It has been postulated that fascia not only surrounds, but also interacts with and impacts, every structure within the body, including the eustachian canal. Ergo, by treating this fascia, we will also impact the eustachian canal, ideally optimizing its function in reducing pressure in the middle ear, and improve the functioning of the tympanic membrane.
Materials: We incorporated the use of tympanograms to measure middle ear parameters, as well as a pain visual-analog scale and a survey to gather pertinent past medical history.
Methods: After gaining IRB approval, we enrolled 10 patients between the ages of 3 and 12, and randomly assigned them to either the treatment or the sham group. After obtaining parental consent, we gathered data prior to treatment and five minutes following treatment via the surveys and the tympanogram. The treatment consisted of a strain-counter-strain technique directed at a tenderpoint over the OA for 90 seconds. The sham treatment consisted of placement of fingers around the ear, and holding for 90 seconds.
Results: The data shows a very strong correlation between patients having a diagnosis of acute otitis media and the presence of a tenderpoint at the OA, ipsilateral to the affected ear. The active group demonstrated resolution of this tenderpoint, while the control group showed no change. Furthermore, patients in the treatment group demonstrated an increase in their maximum tympanic membrane compliance, (t, $p<0.03$), indicating improved tympanic membrane function. The treatment group also showed significant changes, indicating a decrease in middle ear pressure within five minutes following treatment, (t, $p<0.05$). This change is consistent with the drainage of the middle ear through the now patent eustachian canal.
Conclusion: This study illustrates a strong correlation between strain-counter strain treatment of an OA tenderpoint in pediatric patients with acute otitis media, and the improvement in drainage from the middle ear via the eustachian canal. A decrease in middle ear pressure was also demonstrated in the treatment group, which is consistent with improved eustachian canal function.

♦Indicates posters entered in the Student Prize Competition, a judged event that takes place during the Poster Session at the Research Conference.

♦P7

Assessing Educational Impact of Osteopathic Pre-doctoral Teaching Fellows

B.M. Cross, OMS-IV[1], R. Villanueva, OMS-IV[1], J.C. Glover, DO, FAAO[1], R.M. Hiserote, DO[1], G. Davis, MS[2]
[1]Department of OMM, TUCOM-CA, Vallejo, CA, [2]Department of Clinical Education, TUCOM-CA, Vallejo, CA

Background: The incorporation of pre-doctoral teaching fellows in the department of Osteopathic Manipulative Medicine (OMM) at Touro University (TUCOM-CA) began in the spring semester, 2007. The OMM fellows interacted with 1st and 2nd year students by hosting review sessions, assisting in OMM lab, giving 4 lectures and preparing review summaries for exams.

Hypothesis: The incorporation of pre-doctoral fellows into the OMM department demonstrates a favorable impact based on subjective and quantitative student evaluation.

Methods: An evaluation survey was administered to 270 students from the class of 2009 & 2010 in May, 2007. Agreement with items relating to attitudes toward OMM practice, and beliefs about the value of teaching fellows in course performance was measured on a 7 point Likert scale ("Strongly Disagree" to "Strongly Agree") with 3.5 representing "No Opinion". The mean response score, standard deviation and 95% confidence interval for each question was determined. Response rate was 54.8% with 148 surveys collected. IRB approval was obtained.

Results: Student responses show 94% agreement that the pre-doctoral fellows increased knowledge of Osteopathic techniques (mean response (MR) 4.97±0.39), with 72% agreement that working with fellows increased the time spent practicing OMM outside of class time (MR4.23±0.40). Secondly, 88% agreed that their knowledge of Osteopathic theory improved (MR4.99±0.42), and 51% agreed that exposure to fellows increased time spent studying OMM theory (MR3.82±0.39). 75% of students felt their grades on OMM lab practicals improved (MR4.36±0.41), while 54% agreed with an improvement grades in OMM theory (MR3.97±0.40). 79% of respondents agreed that working with OMM fellows increased their knowledge of applying OMM to clinical problems and improved their interest in integrating OMM into patient management (MR4.37±0.44; MR4.63±0.46). In a subgroup analysis of 70 respondents, however, no statistical significance was found in correlating change in OMM grades to exposure time with OMM fellows. This aspect of the study was limited by study design and sample size.

Conclusion: Students believed most strongly that interacting with teaching fellows led to increased knowledge of OMM techniques and theory. The generally positive response to all items leads us to believe that students believe the teaching fellowship is beneficial. Further investigation into change in grades and exposure to OMM pre-doctoral fellows is warranted.

P8

More Consistent Inflammation in Sprague-Dawley Rats Using Carrageenan Versus Capsaicin

C. Fossum, DO (Europe)[1], N. Sargentini, PhD[2], V. Singh, PhD[2], B.F. Degenhardt, DO[1]
[1]A.T. Still Research Institute, A.T. Still University, Kirksville, MO, [2]Department of Microbiology and Immunology, A.T. Still University, Kirksville, MO

Aim of investigation: To develop an animal model of acute inflammatory pain to investigate the short-term effect of manual treatment

Methods: Two different rat strains (Sprague-Dawley and Lewis rats) were used to identify a suitable model to consistently produce acute inflammatory pain. Both capsaicin and carrageenan were tested for their consistency to induce an acute inflammatory response in the ankle joint within 24 hours post injection. The assessment of acute pain was made by observation of the cardinal signs of inflammation consisting of redness, swelling and pain response assessed by determining the withdrawal response using Von Frey monofilaments applied to the hind paws.

Results: While joint swelling was present due to the increased intra-articular fluid volume from injection, the injection of capsaicin did not produce a consistent pain response in either the Sprague-Dawley or the Lewis rats within a 24 hour period post injection. While both strains of rats consistently demonstrated the cardinal signs of inflammation at 24 hours, the Lewis rats were less responsive than the Sprague-Dawley rats.

Conclusions: Although other laboratories have established rat models of acute nociceptive pain, our experiments indicate that researchers' needs to assess the validity of previously reported models in initiating a new line of research in acute nociceptive pain. Although capsaicin is commonly used to induce acute nociceptive pain, our experience indicates it is less effective than carrageenan in producing a consistent inflammatory response within 24 hours post-injection.

P9

Comparing Objective Characteristics of Lumbar and Sacral Somatic Dysfunction Between Low Back Pain and Control Subjects

B.F. Degenhardt, DO, J.C. Johnson, MA, Q. Yang, MS
A.T. Still Research Institute, Kirksville, MO

Aim of Investigation: To determine and compare objective positional asymmetry and motion characteristics in the lumbar and sacral regions of subjects with and without subacute/chronic low back pain (LBP).

Methods: The LBP group had a self-reported history of pain (at least 4 on a 0-10 numerical pain scale) in the lower back region for a minimum of five days a week for at least four weeks. The non-LBP, control group had no history of pain in

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the lower back region. A blinded neuromusculoskeletal medicine specialist evaluated all subjects, performing a standardized diagnostic protocol evaluating the lumbar and sacral regions. A pressure sensor pad (pressure sensing range of 0-5 kg/cm^2; XSensor, Sensor Products, Cherry Hill, NJ) was used to assess pressure and force when performing lumbar segmental motion and sacral springing tests evaluating motion at each quadrant. Reflective markers placed on standardized hand landmarks were used with a 3-D infrared camera system (Vicon Motion System Inc., Lake Forest, CA) to quantify displacement of landmarks during motion testing. Local IRB approval was obtained.

Results: 42 subjects (31 female, 11 male), age range 20-50 (36.0±11.4), participated in the study, 35 with LBP and 7 controls. In both groups, L1–L4 had the right transverse process anterior and preferred rotation to the left. There were statistically significant greater forces applied to the left transverse process for 50% of the spinal segments tested. For the sacral base, the right side was consistently anterior in both groups. Sacral base motion testing showed slight but not significant increased tendency of greater motion on the left side. The sacral inferior lateral angles (ILAs) were posterior and inferior on the left. In the LBP group, the left ILA was most often restricted. Overall, there was no difference between the groups on the forces used at all testing sites.

Conclusions: Characteristics of somatic dysfunction were objectively quantified but were not significantly different between the LBP and control groups. Findings do not support commonly held compensatory models of lumbar and sacral somatic dysfunction except for sacral landmark asymmetry and ILA motion. Additional research using objective measures is necessary to further substantiate these somatic dysfunction characteristics.

Acknowledgment: This grant was funded by the American Osteopathic Association (06-04-550).

Clinical Studies

♦C1

Presentations of Coccidioidomycosis in the Emergency Department

A.D. Moffat, OMS-II, F. LoVecchio, DO
Midwestern University/AZCOM, Glendale, AZ

Introduction: Patients with the fungal infection coccidioidomycosis often have non-specific symptoms that delay their diagnoses. The purpose of this study was to characterize presentations of coccidioidomycosis in the Maricopa Medical Center Emergency Department (ED) over a 5 year period.

Methods: Following IRB approval, a retrospective chart review of all patients presenting to the ED from 1/2002 to 1/2007 was performed. ICD-9, Billing records, and microbiologic culture records were reviewed for pertinent diagnosis. These charts were examined by a trained reviewer and a second reviewer validated the findings. Charts were incorporated if they included coccidioidomycosis as a diagnosis.

Results: From a pool of approximately 450,000 patients, 44 fit the inclusion criteria. The most common symptoms of coccidioidomycosis presenting to the ED were respiratory (58.7%), gastrointestinal (46.7%), and musculoskeletal (44.4%) in nature. Other lesser manifestations included the nervous and integument systems, fever, as well as post-operative and injurious infections. HIV patients presented with more respiratory, gastrointestinal, and fever complaints, while non-HIV patients with more musculoskeletal and disseminated skin problems. Age between the two groups was found to be similar and seemingly not a major factor. It was also noted that 51.1% of all the patient cases were chronic.

Conclusions: Overlooking coccidioidomycosis as a differential in the ED is common and the diagnosis is often delayed. The prevalence of the disease is not limited to HIV patients, or the elderly, and that more than half of patients are chronically infected.

♦C2

Outcomes of Clostridium Difficile: A Surgical Perspective

A. McCague, OMS-IV, J. D'Emilia, MD
Department of Surgery, UMDNJ-SOM, Stratford, NJ

Objective: Clostridium Difficile infection is a changing entity with increased incidence, increased mortality, changed clinical presentations and changing treatment options. Patients consulted by a surgical service face additional challenges and are often sicker patients. Here we investigate what variables lead to an increased or decreased mortality.

Methods: A retrospective chart review was performed on patients with positive Clostridium Difficile toxin assays who were consulted on by the Department of Surgery between 2001 and 2006. Data from 49 patients was included in the statistical analysis of the data.

Results: Forty-nine patients were included in the analysis. Of these patients 10 (20.8%) resolved without surgery, 18 (37.5%) resolved with surgery, 10 (20.8%) expired after surgery and 10 (20.8%) expired without surgical intervention. An ANOVA was performed revealing age (p-value: 0.066), peak WBC (p-value 0.033), and musculoskeletal comorbitities (0.084) as significant variables in predicting death regardless of surgical intervention. A Bonferroni analysis for Multiple Comparisons confirmed that peak WBC is significant in determining outcome with p-value of 0.017. Age and peak WBC were further analyzed by running a Receiver Operating Characteristic and later the Chi-squared and Phi scores were used to determine a cut-off value for each. Using a cut off value for peak WBC of 28 gives a sensitivity of 65%, specificity of 82.1% and a mortality rate of 72.2%. For age, a cut off of 65 gives a sensitivity of 85% and a specificity of 46.4% and a mortality rate of 53.12%. Those patients who

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had both a WBC greater than 28 and age greater than 65 had a mortality rate of 86.7%. The overall morality rate for patients consulted by the Department of Surgery having a diagnosis of Clostridium Difficile infection was 40.8%.
Conclusions: Based on our analysis of patients with Clostridium Difficile infection consulted on by the Department of Surgery at our facility we recommend more aggressive treatment for patients with age greater then 65 and a white blood cell count greater than 28. The increase in mortality seen in patients with these values is significantly higher than that of other patients.

♦C3

Investigating Habit Reversal Techniques as a Treatment Option for Reducing Pain in Chronic Headache Sufferers

C.C. Ryen, BA, OMS-II, A.H. Hanson, BS, OMS, A.G. Glaros, PhD
KCUMB Student Summer Research Fellowship, Kansas City, MO

Aims: Patients with temporomandibular disorders (TMD) and those with headache show high levels of tooth contact. TMD patients report relief from pain with a form of behavioral modification called habit reversal, designed to reduce tooth contact. This trial tested the efficacy of habit reversal as a treatment for those suffering from headaches and received IRB approval from KCUMB.
Methods: Headache patients who participated in a study which investigated the relationship between tooth contact and headache pain were allowed to participate in this clinical trial. Those who accepted the invitation (N = 20) signed an informed consent form and were randomly assigned to a HABIT REVERSAL group or WAIT LIST control group. During the habit reversal session, patients were given information (1) about facial pain and headaches, (2) about the role of oral behaviors headaches; (3) about possible treatments for reducing headaches; and shown how (4) tooth contact can affect the activity of the masticatory muscles (using biofeedback); and (5) to reduce masticatory muscle activity. A "DTMD" approach was used in which subjects were instructed to use external signals from a pager and other cues to Drop their jaws; separate Teeth the width of a pencil; relax Muscles; and breathe Deeply. All individuals completed headache diaries and response cards using experience sampling methods (ESM).
Results: Subjects reporting high levels of tooth contact were included in the analysis. These results include data from formal headache questionnaires, patient examinations by a blinded investigator, and ESM card data. The results showed that patients assigned to the habit reversal group showed significantly ($p<.05$) greater reduction in tooth contact than those in the wait list. Although both groups showed significant reductions in facial pain, the habit reversal group's reduction was much more dramatic.
Conclusion: Treatment using behavioral modification in the form of habit reversal altered clenching behaviors, diminished facial pain, and decreased headache symptoms. The results were encouraging for the use of habit reversal as a treatment for headache pain. The overall power of this study is low due to the small size; further investigation is required using a larger sample of headache patients. Further studies showing that habit reversal was efficacious in reducing headaches could lead to less costly for headache patients.

♦C4

Women Who Continue Exercise During Pregnancy: Are We Missing Anything?

E.M. Smith, BA, OMS-III[1], E. Zare-Maivan, BS, OMS-III[2], L.E. May, PhD[2]
[1]KCUMB-COM, Kansas City, MO, [2]Department of Anatomy, KCUMB-COM, Kansas City, MO

Context: Although there is plethora of research stating the safety and benefits of exercise during pregnancy, the majority of healthy pregnant women choose not to exercise.
Hypothesis: We conducted a survey to determine women's exercise before and during pregnancy, why they chose to engage or not in exercise and self perception of their health. This information will assist physicians in providing better care for mother and child.
Materials and Methods: This project was approved by the IRB committee at KCUMB-COM. Questionnaires were placed in several clinics for three months with an attached cover sheet explaining the purpose of the study, contact information, and an explanation that every question on the survey was optional and could be left blank. There were 16 items on the survey and it was designed to be easy to read and take about ten minutes to complete. General demographic and socioeconomic information was obtained but no personal identifiers. If women were not involved in exercise during pregnancy then they could choose up to eight reasons why they were not active. The average time spent doing common physically active and sedentary daily tasks were included. Each questionnaire was scanned and read by Teleform software. The electronic versions of the questionnaires were then validated by the computer software and the investigator. All data are stored on a password protected computer in a locked room.
Results: The average age of the 224 pregnant women in this study was 28.07 ± 5.61 years. The participating women represent a normal distribution of ethnicities, education levels, and socioeconomic status. Interestingly 60.7% report their physician has talked to them about the benefits and risks of exercise, but only 40.5% have been instructed by their physician on how to exercise. Prior to pregnancy 63.6% reported exercise activity, but only 22.3% continued exercise during pregnancy. Although 71.2% of women reported watching television for 1 or more hours per day, the reasons given for not exercising were: lack of time (33.3%), 'other' (16.4%),

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and not knowing why they did not exercise during pregnancy (12.2%).

Conclusions: This study begins to tell physicians *why* pregnant women decide not to exercise. In order for the osteopathic physician to help pregnant clientele stay healthy and active during their pregnancies, they need to educate their patients how to exercise during pregnancy and the benefits of such.

♦C5

Daily Genistein Injections Stimulate Intestinal Chloride Secretion in Male But Not Female Mice via Estrogen Receptor-Dependent Mechanisms

J. Jensen, OMS-III, N.E. Hale, OMS-III, MS, L. Batia, BS, L. Al-Nakkash, PhD
Department of Physiology, Midwestern University/AZCOM, Glendale, AZ

Intestinal chloride (Cl) secretion in male and female mice (C57BL/6J) was determined following injection with either 600 mg/kg genistein/day (600G) or genistein-free (0G, DMSO vehicle control) for either 1 or 2 weeks. After injections, jejuna were isolated and intestinal Cl secretion measured with Ussing chamber short circuit current (Isc, $\mu A/cm^2$). After 1 week basal Isc was significantly increased in females injected with 600G (198.8 ± 18.9, n=6, $P<0.05$) compared to 0G (128.3 ± 12.8, n=4). Basal Isc was significantly increased in males injected with 600G (183.6 ± 7.6, n=7) compared to 0G (100.8 ± 18.2, n=7) only after 2 weeks. Cl-free ringer reduced the basal Isc by 55%, suggesting a major Cl component. Forskolin-stimulated Isc (10μM bilateral) was significantly increased ($P<0.05$) in both female and male mice injected with 600G compared to those injected with 0G (n=4-9). Similar data were obtained after 2 weeks of injections. The estrogen-receptor antagonist ICI-182780 (25 mg/kg body weight) concomitantly injected with 600G for 2 weeks, significantly decreased basal Isc in males (by 52%, n=3, $P<0.01$) but not females (by 5%, n=4). Villi length and crypt depth were similar in males and females injected with 600G or 0G. These data suggest that male and female mice respond similarly to 600G (longer duration for males), but the effects are mediated via different mechanisms.

Acknowledgment: Jeese Jensen was supported by the Midwestern University Summer Fellowship Program. Nathan Hale was supported via work study. Layla Al-Nakkash was supported by CFF (ALNAKK06P0) and NIH (1R15DK071625-01A2).

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C6

Initiating Pharmacotherapy for Type 2 Diabetes: Better Glycemic Control and Weight Reduction with Liraglutide, a Once-Daily Human GLP-1 Analog, Compared With Glimepiride When Used as Monotherapy

J.S. Freeman, DO[1], P.M. Hale, MD[2], C.T. Chang, PhD[3], B.W. Bode, MD[4], A.J. Garber, MD, PhD[5]
[1]Division of Endocrinology, Philadelphia College of Osteopathic Medicine, Philadelphia, PA, [2]Department of Clinical Pharmacology & Research, Novo Nordisk Inc, Princeton, NJ, [3]Department of Statistics, Novo Nordisk Inc, Princeton, NJ, [4]Department of Endocrinology, Atlanta Diabetes Associates, Atlanta, GA, [5]Department of Endocrinology, Baylor College of Medicine, Houston, TX

Background: GLP-1 receptor agonists, a new class of antidiabetes drugs, stimulate insulin secretion only during hyperglycemia. Liraglutide (lira) is the first human GLP-1 analog. In contrast, sulfonylureas are non glucose-dependent and associated with increased risk of hypoglycemia and weight gain.

Objective: Compare efficacy and safety of lira or glimepiride (glim) monotherapy once daily for 52 wks in subejects with type 2 diabetes (T2D) previously prescribed lifestyle modification.

Methods: Data from a prespecified group (n=272) treated in a randomized, double blind, double dummy, active control trial comparing lira (1.2 or 1.8 mg) to glim (8 mg) were analyzed: mean age: 51 y; disease for 4.3 y, and 73–80% White. Trial was IRB approved.

Results: Lira therapy for 1 yr caused substantial and durable A1C, FPG, PPG (1.8 mg) and weight reductions compared to glim. Considerably more subjects reached A1C targets with lira, while minor hypoglycemia, measured as PG<56 mg/dL, was much lower. While nausea was higher with lira, it generally occurred during week 1 and dissipated within 16 weeks. *(See table facing page.)*

Conclusion: Lira was significantly more effective in improving glycemic control and reducing weight with less hypoglycemia compared with a maximal dose of glim in subjects with T2D not responding to lifestyle modification.

Acknowledgment: Supported by Novo Nordisk.

♦C7

Location of Out-of-Hospital Cardiac Arrests in Manatee County Florida

M. Frank, OMS-IV, A. Moradi, MD, MPH
Department of Public Health, Lake Erie College of Osteopathic Medicine, Erie, PA

Context: Cardiac arrest is a medical emergency that, in certain groups of patients, is potentially reversible if treated early enough. Sudden cardiac arrest mortality is estimated to be about 400,000 lives annually in the United States. Two thirds of unexpected cardiac deaths occur without prior recognition of cardiac disease and about 60 percent of unexpected cardiac deaths are treated by emergency

Variables (ITT, LOCF)	Liraglutide 1.2 mg n=91	Liraglutide 1.8 mg n=87	Glimepiride 8 mg n=94
Baseline A1C, % (SD)	8.43 (1.29)	8.59 (1.29)	8.59 (1.25)
Final	7.23 (1.47)	6.95 (1.24)	7.72 (1.28)
Change from baseline	–1.19 (1.40)*	–1.60 (1.29)**	–0.88 (1.23)
% A1C <7.0%	58*	62**	31
% A1C <6.5%	44**	49**	15
Baseline weight, kg (SD)	92.0 (19.0)	90.4 (19.4)	96.4 (18.1)
Final	90.5 (19.0)	88.6 (19.3)	97.8 (18.3)
Change from baseline	–1.88 (4.26)**	–1.75 (3.91)**	+1.46 (3.88)
Baseline FPG, mg/dL (SD)	179.2 (48.8)	188.3 (50. 9)	185.1 (47.3)
Final	148.0 (53.5)	141.6 (40.8)	168.7 (49.8)
Change from baseline	–31.5 (46.0)*	–45.4 (49.3)**	–15.1 (56.3)
Baseline mean PPG, mg/dL (SD)	214.2 (48.6)	218.8 (48.9)	215.2 (53.4)
Final	170.3 (47.6)	158.6 (35.2)	179.7 (44.7)
Change from baseline	–44.9 (49.1)	–52.5 (41.2)*	–36.8 (60.1)
% reporting minor hypoglycemia	8.8*	12.6*	25.5
Events/subject/ year	0.22*	0.43*	1.87
% reporting nausea	28*	30*	10

*p<0.05 or **p<0.0001 vs. glimepiride (ANCOVA or logistic regression). FPG: fasting plasma glucose; PPG: postprandial plasma glucose. Data are mean (SD).

medical services (EMS).

Objective: To identify the type of location of out-of-hospital cardiac arrests (OHCA) in Manatee County Florida to aid the determination of automated external defibrillator (AED) placement in areas of most common occurrence.

Methods: Retrospectively, the Manatee County Emergency Medical Service (EMS) database storing all EMS call reports was searched for cardiac arrest. Data for a 22-month period was obtained. Cardiac arrests were categorized into two categories. Those occurred in a private residence and those occurred outside of a private residence. The cardiac arrests that occurred outside of a residence were then subcategorized according to the type of location.

Results: In the 22-month period, 1085 OCHAs occurred in Manatee County. There was no information regarding the type of location for 119 (11%) arrests, these were excluded, leaving 966 OHCAs. Private residence accounted for 690 (71%). Non-private residence accounted for the remaining 276 (29%). The 276 non-residential OHCAs were further subcategorized. Nursing facility 167 (17.3%), a roadway 33 (3.4%), an office/business/restaurant/bar 14 (1.5%), a clinic/physicians office 9 (0.93%), public /wilder ness/recreational areas 23 (2.4%), beach 2 (0.2%), and religious facility 4 (0.41%). The remaining 24 (2.5%) non-residential OCHAs were documented on the EMS chart as having occurred in "other".

Conclusion: Unsurprisingly, the majority of OHCAs were found to have occurred in a private residence, while less than one-third occurred out of a private residence. The majority of non-residential OHCAs occurred in nursing facilities, followed distantly by roadways. The focus of this study was to identify the type of location of OHCAs to aid in the determination of automated external defibrillator (AED) placement.

C8

Effect of OMT in the Treatment of Initial Vascular Wall Alteration

F. Cerritelli, DO[1], F. Carinci, MS[2], G. Barlafante, DO, MD[2], G. Pizzolorusso, DO[2], P. Turi, DO[2], V. Cozzolino, DO, MD[2], C. Renzetti, DO, MD[2], F. Pizzolorusso, DO[2], F. Orlando, DO[2]
[1]Research Department, AIOT, Pescara, IT, [2]Research Department, AIOT, Pescara, Abruzzo

Hypothesis: Research studies document the relationship between vessels wall alterations and the modification of cardio-circulatory functions, as well as the association between a change of the endothelial carotid wall, hypertension and the occurrence of cardiologic events. So far, the efficacy of osteopathic treatment on the improvement of cardiovascular function concentrated has never been tested. Aim of the present study is to investigate the existence of an association between osteopathic treatment and intimae media thickness in terms of intermediate outcomes of long-term cardiovascular disorders at 12 months follow-up.

Materials and Methods: Non-randomized trial, including a treated and control group of consecutive subjects resulting affected by vascular alterations at a cardiologic visit. Individual characteristics, including intimae media thickness, height, weight, rest rate, and use of prescribed drugs, were measured at entry and after 12 months follow-up. Osteopathic treatment was administered by a group of osteopaths. Pre-post differences at 12-months in intimae media thickness were used as primary endpoints. Statistical analysis was performed using univariate t tests and multivariate linear regression.

Results: Out of a total of 63 patients entering the study, 31 were administered osteopathic treatment and followed up for 12 months. Univariate statistical analysis showed no significant imbalances among treated and control groups in terms of main characteristics measured at baseline. At the end

of the follow-up, heart rate and osteopathic treatment were significantly associated to change in intimae media thickness. All the factors, including a change in pre-post measurements of main endpoints, were used as potential confounders in a multivariate linear regression. After adjusting for all such characteristics, osteopathic treatment was found to be significantly and independently associated to a change in intimae media thickness (mean difference between change in treated and control groups: -0.602; 95%c.i.:-0.745 – -0.459).
Conclusions: Our study, targeting a selected population of patients affected by cardiovascular disorders, shows that after a one-year follow-up, as measured by main clinical parameters, osteopathic treatment is independently associated to an improvement in intimae media. However our approach, mainly exploratory and hypothesis generating, should be further extended to avoid the potential bias induced by the particular study population.

C9

Maternal and Neonatal Outcomes in Pregnancies Complicated by Nasopharyngeal Carriage of Methicillin Resistant Staphylococcus Aureus (MRSA)

R. Patel, DO
Department of Maternal Fetal Medicine, Rockford Health System, Rockford, IL

Objective: MRSA infections have increased significantly over the past decade. Routine screening of patients for MRSA upon hospital admission is increasing. The objective of this study was to determine if there was a correlation between positive screen results and increased risk of adverse maternal and / fetal outcomes and MRSA status.
Study Design: All pregnant patients admitted to our institution have MRSA screening via nasal swab as part of the admission protocol. A 4 month retrospective chart review was performed. MRSA carriage rates were computed. Newborns to mothers who were screen positive received nasal and umbilical MRSA swabs. NICU admissions and neonatal sepsis workups were noted. Maternal postoperative infections were noted. APGARS at birth were compared with a control group which comprised the 2 neonates delivered after the neonate in the control group.
Results: A total of 562 patients were tested. 19 patients tested positive for an overall incidence of 3.4%. 14 of the 19 patients delivered at our institution. 5 patients were excluded. 4 patients were preterm and discharged home. 1 patient had an early miscarriage. There were no positive neonatal MRSA screens. There were no 5-minute APGAR scores < 7. There was not a statistical difference in 1 or 5 minute APGAR scores between the 2 groups. There were 3 NICU admissions, with 1 sepsis workup which was negative. There was 1 postoperative patient treated with prophylactic antibiotics, admitted with hematoma attributed to over anticoagulation with Coumadin.
Conclusions: Maternal nasopharyngeal carriage of MRSA was not associated with adverse maternal and neonatal outcomes. Further studies are needed with a larger group of patients to help determine optimal management of MRSA positive patients in pregnancy. Future studies will attempt to correlate nasal MRSA carriage with vaginal MRSA carriage.

♦C10

Telesonography Adoption and Use to Improve the Standard of Patient Care Within a Dominican Community

J.E. Sutherland, DO[1], H.D. Sutphin, PhD[2], K.J. Redican, PhD, MPH[3], J.K. Burton, PhD[3], F.A. Rawlins, DO[4]
[1]Virginia College of Osteopathic Medicine, Blacksburg, VA, [2]Department of International Outreach, Virginia College of Osteopathic Medicine, Blacksburg, VA, [3]Department of Education, Virginia Polytechnic Institute and State Univ., Blacksburg, VA, [4]Department of Emergency Medicine, Virginia College of Osteopathic Medicine, Blacksburg, VA

Overview: The role of teleradiology has far reaching implications for the health of remote and underserved populations. The ability to coordinate radiographic evaluation and diagnosis from a distance has the potential to raise the standard of patient care throughout the world. Perhaps the safest and most cost effective mode of teleradiology today is telesonography. The current project attempts to determine the extent that telesonography improves the standard of care within a rural government-run primary clinic within the Dominican Republic.
Hypothesis: The use of a store-and-forward telesonography system in this setting will improve the standard of patient care by increasing the number and speed of sonographic reports successfully returning to the referring physician while also increasing the number and speed of post-sonography patient follow-ups.
Methods: Participants were randomized into experimental and control groups over a 9-week implementation period. The experimental group received the telesonography service and the control group received traditional ultrasound consults.
Materials: Consent Form, Request for Interpretation (RFI) Form, Sonosite Titan portable ultrasound with SiteLink Image Manager 2.2, Dell and Apple laptop computers with wireless Internet connectivity and Irfanview 3.31, DSL Internet connection with wireless router.
Sample: A convenience sample of 100 low-income Dominican and Haitian patients 13 years old or greater that utilize the primary care clinic of Veron, Dominican Republic.
Results: The telesonography system implemented during this study along with patient awareness of such a system provided a 4-fold increase in the proportion of patient follow-ups, 6-fold increase in the proportion of returned radiological reports, and delivered those reports to the referring physi-

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cian 6-times faster than the was recorded in the control group.
Conclusion: The telesonography system utilized in this study, while having no appreciable effect on the elapsed time to post-sonography patient follow-up, provided an increase in the number of post-sonography patient follow-ups while simultaneously increasing the number and speed of delivered sonographic reports to the referring physician. Future research should focus on the sustainability of a telesonography system in this setting and its long-term effect on patient outcomes.

C11

Severity and Recurrence of Menstrual Migraine Treated With Patient's Usual Migraine Therapy: An Intrapatient Analysis

T. Victor, PhD[1], B.L. Peterlin, DO[2], X. Hu, PhD[1], Q. Xiang, PhD[1], R.A. Puenpatom, PhD[1], W. Chen, MPH[1], J. Campbell, BSc[1]
[1]Endo Pharmaceuticals Inc., Chadds Ford, PA., [2]DUCoM Headache Clinic, Philadelphia, PA

Hypothesis: Women have a 3-fold higher prevalence of migraine (vs men) and 50%-60% of female migraineurs have migraines associated with menses (menstrual migraine [MM]). Research suggests that MM is longer, more severe, has more symptoms, and is harder to treat than non-MM. This intrapatient subanalysis evaluated severity and recurrence of MM and non-MM in women using their usual migraine therapy.
Materials and Methods: Data were derived from an IRB-approved open-label study in which women (N=153) treated all migraines with their usual care for 1 month (included 1 menses). Maximum pain severity per episode and recurrence rate according to migraine type (MM and non-MM) was assessed using within-patient data. MM occurred between days –2 to +3 (inclusive, menses start=day 1) and non-MM occurred before day –2 or after day +3 relative to menses. A migraine episode encompassed the time from treatment initiation until pain-free response or use of additional medication. Severity was scored as no, mild, moderate, or severe pain. Recurrence per episode was defined as return of headache of any severity within 24 hours after a pain-free response at any time. Mathematical modeling determined the sources of variability for severity and recurrence and examined the intrapatient differences between the 2 migraine types.
Results: Women were predominantly white (88.2%) and had a mean (SD) age of 37.6 (8.4) years. They averaged 13.5 (6.8) MM per year and 2.6 (3.5) non-MM per month; 53% of women were using triptans as their usual care. Over 1 month, 212 (59.2%) MM and 146 (40.8%) non-MM episodes occurred. Of these, 130 were moderate or severe: 84 MM (64.6%) and 46 non-MM (35.4%). The odds of a higher category of severity were 1.65 times greater for MM than non-MM (P=0.03). There were 56 recurrences: 41 (73.2%) MM and 15 (26.8%) non-MM. The odds of MM recurrence were 2.66 times that of non-MM recurrence (P=0.01). Within-subject variation accounted for approximately 30% of the total variance in migraine severity (interclass correlation coefficient [ICC], 0.33) and recurrence (ICC, 0.27).
Conclusions: In women treating migraines with their usual care, including triptans, MM were more severe and recurrent than their non-MM episodes. These findings support previous research and highlight the need for effective treatment options for MM. The preponderance of variability in the outcomes (>70%) are not idiopathic in nature, suggesting that they are potentially treatable.

♦C12

Withdrawn

♦C13

A Retrospective Analysis of Reasons for Discharge from a Multi-Disciplinary Chronic Pain Center

H. Baye, OMS-II[1], M. Suarez, OMS-II[1], K. Gupta, DO[2]
[1]UMDNJ-SOM, Stratford, NJ, [2]Department of Pain Medicine, UMDNJ-SOM, Stratford, NJ

Background: It is common practice among pain clinics to implement an agreement which is signed both by the physician and patient. Agreements may state guidelines, goals for treatment, and most importantly rules of compliance. Establishing an honest patient-physician relationship early on is vital in successful pain management. Use of agreements has come about due to the addictive effects of opioid use. The reason for these stringent measures is due to inconsistent self-reporting given by patients on current drug use. This includes both prescribed drugs and illicit drugs. A literature review was conducted in the time frame of 1987-2007 on previous research of pain center discharge. It was found that no previous study was performed as of August 2007 detailing the reasons for discharge. Our study highlights the importance of maintaining strict guidelines in compliance with the opiate agreement.
Design/Methods: The following data is a retrospective chart review. It is a cohort study of the patients discharged from UMDNJ pain Center from 1999-2007. 614 charts were analyzed.
Setting: This research was performed within the UMDNJ multidisciplinary chronic pain center.

(continued on the next page)

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Results:

Table
Reason for Discharge from Pain Center

Reason for Discharge	Total	Percentage
Non compliance with agreement	225	40.1
Drug test positive for illegal substances	154	27.5
Patient received pain medications from another source	123	21.9
Drug test negative for prescribed medication	59	10.5

Conclusions: Our findings emphasize the importance of maintaining a strict adherence to the agreement signed by both patient and physician. Essentially the patient agrees to be compliant (abstain from alcohol, refute any pain prescriptions from another physician, and be prepared for random drug screenings) and the physician commits to providing the best pain management for the patient. Maintaining the following of pain agreement guidelines is important in giving patients the best care possible for improvement of their quality of life. A key finding was that 21.9% of the discharged patients received pain medication from another source including other physicians or family members. This establishes the importance of communication among the different physicians providing care, pain-related or not.

♦C14

Anatomical Correlates to Birth Order

B.J. Teran, OMS III[1], J.T. Martin, Dr. rer. nat[2]
[1]WesternU/COMP, Pomona, CA, [2]Department of Basic Medical Sciences, WesternU/COMP, Pomona, CA

Objective: Numerous studies in the psychological literature which have demonstrated correlations between behavior and birth order. In contrast, there are very few studies which examine the correlation between anatomical measurements and birth order. Sex differences exist in skeletal growth and these differences can be traced back to hormonal changes during the prenatal period. Sex steroids play a role in adult diseases such as diabetes and breast cancer, and these hormones also influence skeletal growth in childhood and adolescence. Demonstrating a relationship between anatomical variables and birth order would benefit our understanding of how prenatal endocrine activity influences adult disease processes.

Hypothesis: Since the mother's gestational steroid profile may be transmitted to the fetus via the placenta and also may vary systematically from one pregnancy to the next, we hypothesized that bones which are known to have sexually dimorphic growth patterns might also be sensitive to variation in sex steroids related to sibship position.

Methods: Volunteers for this study were obtained at various nearby hospitals and clinics with IRB approval. The subjects completed a questionnaire on medical history and family background, an informed consent for each participant and seven anatomical measurements of the arm and hand were made with a caliper and osteometric board. Statistical analysis was done on subgroups based on sex and ethnicity and on individuals from sibship positions of 1-4.

Results: An analysis of variance of female subjects showed that ulna length, adjusted for differences in stature (ulna to stature ratio), and adjusted hand length were significantly influenced by birth order ($F_{3,256}$= 3.95; p = .0089). Second born subjects had the lowest bone growth. No relationship was found between the ratio of the second digit to the fourth digit (2D:4D) and birth order.

Conclusions: A portion of variation in certain long bones lengths is related to birth order. Efforts to understand how adult disease is influenced by early hormone exposure should include birth order as a variable. Not all anatomical measurements in this study are related to birth order, and furthermore, factors related to birth order other than hormonal profile may have caused the effects seen in this study.

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C15

Failure of Clinical Practice to Comply With Guidelines for Opiate Use in Chronic Pain

T. Victor, PhD[1,2], N. Alvarez, PharmD[1], E. Gould, PhD
[1]Endo Pharmaceuticals, Chadds Ford, PA, [2]College of Psychology, PCOM, Philadelphia, PA

Hypothesis: Current guidelines recommend extended-release (ER) rather than immediate-release (IR) opioids for chronic pain (AGS Panel on Persistent Pain in Older Persons, 2002; American Pain Society, 2002). However, the extent to which clinicians adhere to these guidelines remains unclear. To clarify this issue, we examined the use of ER opioids relative to IR opioids in the treatment of chronic pain.

Materials and Methods: Data from the i3 Innovus Lab/Rx Database were used in this analysis. Enrollees having at least 1 pharmacy claim for an opioid between June 2003 and May 2006 and having at least 1 year of continuous enrollment beyond the date of their first observed opioid pharmacy claim were included in this analysis. Opioid-related treatment episodes were created by combining contiguous days of therapy allowing for a maximum of 7 days between dispensations of medication. Opioid-related treatment episodes were classified as chronic pain if duration of treatment was ⩾60 days. Outcomes were reported in the form of probabilities and odds ratios (ORs).

Results: A total of 3,993,011 opioid-related treatment episodes were derived from 1,967,898 enrollees. Overall, treatment with IR opioids was more prevalent (97.7%) than treatment using ER opioids (2.3%). ER opioids were approximately

11 times more likely to be used for chronic pain than for pain of shorter duration, compared with IR opioids (OR=10.7). However, the vast majority of chronic pain was treated with IR opioids (84.8%). The data were further stratified by prescriber type (specialist vs nonspecialist). Pain specialists were about 50% more likely to treat chronic pain with ER opioids than nonspecialists (OR=1.49). Nonetheless, the probability of a pain specialist prescribing ER opioids for chronic pain was only 19.1% and for nonspecialists was 13.7%, indicating that both prescribed IR opioids for >80% of chronic pain, contrary to treatment guidelines.
Conclusions: These data suggest that clinical practice does not follow accepted treatment guidelines for opiate use in chronic pain. Further research is needed to better understand physician prescribing behaviors as they relate to chronic pain and to identify gaps in the dissemination, knowledge, acceptance, and implementation of treatment guidelines.

♦C16

What Are the Normal Ratios Among Left-Sided Cardiovascular Structures in Children?

E.M. Smith, BA, OMS-III[1], E. Zare-Maivan, BS, OMS-III[2], W.B. Drake, MD[3], L.E. May, PhD[2]
[1]KCUMB-COM, Kansas City, MO, [2]Department of Anatomy, KCUMB-COM, Kansas City, MO, [3]Pediatric Cardiology, The Children's Mercy Hospital, Kansas City, MO

Context: Currently there is a scarcity of information available regarding the correlation among left sided cardiac structures and the great vessels within the pediatric population. It may be clinically useful to understand the degree and strength of correlation between the size of the left sided cardiac valves, left ventricle, and aorta.
Hypothesis: The focus of this project was to determine if normal ratios exist among internal structures of the heart and great vessels and to find a correlation among them.
Materials and Methods: This research project was approved by the Institutional Review Board at KCUMB-COM and Children's Mercy Hospital (CMH) in Kansas City, Missouri. This project reviewed echocardiographs performed at CMH between January 1, 2000 and December 11, 2007. The echocardiographic database was queried using TOAD software. A total of 812 normal echocardiographs, based on pediatric cardiologists' notes, were reviewed. Measurements were taken using Encompass software (Agfa-Heartlab) and from four views: 1) the long axis view (measured the mitral valve annulus, aortic valve annulus, aortic bulb, sinotubular junction, and the ascending aorta), 2) apical four chamber view (measured the mitral valve annulus), 3) apical five chamber view (measured the aortic valve annulus), and 4) suprasternal notch view (measured the descending aorta). All measurements were placed in an Excel spreadsheet with the following additional information: the last six digits of the chart number, the date of the study, height, weight, and body surface area.
Results: There are strong positive correlations (R^2 greater than 0.8) among internal and outflow structures: aortic valve to mitral valve, LV end diastolic diameter and aortic valve, aortic valve to sino-tubular junction (STJ), aortic sinus to STJ, and aortic sinus to ascending aorta. Weaker correlations (R^2 between 0.6 – 0.79) are seen among the cardiac structures and the aortic arch or descending aorta.
Conclusions: Given the close proximity of the aortic valve, aortic sinuses and ascending aorta, it logically follows that there is a high developmental correlation between the sizes of these structures. The distal arch and descending aorta may have weaker correlations to aortic valve size due to slight differences in flow across the ductus arteriosus in the fetus. This information will allow pediatric cardiologists to more accurately detect abnormalities among these crucial structures.

C17

An Epidemiological Examination of Cardiovascular Risk Factors in Patients With Osteoarthritis

R.A. Puenpatom, PhD[1], E. Angel, MA[2], T. Victor, PhD[1,3]
[1]Endo Pharmaceuticals, Chadds Ford, PA, [2]Angelic Productions, LLC, Jenkintown, PA, [3]College of Psychology, PCOM, Philadelphia, PA

Hypothesis: The use of systemic nonsteroidal anti-inflammatory drugs and cyclooxygenase-2 inhibitors is a significant concern in patients with increased cardiovascular (CV) risk, particularly in chronic pain patients who may have prolonged drug exposure. Although several factors (eg, obesity, age) are known to increase both CV and OA risk, there is currently little information available regarding the prevalence of CV risk in patients with chronic osteoarthritic pain to help guide treatment decisions. The objective of this study was to characterize and contrast the prevalence of CV risk factors in representative samples from the adult general (GP) and osteoarthritis (OA) populations.
Materials and Methods: The adult GP and OA samples were derived from the National Health and Nutrition Examination Survey III from 1988-94 conducted by the Centers for Disease Control and Prevention. Subjects were classified as having OA if they were diagnosed with *International Classification of Diseases, Ninth Revision, Clinical Modification* code 715 and 721, had ⩾1 knee OA record from radiograph files, or had been told by a doctor that they had OA. Prevalence rates and odds ratios (ORs) for CV risk factors according to age, sex, ethnicity, marital status, education, geographic location, and OA status were calculated.
Results: The OA study group was comprised of 975 subjects. The GP sample included 7714 subjects aged 18–90 years. Compared with the GP sample, the OA population had a higher prevalence of hypertension (75% vs 38%), hyperglycemia (30.2% vs 12.5%), low high-density lipoprotein cholesterol (44.1% vs 38.4%), elevated triglycerides (46.9% vs

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31.7%), and central adiposity (63.3% vs 37.5%). The prevalence of metabolic syndrome was 54.5% in the OA population and 26.5% in the GP sample. In ordered logistic regression analyses, CV risk factors were positively and significantly associated with age, race, marital status, and having OA. Among these factors, OA was most strongly associated with a higher number of CV risk factors both in an unadjusted analysis (OR, 3.67) and after adjusting for age (OR, 1.89).

Conclusion: Having OA is positively associated with having an increased number of CV risk factors (+90%). For patients with chronic pain due to OA, it may be prudent to assess patients' CV risk when making treatment decisions regarding analgesic medications.

C18

Transitioning From Oral Monotherapy to Combination Therapy in Type 2 Diabetes Mellitus: Comparison of Either Liraglutide, Glimepiride, or Placebo, in Combination With Metformin

J.S. Freeman, DO[1], M.A. Nauck, MD[2], M. Düring, PhD[3], M. Zdravkovic, MD[4], D.R. Matthews, DPhil, BM[5]
[1]Division of Endocrinology, Philadelphia College of Osteopathic Medicine, Philadelphia, PA, [2]Diabetologie, Diabeteszentrum Bad Lauterberg, Bad Lauterberg im Harz, Germany, [3]Statistics, Novo Nordisk A/S, Bagsvaerd, Denmark, [4]Medical Affairs, Novo Nordisk A/S, Bagsvaerd, Denmark, [5]OCDEM, University of Oxford, Oxford, Oxon, UK

Background: The ADA recommend metformin (met) and lifestyle modification initiation when T2D is diagnosed, but no consensus on what to do next when target glycemic control is not achieved exists. Glucose, risk of hypoglycemia (hypos), and weight gain should be considered when initiating combination therapy.

Objective: Compare efficacy & safety of adding either QD human GLP-1 analog liraglutide (lira) or glimepiride (glim) QD added to meet BID in 385 subjects with T2D previously treated with one OAD.

Methods: Data from a prespecified group (mean age: 55 y; White: 87%; T2D for 6 y) in a 26 week randomized, double blind, double dummy, IRB-approved trial were analyzed.

Results: Lira + met substantially improved glycemic control with weight loss and minimal hypos. 0.6 mg dose had lower efficacy. Glim + met also improved A1C, but with clinically significant weight gain and a 5 fold greater rate of hypos. Although nausea was higher with lira, it usually dissipated after week 4. *(See table next column.)*

Conclusions: Lira added to met substantially improves glycemic and weight control compared with met alone, with low risk of hypos. Adding glim + met improves glycemic control, but substantially increased risk of hypoglycemia and weight gain.

Acknowledgment: Supported by Novo Nordisk.

Variable (ITT, LOCF) Mean (SD)	Lira 1.2 mg + Met n=90	Lira 1.8 mg + Met n=83	Met n=41	Glim + Met n=89
Baseline A1C, %	8.37 (1.22)	8.23 (1.08)	8.36 (1.18)	8.17 (1.04)
Final	7.11 (0.94)	6.95 (1.09)	7.91(1.36)	7.05 (1.00)
Change (52 weeks)	–1.28 (1.16)††	–1.30 (1.07)††	–0.46 (1.32)	–1.11 (0.85)
% A1C <7.0%	53†	66††	23	56
% A1C ≤6.5%	32†	39†	8	37
Baseline weight, kg	87.1(17.1)	89.4 (17.0)	89.8 (18.3)	87.0 (17.3)
Final	85.3 (17.2)	87.0 (17.6)	88.6 (18.5)	88.7(17.2)
Change	–2.09 (3.04)**	–2.39 (4.59)**†	–1.18 (3.04)	+1.19 (2.75)
Baseline FPG, mg/dL	162 (43.7)	161 (36.1)	161(43.0)	163 (36.4)
Final	135 (35.2)	138 (38.1)	171 (53.4)	146 (42.3)
Change	–26.7 (43.9)*††	–25.0 (39.9)††	+8.70 (40.7)	–16.8 (33.8)
Baseline PPG, mg/dL	201 (41.8)	200 (43.3)	202 (55.6)	198 (43.1)
Final	162 (31.9)	161 (36.4)	192 (49.1)	165 (40.0)
Change	–40.4 (38.4)††	–39.4 (37.8)††	–8.10 (41.1)	–33.5 (42.5)
Minor hypos (PG <56 mg /dL) (%)	1**	5**	2	27
Events/ subject/year	0.05**	0.17**	0.21	2.17
% reporting nausea	17*	21*	10	5

*p<0.05 or**p≤0.0001 vs. glim + met †p<0.05 or ††p<0.0001 vs. met (ANCOVA or logistic regression)
FPG: fasting plasma glucose; PPG: post-prandial glucose; PG: plasma glucose

C19

Diclofenac Sodium Topical Gel 1% in Patients with Primary Knee Osteoarthritis: A Randomized, Double-Blind, Placebo-Controlled Trial

H. Barthel, MD[1], D. Haselwood, MD[2], S. Longley, MD[3], M. Gold, ScD[4], R. Altman, MD[5], S. Brunk, DO[6]
[1]Private Practice, Santa Barbara, CA, [2]Med Investigators, Fair Oaks, CA, [3]Arthritis Associates, Gainsville, FL, [4]Novartis Consumer Health, Parsippany, NJ, [5]The David Geffen School of Medicine, Los Angeles, CA, [6]Family Medical Group, St. Peters, MO

Hypothesis: Nonsteroidal anti-inflammatory drugs (NSAIDs) relieve symptoms of knee osteoarthritis (OA); however, orally administered NSAIDs may cause systemic adverse events (AEs), including gastrointestinal (GI) bleeding and ulcers, cardiovascular events, and renal failure. Topical NSAIDs may permit effective treatment while avoiding systemic drug exposure. In this study we tested the hypothesis

that diclofenac sodium topical gel 1% (DSG) would be efficacious in the treatment of mild to moderate symptoms of knee OA.

Materials and Methods: After approval by institutional review boards and informed consent 492 adults aged ≥35 years with symptomatic knee OA of ≥6 months' duration entered a double-blind vehicle-controlled trial. Following washout of analgesics, patients were randomized to DSG 4 g (n=254) or vehicle (n=238) 4 times daily for 12 weeks. Rescue acetaminophen (≤4 g/d) was allowed throughout the study. Primary efficacy outcomes at week 12 were Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) pain subscale, WOMAC physical function subscale, and global rating of disease (GRD). These outcomes were also assessed after 1, 4, and 8 weeks, and pain on movement (POM) was assessed on a 100-point Visual Analog Scale. AEs in any patient receiving study medication were recorded.

Results: At week 12, the DSG group exhibited significant improvements compared with the vehicle group on the WOMAC pain subscale (P=0.03), WOMAC physical function subscale (P=0.002), and mean global rating of disease (P=0.001). Mean symptom scores improved by 42%, 39%, and 43%, respectively, for these outcome measures in the DSG group. DSG was significantly superior to vehicle on all 3 primary efficacy measures and on the POM assessment at all visits, starting at week 1. The overall incidence of AEs was 60.2% with DSG and 53.8% with vehicle. The incidence of GI AEs was 5.9% with DSG and 5.0% with vehicle. 1 episode of nausea (0.4%) and 1 episode of dyspepsia (0.4%) in the DSG group were considered to be related to the study drug. No patients discontinued because of a GI AE. No ulcers, gastrointestinal bleeds, or serious treatment-related AEs were reported. Application-site dermatitis occurred in 4.3% and 1.7% of patients in the DSG and vehicle groups, respectively.

Conclusions: Topical treatment with DSG achieved significant improvements of pain and function in patients with knee OA. DSG was not associated with serious gastrointestinal or other systemic AEs.

♦C20

Geographic Variation in the Prescription of Stimulants for Attention Deficit Hyperactivity Disorder (ADHD) by U.S. Physicians

A.V. Bahel, BA, OMS-III
KCUMB-COM, Kansas City, MO

Purpose: To utilize the largest national database to determine if the prescription of a stimulant for ADHD has a geographical bias as well as to determine any possible medication class utilization disparities based on patient characteristics.

Methods: The study utilized the 1993-2005 National Ambulatory Medical Care Survey (NAMCS) and both components of the National Hospital Ambulatory Medical Care Survey (NHAMCS). The dependent variable was use of stimulant medication in the ADHD study population with independent variables assessed, via univariate and multivariate analyses, including region of the country, age group, gender, race, form of payment, ethnicity and year of study.

Results: A total of 1,126,506 office/site visits were captured by both surveys during the 13 study years, with 7,642 office/site visits associated with an ADHD diagnosis. When utilizing the national weighting variable these captured office/site visits represent a national estimate of 12,851,607,060 office site visits with 80,890,863 associated with an ADHD diagnosis. It was shown that relative to the Northeast, people living in the South were 31% less likely to receive a stimulant. Patients from the West were 35% less likely to receive a stimulant. The Midwest did not produce a statistically significant result. It was also shown that compared to male ADHD patients, female ADHD patients were 19% less likely to receive a stimulant. Compared to ADHD children of ages 0-14 years, ADHD patients between 15-24 years of age were 28% less likely to receive a stimulant and patients 25-44 years were 37% less likely to receive a stimulant. From 1993 to 2005, there was an increasing trend in the use of stimulants to treat patients with ADHD.

Conclusion: There continues to be a regional aspect to the treatment of ADHD in the US. It now seems that research methodology is the primary determining factor in which region predominates in stimulant use for treatment of ADHD.

C21

Efficacy of Frovatriptan as Acute Treatment in Female Migraineurs: A Pooled Analysis

B.L. Peterlin, DO[1], K. Ryder, PhD[2], K. Schuler, MS[2], T. Victor, PhD[3], J. Campbell, BSc[3]
[1]DUCoM Headache Clinic, Philadelphia, PA, [2]Complete Healthcare Communications, Chadds Ford, PA, [3]Endo Pharmaceuticals, Chadds Ford, PA

Hypothesis: Migraine, though often initially seen in the primary care setting, continues to be underdiagnosed and undertreated. Migraine is a particular problem in women, who have a 3-fold higher prevalence versus men, and many female migraineurs (60%) have menstruation as a predominant trigger, which is thought to be elicited by low estrogen levels at the start of menses. Triptans are generally effective and safe when used in the appropriate patients as acute treatment for moderate to severe migraine. This pooled analysis evaluated the efficacy of acute treatment with frovatriptan in female migraineurs.

Materials and Methods: Data were derived from 4 double-blind, placebo-controlled, IRB–approved clinical trials (n=1,

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phase II; n=3, phase III) of acute frovatriptan for treatment of migraine. Women administered frovatriptan (2.5 mg) when the migraine was moderate or severe. Migraine response (complete [grade 0] or almost complete [grade 1] relief in women with moderate [grade 2] or severe [grade 3] migraine) at 2 and 4 hours after the first dose of study medication and migraine recurrence within 24 hours of the first dose of study medication were evaluated. Recurrence was defined as a worsening from no or mild migraine to moderate or severe migraine in women with a response at 4 hours.

Results: The intent-to-treat pooled population was comprised of 2321 women who were randomized in similar proportions to the frovatriptan (88%, 1324/1505) and placebo groups (87%, 706/816). Acute frovatriptan effectively treated migraine in women across all studies. The response rates at 2 hours postdose were 43% (516/1214) with frovatriptan vs 24% (156/657, $P<0.05$) with placebo; at 4 hours they were 63% (669/1061) vs 35% (203/573, $P<0.05$), respectively. In addition, headache recurrence was lower with frovatriptan: in women who reported headache response at 4 hours, 22% (145/669) of women using frovatriptan reported recurrence within 24 hours compared with 28% (57/203) of placebo-treated women. Frovatriptan was generally well tolerated and the types of adverse events reported by patients were similar to placebo-treated patients and consistent with the product labeling.

Conclusions: Pooled findings from 4 randomized, double-blind, placebo-controlled trials demonstrate good response rates at 2 and 4 hours postdose and low migraine recurrence in women using frovatriptan 2.5 mg. These findings support the efficacy of frovatriptan as an acute treatment for migraine in women.

C22

Treatment of Chronic Moderate to Severe Pain of Osteoarthritis of the Hip or Knee with Morphine Sulfate Extended-Release Capsules Containing Sequestered Naltrexone Hydrochloride

J. Stauffer, DO[1], M. Hale, MD[2], J.B. Jones, MD, PharmD[1], G. Wagner, BS[3], D. Morris, PhD[3]
[1]Alpharma Pharmaceuticals, LLC, Johns Hopkins U Hospital, Piscataway, NJ, [2]Gold Coast Research LLC, Plantation, FL, [3]WebbWrites LLC, Northern Illinois University, Durham and DeKalb, NC and IL

Introduction: While guidelines for treatment of chronic moderate to severe pain include use of opioids, concern over misuse, abuse and diversion has made some clinicians reluctant to prescribe opioids when needed, resulting in undertreatment of pain.[1,2] Several pharmaceutical products under development are intended to provide effective analgesia while discouraging tampering to access opioid. ALO-01 (morphine sulfate extended-release with sequestered naltrexone hydrochloride) Capsules is an investigational product under development for chronic moderate to severe pain. The naltrexone, an opioid antagonist, is intended for release only upon tampering (such as by crushing or chewing) to mitigate morphine-induced positive effects and render the product less desirable for abuse.

Objective and Methods: This multicenter, randomized, double-blind, placebo-controlled IRB approved study assessed efficacy of ALO-01 administered BID over 12 wks to patients (N=547) age ⩾21y with chronic moderate to severe pain of osteoarthritis (OA) of the hip or knee (Am Coll of Rheumatology criteria). All pain medications (except acetaminophen as rescue) were stopped to induce pain flare, defined as Brief Pain Inventory (BPI) average pain score ⩾5 (0=no pain, 10=worst pain).3 Dose was titrated with ALO-01, 20-80mg BID to effective tolerated dose (BPI average pain score ⩽4 and 2 point drop from flare). Patients were randomized to be maintained on ALO-01 at this dose or tapered to placebo during the 12wk maintenance phase. Patients recorded BPI pain scores (worst, least, average over 24h and current pain) in daily diaries. The goal during maintenance phase was to maintain the level of pain relief attained during titration.

Results: During maintenance phase ALO-01 yielded reduced and statistically different mean change from baseline (day of first dose during maintenance) to wk 12 in BPI scores vs placebo for worst (0.3±2.0 vs 0.9±2.0; p=.003), least (0.3±1.8 vs 0.8±1.8; p=.036), average (0.3±1.9 vs 0.9±1.9; p=.003) and current pain (0.4±2.0 vs 0.9±2.1; p=.026). Significant difference was evident beginning at wk 1 through wk 12.

Conclusions: ALO-01 provided greater analgesia over a 12wk maintenance period vs placebo in patients with chronic moderate to severe pain due to OA of the hip or knee.

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C23

Elevated D-Lactate Concentrations in Serum and Urine of Diabetic Patients

A. Dyachenko, MS[1], K. Mészáros, MD, PhD[2], J. Schulze, BS[1], A. Gugliucci, MD, PhD[1], J. Schwarz, PhD[1], S. Kimura, MD, PhD[3]
[1]Touro University-College of Osteopathic Medicine, Vallejo, CA, [2]College of Pharmacy, Touro University, Vallejo, CA, [3]Department of Laboratory Medicine, Showa University Northern Yokohama Hospital, Yokohama City, Japan

Background: Metabolic disturbances in diabetes mellitus lead to increased D-lactate production, which also indicates enhanced formation of other, harmful metabolites. Accurate determination of D-lactate is challenging due to the presence of its stereoisomer, L-lactate at much higher concentrations.

Hypothesis: D-Lactate is higher in plasma and urine of diabetic patients than in controls.

Methods: Lactate (both D *and* L isomers) was purified from serum and urine of diabetic and control patients by deproteinization and ion exchange chromatography. The derivatized lactate isomers were separated and quantified by

GC/MS, using a chiral column. Glucose, L-lactate, HbA1c and creatinine were determined by standard clinical laboratory methods.

Results: The study included 14 diabetic patients and 11 control subjects. The diabetics displayed both hyperglycemia (10.9 ± 4.1 vs. 5.2 ± 1.0 mmol/L, $p<0.001$) and elevated HbA1c (8.1 ± 1.4 vs. 5.1 ± 0.2 %, $p<0.001$). L-Lactate, a normal metabolite, was in the normal range in the sera of both groups (1.9 ± 0.5 and 2.1 ± 0.8 mmol/L), but it was markedly increased in the urine of diabetics (0.99 ± 0.45 vs. 0.59 ± 0.28 mmol/L, $p<0.03$). Our main finding was the more than two-fold increase of D-lactate in diabetic patients both in the serum (56 ± 32 umol/l vs. 24 ± 19 μmol/L, $p<0.012$; note that the units are micromoles/L) and the urine (410 ± 350, vs. 130 ± 100 μmol/L, $p<0.02$). While normal urine did not contain detectable amounts of glucose, several urine samples from diabetics contained substantial amounts (up to 1 g/dL). In order to exclude the possibility of bacterial production of D-lactate from glucose in the urine of diabetics, the samples were shown to be free of bacterial contamination by means of a nitrite assay. The difference in urinary D-lactate remained unchanged after correction for glomerular filtration rates based on creatinine clearance.

Conclusions: Our study confirmed the increased production of D-lactate in diabetic patients, using a highly specific procedure for the separation of this trace metabolite from its - much more abundant - stereoisomer, L-lactate. This finding is relevant to the complications of diabetes which have been attributed, at least in part, to protein glycation. Methylglyoxal, a precursor of D-lactate, is one of the most aggressive glycation agents. Elevated D-lactate levels indicate enhanced production of methylglyoxal, and thus enhanced protein glycation.

♦C24

Cancer Screening Practices Among Community Health Fair Participants

A.J. Caban-Martinez, MPH, OMS-III[1], C. Siano, DO[2], A.M. Perez, JD, LCSW[3], S. Ledbetter, DO[4]

[1]Department of Osteopathic Principles and Practice, NSU-COM, Fort Lauderdale, FL, [2]Department of Emergency Medicine, Miami Children's Hospital, Miami, FL, [3]Master of Public Health Program, NSU-COM, Fort Lauderdale, FL, [4]Department of Family Medicine/Geriatrics, NSU-COM, Fort Lauderdale, FL

Objective: Understanding and elucidating healthcare access, insurance status and cancer screening practices among minority populations remains a priority for the U.S. Healthy People 2010 guidelines. The burden of cancer is not distributed equally across U.S. populations. Ethnic minority groups suffer from higher incidence, higher mortality, and poorer survival rates than white Americans. Uncovering data on minority populations and promoting changes that could improve minority health is highly warranted. Using a health behavior survey, this study assessed the proportion of community-based health fair attendees that engage in cancer screening practices.

Methods: A modified 57-item version of a validated cancer screening questionnaire was randomly administered to 117 adult participants during an annual health fair held April 19, 2008 in Davie, Florida. Descriptive analyses of the 10 selected variables from 117 completed surveys were tabulated using SPSS. Informed consent was secured from all subjects prior to participation in the study and approved by the Nova Southeastern University institutional review board.

Results: One hundred and seventeen participants (117) completed the health behaviors surveys, of those, 26.5% were males and 73.5% were females, 30.8% White, 28.2% Hispanic, 17.1% Other, 16.2% Black, and 7.7% Asian. Ages ranged from 19-99 years old (mean ± SE; 48.5±17.5), height from 55-83 inches (64±5), weight from 105-260 pounds (156±31), and BMI from 17.4-41.8 lb/in2 (27.5±9.8). Data regarding cancer screening practices showed that only 21.5% of individuals had ever received a complete skin examination by a physician, 60% of Hispanics had a pap smear, 27.2% had prostate evaluation using PSA, and 60.4% reported having a colonoscopy when indicated by guidelines. Fisher's test performed for cancer screening type versus gender, demonstrated a significant difference for colonoscopy screening between gender, with a higher proportion of screened males meeting national guidelines ($p=0.024$).

Conclusion: Findings from this study indicate there is a considerable disparity in select cancer screening practices among minority populations. Community-based health fairs provide a formidable venue to address health prevention and promotion needs among this vulnerable population. Encouraging primary care physicians to engage in cancer screening promotion and community-based health fairs is paramount to improving the gap in cancer disparity.

♦C25

Relationship of Osteopathic Manipulative Treatment During Labor and Delivery on Selected Maternal Morbidity Outcomes: A Randomized Controlled Trial

A. Keurentjes, DO[1], A. Showalter, DO[2], C. James, DO, PhD[3], A. Vawter, DO[4], B.M. Cross, OMS-IV [5]

[1]VCOM, Blacksburg, VA, [2]PNWU, Yakima, WA, [3]Vallejo, CA, [4]University of Washington, Yakima, WA, [5]TUCOM-CA, Vallejo, CA

Osteopathic Manipulative Treatment (OMT) has been used for more than 100 years to enhance the physiologic process of labor and delivery by normalizing pelvic structures and providing adequate blood supply to the uterus. Maternal morbidity and mortality is a major health concern for developing countries and it was desirable to explore the benefits that OMT might have to offer. A randomized controlled trial in Santo Domingo, Dominican Republic at Hospital Mater-

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nidad Nuestra Señora de la Altagracia explored the relationship of OMT during labor and delivery on rates of cesarean section and perineal lacerations/ episiotomies. A randomized sampling technique was utilized where each qualifying candidate received the next sequentially numbered envelope with a randomized number assigning her to either the treatment or control group. The staff physicians at the hospital managed the women in the control arm in the usual manner. Four Osteopathic Physicians and one pre-doctoral OMM fellow performed OMT on women during the first and second stages of labor and performed their deliveries. There were 33 parturients in the OMT Treatment group and 32 in the control, for a total of 65 in the trial. The results of a logistic regression analysis using Wald criterion, showed statistical significance $P<0.05$ in the treatment group for reduced rates of episiotomies in the primaparous ($P = .04$) and marginal significance in the combined primaparous and multiparous population ($P = .05$). The percentage of episiotomies in the primaparous treatment group was 35.29% and 75% in the control group. The percentage of episiotomies in the combined primaparous and multiparous groups were 15.15% in the treatment group and 37.5% in the control group. The cesarean rate for the treatment group was 9.09% and 18.75% for the control group ($P = 0.098$). The percentages of grade I & II perineal lacerations were 15.15% for the treatment group and 12.5% for the control group ($P = 0.55$) due to the extensive use of episiotomies in the control group. Cross-cultural issues made it difficult to perform the research as originally intended, yet the evidence shows Osteopathic Obstetrics provides a benefit to parturients. A multi-institutional randomized controlled trial is proposed as the next step for the evaluation of OMT during labor and delivery.

C26

Characteristics of Hip Bone Somatic Dysfunction in Subjects With and Without Low Back Pain

B.F. Degenhardt, DO, J.C. Johnson, MA, Q. Yang, MS
A.T. Still Research Institute, Kirksville, MO

Aim of Investigation: To determine objective characteristics of lateralization and positional asymmetry tests for the hip bone (innominate) in subjects with and without subacute/chronic low back pain (LBP).

Methods: The LBP group had a self-reported history of pain ($\geq$4 on a 0-10 numerical pain scale) in the lower back region for a minimum of 5 days a week for at least 4 weeks. The control group had no history of pain in the lower back region. All subjects were evaluated by one neuromusculoskeletal medicine specialist, blinded to group, who performed a standardized diagnostic protocol evaluating the pelvis. Reflective markers placed on standardized locations on the examiner's hands were used with a 3-D infrared camera system (Vicon Motion System Inc., Lake Forest, CA) to localize finger placement for each test. The coordinates for each landmark within the appropriate plane were compared by subtracting the value of the subject's left side from the right to quantify the positional asymmetry of the landmarks. Local IRB approval was obtained.

Results: 42 subjects (31 female, 11 male), age range 20-50 (36.0 ± 11.4), participated in the study, 35 with LBP and 7 controls. With the standing flexion test, there was more right PSIS motion in both groups (LBP: 4.54 ± 4.58 mm, 95% confidence interval [CI] 2.97-6.11; Control: 3.18 ± 4.60 mm, 95% CI -1.07-7.43). The seated flexion test was also positive to the right side (LBP: 3.43 ± 5.61 mm, 95% CI 1.50-5.35; Control: 6.08 ± 4.91 mm, 95% CI 1.54-10.62). The ASIS compression test showed greater right innominate displacement (LBP: 3.37 ± 3.47 mm, 95%CI 2.18-4.56; Control: 8.89 ± 5.67 mm, 95% CI 3.65-14.14), indicating a positive test on the left. Iliac crest height evaluated in the standing (LBP: -2.63 ± 6.28 mm, 95% CI -4.79- -0.47; Control: -6.01 ± 7.39 mm, 95% CI -12.85-0.82) and prone (LBP: -5.58 ± 10.22 mm, 95% CI -9.09- -2.07; Control: -4.95 ± 13.46 mm, 95% CI -17.40-7.50) positions were elevated on the left side in both groups. Pubic tubercle asymmetry showed that the right side was more consistently anterior in the LBP group (LBP: 3.60 ± 3.98 mm; Control: -0.26 ± 2.72 mm; $P=0.01$).

Conclusions: Most positive findings were not significantly different between the LBP and control groups. The observed disagreement between flexion and ASIS compression tests is not consistent with the currently accepted pelvic screening model and should be further investigated.

Acknowledgment: Funded by the American Osteopathic Association (06-04-550).

♦C27

Comparison of 0.5% Vs. 0.75% Ropivacaine Interscalene Brachial Plexus Block (ISB) Prior to Elective Total Shoulder Replacement Surgery on Use of Analgesic Medication During Post-Discharge Week

K.V. Tuitt M.S., OMS-II[1], F.J. Goldstein, PhD, FCP[2], D.A. Steinberg, M.D[3], E. Anvari, M.S., OMS-II[1], A. Gianitsos, D.O. [3], N. Suleiman, M.D.[3], C. Wells, M.D. [3], R. Olexa, M.S., OMS-III[1]
[1]Philadelphia College of Osteopathic Medicine, Philadelphia, PA, [2]Dept of Neuroscience, Physiology and Pharmacology, Philadelphia College of Osteopathic Medicine, Philadelphia, PA, [3]Dept. of Anesthesiology, Methodist Hospital Division, Thomas Jefferson University, Philadelphia, PA

Context: Ropivacaine is a local anesthetic commonly used in 0.5% and 0.75% concentrations for interscalene brachial plexus blockade (ISB) to decrease pain after total elective shoulder replacement surgery. There is little evidence to support that one is more beneficial than the other in relieving post-operative pain; however, severe adverse reactions such as seizures and ventricular arrhythmias can occur after its administration. This may be associated with high plasma concentrations due to intravascular injection, over-dosage,

♦ Indicates posters entered in the Student Prize Competition, a judged event that takes place during the Poster Session at the Research Conference.

or increased sensitivity to the drug.
Objectives: To investigate whether the lower concentration of ropivacaine was as effective as the higher one in regard to use of analgesic medication for seven days at home following surgery.
Methods: IRB approval was obtained on June 12, 2006 from Methodist Hospital Division of Thomas Jefferson University; 46 patients undergoing elective shoulder replacement surgery were recruited for this two-part single blind, randomized pilot study. Consented patients spent 48 hours within the hospital. To evaluate the efficacy of each ropivacaine concentration, the following data were recorded in-house: onset time of motor and sensory blockade; amount of patient-controlled analgesia (PCA) morphine consumed (μg/kg/hr); pain scores (0-10), and total amount of postoperative pain medications taken prior to discharge. Upon release (post-discharge study), patients were given pain and medication diaries to complete for 7 successive days. They recorded the total amount of Percocet tablets taken at home each day, in addition to pain scores (0-10) in the morning, afternoon and evening.
Results: Thirty-nine patients completed the in-house study while 27 completed the post-discharge study. Data from the previously reported in-house study indicated no significant difference between groups in regards to the amount of immediate post-operative analgesic medications consumed (PCA morphine; prescribed tablets) and post-operative pain. For 7 successive days at home, there was no difference between groups in regard to pain; however, patients in the 0.75% group unexpectedly took more tablets ($p<0.05$).
Conclusion: From these results, both concentrations of ropivacaine provided similar post-operative analgesia; thus, there would be a lesser chance of cardiovascular and central nervous system toxicity. Therefore, 0.5% ropivacaine should be the sole choice for ISB in patients undergoing elective total shoulder replacement surgery.

C28

Depressive Symptoms and Self-Rated Mental Health Among Firefighters

S. A. Pyle PhD[1], R. Suminski, PhD, MPH[2], G. Desai, DO[3], A. Glaros, PhD[4]
[1]Departments of Family Medicine & Preventive Medicine, KCUMB-COM, Kansas City, MO, [2]Department of Physiology, KCUMB-COM, Kansas City, MO, [3]Department of Family Medicine & Medical Affairs, KCUMB-COM, Kansas City, MO, [4]Department of Basic Medical Sciences, KCUMB-COM, Kansas City, MO

Hypothesis: In recent years, firefighters have assumed increasing responsibility for responses to emergency situations. At one time, firefighters' sole responsibility was fighting fires but they now include responding to a range of medical emergencies, natural disasters, and other traumas. Some evidence exists that there is a negative psychological toll on firefighters from this repeated exposure. The current project hypothesizes that firefighters rates of clinical depression as measured by a depression screening and a self rating of their mental health will be higher rates than those seen in the general population.
Methods: A cross-sectional, self report survey was completed by a sample (N=132) of firefighters in the midwestern region. The study was approved by the KCUMB IRB and all participants were consented. Participants were asked to provide a self rating of their overall mental health on a five point likert scale and to complete the Center for Epidemiological Studies Short Depression Scale (CES-D 10).
Results: On the CES-D 10, 15.6% of respondents were within the range of clinical depression. Symptoms such as sleep disturbance (29.1%) and trouble concentrating (17.5%) were the most commonly endorsed symptoms. On the single item self-rated mental health question, 0.8% of the total sample reported their mental health as poor, 3.1% rated their mental health as fair, 17.2% rated their mental health as good, 53.1% as very good and 25.8% as excellent. Of those who scored in the clinical range for depression, 75% rated their mental health as good, very good or excellent.
Conclusions: Among the firefighters surveyed, rates of depression where higher than those found in the general population. However, their responses on the CES-D were not reflected in the responses to the self rated health question. It may be that firefighters underestimate the negative psychological toll they experience or that they misattribute the symptoms of depression as being related to something other than their mental health. It also is possible that the CES-D is not the most accurate measure of clinical depression among this population.

C29

Neighborhoods on the Move: a Community-Based Participatory Research Approach to Promoting Physical Activity

R. R. Suminski MPH, PhD[1], S. Pyle, PhD[2]
[1]Department of Physiology, KCUMB-COM, Kansas City, MO, [2]Department of Preventive Medicine, KCUMB-COM, Kansas City, MO

Background: There is both a scientific and practical need for high quality, effectiveness studies of physical activity interventions in "real world" settings.
Objective: To utilize a community-based participatory research (CBPR) approach to develop, implement, operate, and evaluate an intervention for promoting physical activity called Neighborhoods on the Move. It was hypothesized that more positive changes in primary outcomes would be seen in the community participating in Neighborhoods on the Move compared with a comparison community.
Methods: Two communities with similar physical and social characteristics participated in this study. One community (i.e., treatment) participated in Neighborhoods on the Move while the other was used as the comparison group. Academic personnel and residents and organizations in the treatment community worked together to create an envi-

ronment that was more conducive for physical activity (e.g., increased program availability). Pre- and post-intervention data on new initiatives promoting physical activity, existing physical activity programs, and business policies supporting physical activity were collected simultaneously in both communities. Prior to data collection, all study procedures were approved by The Ohio State University IRB (protocol #2004B0193).

Results: The success of the CBPR approach was evidenced by several developments including substantial resident involvement and the formation of a leadership committee, marketing campaign, and numerous community partnerships. The number of businesses with policies promoting physical activity and the breadth of existing physical activity programs (participants, activities, hours) increased substantially more in the treatment than in the comparison community. A total of 60 new initiatives promoting physical activity were developed and implemented in the treatment community during the intervention.

Conclusions: The CBPR approach is an effective strategy for educing environmental changes that promote physical activity. Additional research is needed to expound the portability and sustainability of the intervention.

C30

Pain Reduction in Soft Tissue Injuries Over Time After Treatment With Diclofenac Epolamine Topical Patch

J. Stauffer DO[1], J. Yanchick, PharmD, CDE[1], S. Rovati, PhD[2], M. Magelli, PharmD[1], C. Fuller, PhD[3], K. Blackburn, MS[3], K. Kuehl, MD, DrPh[4]

[1]AlpharmaPharmaceuticals LLC, JohnsHopkinsU Hospital, Piscataway, NJ, [2]Institute Biochimique SA, Pambio-Noranco, Switzerland, [3]MMS Holdings, Canton, MI, [4]Oregon Health and Science University, Portland, OR

Introduction: Soft tissue injuries cause pain and swelling, resulting in restricted activity and further deconditioning. Such injuries may be treated with non-steroidal anti-inflammatory drugs (NSAIDs) to reduce pain and swelling, but oral NSAIDs are associated with risk of significant gastrointestinal adverse effects (AEs). Topical NSAIDs are intended to provide targeted analgesia at injury site with minimal systemic absorption and lower potential for AEs.[1] Diclofenac epolamine topical patch (DETP) is the first topical NSAID patch approved in the United States for treatment of acute pain of minor strains, sprains, and contusions.[2] The formulation allows release of medication over a 12-hour period[3] and has been shown to provide relief of pain of minor soft tissue injuries.[4]

Objective: To evaluate data from a double-blind, randomized, placebo-controlled trial to test the hypothesis that DETP could yield lower pain scores vs placebo when assessed over time in patients with minor soft tissue injury.

Methods: After signing informed consent for this IRB-approved trial, outpatients aged 18-65y with minor pain of ⩾5 (0-10 scale; 0=no pain, 10=worst pain) due to strain, sprain, or contusion occurring within 7 days of study entry were randomized to receive either DETP or placebo patch. Patients were instructed to apply study patch and record pain on a 0-10 Visual Analog Scale (VAS) twice daily (every 12h) for 14d or earlier if pain resolved (4 scores ⩽2). If needed, VAS scores were imputed by last observation carried forward.

Results: Of 418 patients, most were women (50.7%) and white (99.5%); mean age was 38.9y. VAS pain scores were significantly lower after DETP vs placebo on day 1 at time of removal of the second patch (6.05 vs 6.62, $p = 0.002$). VAS scores after DETP remained significantly lower at most time points throughout the 14d observation. The lowest VAS score was reached on day 13 (1.97 vs 2.94, $p < 0.002$).Incidence of AEs was similar between treatment groups (DETP 14.8%, PP 16.8%; $p = 0.59$).

Conclusion: This study in more than 400 patients demonstrated that DETP, applied twice daily for up to 14 days, was more effective than placebo in reducing pain of minor soft tissue injuries over the time period and was equally well tolerated.

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[3]Assandri A et al. *Drugs Exp Clin Res*. 1993.
[4]Galer BS et al. *J Pain Symptom Manage*. 2000.

Basic Sciences

♦B1

Stem Cell Proliferation and Hippocampal Repair Following Status Epilepticus in the Juvenile Period

Y. Khalil, OMS-IV, H. Hong, BS, E. Lopez, OMS-III, I. Sampson, L. K. Friedman, PhD

Dept. of Neuroscience, New York College of Osteopathic Medicine, Old Westbury, NY

Introduction/Hypothesis: In rat pups neurogenesis of the hippocampus is constrained by seizures whereas in adult rats it is provoked. We hypothesized that there is a critical developmental age when the "switch" occurs so that inhibition or stimulation of progenitors may depend upon the number of juvenile seizures and time point examined.

Materials and Method: Seizures were induced with kainic acid (KA) once on postnatal (P) day 30 (1x KA), or twice on P25 and P30 (2x KA). Immunohistochemistry was used to examine newly dividing cells throughout the hippocampus with the Ki67 antibody. Ki67 labeled sections were counterstained with DAPI to mark newly dividing cells and injured cells simultaneously. Specimens were viewed with an Olympus DP70 microscope equipped with selective excitation/emission filters for Texas Red and DAPI. Hematoxylin and eosin staining was used in adjacent sections to asses hippocampal injury following seizure activity.

♦Indicates posters entered in the Student Prize Competition, a judged event that takes place during the Poster Session at the Research Conference.

Results: In control rats, Ki67 labeled nuclei were few in number and located at the hilar border of the dentate gyrus (DG). Few or no progenitors were counted in other hippocampal layers. After 1x KA, modest increases in proliferation were observed in the granule cell layer (GCL), hilus, and CA3 whereas large elevations were in the CA1 within 48 hrs. After 2x KA, proliferation in the DG was similarly elevated but the MCL, CA1 and CA3 subregions exhibited less new born cells relative to 1x KA animals. Histological analysis revealed robust CA1 injury after 1x KA but spared CA1 neurons after 2x KA. In all cases, the highest proliferation rates and greatest hippocampal damage was observed in those animals who endured the strongest seizures. After 9 days, progenitor counts returned to control or lower levels in the DG and CA1 in both groups. Histological injury was minimal at this time in either group.
Conclusion: Seizure scoring and analysis of corresponding animal tissue suggests that high proliferation rates are associated with seizure severity and hippocampal injury. Minimal increases in hippocampal proliferation and low levels of injured CA1 neurons observed after 2x KA suggest tolerance was induced by the first seizure. In addition, reversed levels of proliferation following a 9 day recovery period, indicate that stimulated proliferation and injury in the juvenile period is transient after 1x KA and even more so after 2x KA possibly due to progenitor replacement of dying pyramidal neurons and tolerance.

♦B2

Anti-Inflammatory Effect of HMGCoA Reductase Inhibitor on Human Aortic Endothelial Cells (HAEC) in the Presence of Chlamydia Pneumoniae Antigen

J.C. Yedowitz, OMS-III, M. Frieri, MD, PhD
Dept. of Internal Medicine, NYCOM, Westbury, NY

Background: Atherosclerosis is an inflammatory process that can be mediated by the presence of a chronic infection within endothelial cells. Chlamydia pneumoniae (Cp) has been shown to exist within many coronary and carotid plaques, and possibly contribute to atherogenesis. Inflammatory processes play a critical role in the pathogenesis of atherosclerosis and statins have been shown to decrease pro-inflammatory markers, increase the number and function of endothelial progenitor cells (EPCs) within the circulation and reduce cardiovascular events aside from their lipid lowering ability.
Material and Methods: Human aortic endothelial cells (HAEC) were grown to confluence in EGM2 media supplemented with growth factor and 2% FBS at 37C in 5% $C0_2$. Cells were then incubated for 24 hrs with recombinant Cp heat shock protein (HSP 60) in a dose response at a concentration of 0-5μg/ml. The effect of statins on inflammation was assessed by pretreatment with 500ng/ml (1μM) of simvastatin. Secretion of vascular endothelial growth factor (VEGF) was determined by a sensitive ELISA.
Results: Dose response studies with HAECs incubated with 0-5μg/ml of HSP-60 showed a significant increase in VEGF secretion as compared with control. Basal level of secretion revealed 848pg/ml in mock-induced cells, while incubation with 5μg/ml of HSP-60 showed 2128pg/ml secretion. Pretreatment with simvastatin for 24 hours resulted in a statistically significant decrease in VEGF secretion incubated with HSP-60 (p=0.003).
Conclusion: EPCs possess the ability to mature into endothelial cells that line the lumen of blood vessels and the mobilization and incorporation of EPCs have been shown to modulate reendothelialization at sites of endothelial cell damage. From this data we can conclude that in-vitro, HAEC VEGF secretion is increased by the presence of Cp HSP-60. This may parallel the effect of Cp HSP-60 in-vivo on coronary and carotid endothelial cells and suggests a potential pathogenic mechanism for Cp associated atherosclerosis. The addition of simvastatin in our model decreased this response significantly, highlighting a potentially important anti-inflammatory effect of this medication, with implications for atherosclerosis prevention.

♦B3

Protective Effects of Craniocervical Osteopathic Manipulation on Cell Proliferation in the Developing Brain

G.N. LaTorre, OMS-III, T. Webster, DO, J. Avallone, DO, B. Hallas, PhD, L. Friedman, PhD
Dept. of Neuroscience, New York College of Osteopathic Medicine, Old Westbury, NY

Rationale: Multiple early-life seizures inhibit the production of newly-diving cells of the hippocampus by possibly enhancing the stress hormone levels associated with the insult. The effect of craniocervical osteopathic manipulative treatment (COMT) on cell proliferation after perinatal seizures is unknown.
Hypothesis: We hypothesized that COMT performed on infant rat pups prevents the reduced rate of proliferation induced by recurrent neonatal seizures, possibly by decreasing the seizure-induced corticosteroid stress response.
Materials and Methods: Kainic acid (KA) was used (2 mg/kg) to induce seizures in rat pups on postnatal (P) days P9, P10 and P12. COMT was performed for 30 minutes on the occipital region and cervical musculature 1.5 hrs after each seizure. Bromo-deoxyuridine (BrdU) and Ki67 immunohistochemistry was used to track newly dividing progenitors of the hippocampus in control and experimental groups at 48 hrs following the 3rd seizure. Radioimmunoassay was performed to measure circulating plasma corticosteroids from trunk blood. Proliferating cell counts and corticosterone plasma levels were subjected to One-way ANOVA to determine statistical significance.
Results: In COMT rat pups, cell proliferation of the hip-

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pocampus was not altered compared to age-matched controls. After three neonatal seizures, proliferating cells decreased in number within the dentate gyrus, but this reduction was attenuated in animals with COMT. Elevation of corticosterone plasma levels was also attenuated by approximately 40% after KA with COMT compared to KA alone.

Conclusions: Results indicate that COMT does not alter cell proliferation of healthy developing rats, but instead prevents loss of progenitors which is anticipated to allow normal brain development and improve cognitive outcome following early-life seizures. Reduced corticosteroid release after COMT may be responsible for the protective effects.

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♦B4

Developmental Regulation of Tyrosine Hydroxylase Expression in Rat Hippocampus

J.M. Mancuso, BS, OMS-III, H. Hong, BS, L.K. Friedman, PhD
New York College of Osteopathic Medicine/NYIT, Old Westbury, NY

Background: Seizure susceptibility and brain damage are age-dependent. Norepinephrine (NE), a potent antiepileptic, is detectable within a sparse population of interneurons of the hippocampus in adult rats. However, the developmental profile of NE expression within the hippocampus is unknown. We hypothesized that the pattern of hippocampal NE expression depends upon the age of the animal.

Material and Methods: To assess developmental regulation of NE protein expression, immunohistochemistry was used with a specific antibody for tyrosine hydroxylase (TH), the rate limiting enzyme for synthesis of NE. Distribution of TH positive neurons of the rat hippocampus was examined at various postnatal (P) ages (P6, 13, 20 and 60), at all levels of the hippocampus. Nissl staining was performed in adjacent sections to identify hippocampal levels according to the rat brain atlas.

Results: At P6, little specific expression was observed; faint staining was noted in occasional interneurons of middle levels of the hippocampal CA3 subregion. At P13, specific labeling occurred in few pyramidal cells and interneurons of the CA3 stratum oriens and in fewer granule cells located at the tip of posterior levels of the ventral blade of the dentate gyrus (DG). In contrast, at P20, many interneurons were prominently labeled throughout several levels of the CA1 stratum lucidum, oriens, subiculum and hilus, whereas interneurons of the CA3 were only weakly stained. Moreover, numerous granule cells were intensely stained along the hilar border of dorsal and ventral blades. At P60, a select population of interneurons was intensely labeled, but these were restricted to the CA3 stratum lucidum and located deep within the hilus at posterior levels. Only tips of the hilar border of the ventral blades over a short distance expressed TH. Pyramidal cells were labeled in the CA1 and CA3, but also only at certain posterior levels. A unique population of neurons was also identified in the subiculum along the midline at the level of the 3rd ventricle.

Conclusion: Spatiotemporal changes in TH expression occur with maturation so that the pattern of hippocampal TH expression depends upon the age of the animal. Different effects on neuronal activity due to transient upregulation of TH within dentate granule cells and inhibitory interneurons are expected to affect the seizure threshold and contribute to the resistance of the juvenile brain to epileptogenesis and seizure-induced brain damage.

♦B5

Acute Phytoestrogen Treatment on Physical Characteristics and Cardiac Function in Ovariectomized Rats

B. Markus, BS, OMS-III[1], L. Batia, BS[2], K. Bowden, DO[1], T. Broderick, PhD[2], L. Al-Nakkash, PhD[2]
[1]Midwestern University/AZCOM, Glendale, AZ, [2]Dept. of Physiology, Midwestern University/AZCOM, Glendale, AZ

Genistein, a naturally occurring isoflavonic phytoestrogen, has been associated with reduced incidence of heart disease and thus may be a possible alternative treatment for postmenopausal women with heart disease. This study aimed to examine the effects of acute and short-term genistein on *in vitro* heart function in ovariectomized (OVX) Sprague-Dawley rats.We found no change in the following parameters following 2 days of genistein injections (0.25 mg/kg): body weight, uterine weight, uterine/body weight, heart weight, heart/body weight, and fat pad weight. Blood pressure, measured in conscious rats by the tail-cuff method, was not altered by genistein treatment. Interestingly, femur weight was significantly increased after the 2-day genistein treatment ($P<0.01$). Furthermore, acute addition of increasing doses of genistein (10-150 mM) on *in vitro* heart function resulted in a maximum increase in contractility and cardiac output with 30 mM genistein in OVX (n = 5) rat hearts. In a separate series of experiments, OVX rats (n = 7) were treated either with genistein (0.25 mg/kg) dissolved in DMSO or DMSO alone, daily for two days. Following treatment, *in vitro* heart function was assessed by perfusion with 11 mM glucose, 1.2 mM palmitate and 3% albumin. Hearts were perfused under aerobic conditions and then subjected to 25 min of global ischemia followed by 30 min of reperfusion. During reperfusion, there was a significant improvement in recovery of contractility and cardiac output in the OVX rats given genistein compared to OVX rats given DMSO. Our results show that physical characteristics of OVX rats are unchanged following an acute 2-day treatment of genistein. The same treatment period, however, induces a significant cardioprotective effect in OVX rats, suggesting a potential therapeutic role in postmenopausal women.

♦Indicates posters entered in the Student Prize Competition, a judged event that takes place during the Poster Session at the Research Conference.

♦B6

Genistein Induces Estrogen-like Effects in Ovariectomized Rats but Fails to Increase Cardiac GLUT4 and Oxidative Status

B. Markus, BS, OMS-III[1], L. Batia, BS[2], W. Prozialeck, PhD[3], T. Broderick, PhD[2], L. Al-Nakkash, PhD[2]
[1]Midwestern University/AZCOM, Glendale, AZ, [2]Dept. of Physiology, Midwestern University/AZCOM, Glendale, AZ, [3]Dept. of Pharmacology, Midwestern University/CCOM, Downers Grove, IL

We have shown that 2-day treatment period of ovariectomized (OVX) Sprague-Dawley rats with genistein (0.25 mg/kg) did not induce changes in physical characteristics of rats but exerted a significant cardioprotective effect. Genistein, a naturally occurring isoflavonic phytoestrogen, has been associated with reduced incidence of heart disease and thus may be a possible alternative treatment for postmenopausal women with heart disease. This purpose of this study was to determine whether 2-week treatment protocol with genistein induces estrogen-like effects in OVX rats and if the cardioproective effect of genistein is associated with changes in GLUT4 and oxidative stress. Physical characteristics, blood pressure, cardiac GLUT4 content, and oxidative stress measured by glutathione and thiobarbituric acid reactive substances (TBARS) were determined after treatment. Uterine weight, uterine body weight, heart/body weight, femur weight were all significantly increased following genistein treatment in OVX rats. On the other hand, there was no effect of genistein on body weight, heart weight, and fat pad weight. Similarly, in these rats, genistein did not affect blood pressure. Genistein treatment had no effect of cardiac GLUT4 protein or oxidative stress, although ovariectomy was associated with a down-regulation of cardiac GLUT4 protein. Our results show that a two-week treatment protocol with genistein produced favorable estrogen-like effects on physical characteristics in OVX rats. However, based on our experimental conditions, the cardioprotective effects of genistein are not mediated by cardiac GLUT4 or changes in oxidative stress.

♦B7

Uterine Artery Vasoconstrictor Response to Sympathetic Stimulation During Pregnancy in Rabbits

J.J. Siegert, OMS-III[1], K.P. O'Hagan, PhD[2], R.J. Murphy, MS[1]
[1]Midwestern University/CCOM, Downers Grove, IL, [2]Department of Physiology, Midwestern University/CCOM, Downers Grove, IL

Hypothesis: We hypothesized that both systemic adjustments and the local presence of a fetus during advancing pregnancy contribute to the attenuation of the uterine artery vasoconstrictor response to sympathetic stimuli.

Materials and Methods: Uterine artery conductance (UtC) and blood flow (UtBF) (Transonic flow probe) were measured in the gravid and nongravid uterine horns of 5 NZW rabbits during the non-pregnant state and at days 10, 20 and 28 (term) of gestation. UtC was evaluated at rest as well as in response to nasopharyngeal reflex (NPR) stimulation (cigarette smoke exposure), the autonomic ganglia stimulant DMPP (25 mcg/kg IV), and the α_1-adrenergic receptor agonist phenylephrine (PE, 2.5 μg/kg IV). NPR and PE doses were repeated under treatment with nonspecific α-adrenergic receptor antagonist, phentolamine (2 mg/kg x 2). Data are analyzed using a general linear model with repeated measures and values are mean [SD].

Results: Resting UtC and UtBF increased progressively over gestation in the gravid horn. The vasoconstrictor response (% change in UtC) to DMPP did not change over gestation in the gravid horn, but displayed a greater response in the nongravid horn at days 20 and 28 ($P<0.05$). Strong stimulation of the NPR produced a similar vasoconstrictor response in both the gravid and nongravid horns over gestation, however, α-blockade effectively reduced the NPR response only in the gravid horn, particularly at days 20 and 28 ($P<0.05$). The largest difference between NPR and PE responses after α-blockade occurred in the gravid horn during the nonpregnant state (-67% vs. -16%, $P<0.001$), but this difference became progressively smaller by term (-9% vs. -27%).

Conclusion: Preservation of vasoconstrictor responses to DMPP and NPR throughout gestation indicate functional sympathetic control of uterine vasculature is not attenuated in uterine horns with growing fetuses. Uterine vascular responsiveness to α_1-agonists was also well preserved during gestation. Pregnancy, however, altered the ratio of adrenergic to non-adrenergic mechanisms that underlie uterine vasoconstrictor responsiveness to NPR stimulation in the gravid horn. The local presence of a fetus appeared to reduce the non-adrenergic component of reflex sympathetic response.

This project was approved by the Midwestern University IACUC (protocol number 1402).

♦B8

Induction of SIRT1 by Resveratrol Targets Proteins Involved in Mood Disorders

K. Svokos, OMS-III, J. Leheste, PhD, B. Hallas, PhD, G. Torres, PhD
Dept. of Neuroscience, New York College of Osteopathic Medicine, Old Westbury, NY

Context: Interactions between proteins are critical to understanding normal biological processes and disease progression. The protein deacetylase SIRT1 acts within cells to target proteins involved in signal transduction cascades, including p53 and NFkappaB which affect gene transcription *via* nucleosomal histone hypoacetylation. Identifying SIRT1 protein targets would provide a more comprehensive understanding of protein-protein interactions and cellular functions. Here, we used a modified chromatin immunoprecipitation (ChIP) technique to identify DNA targets induced by resveratrol. Resveratrol, a constituent of red wine, induces SIRT1 in cer-

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tain cells to enhance stress resistance and extend the lifespan of organisms from yeast to vertebrates.
Hypothesis: Using a ChIP technique, we may identify more SIRT1 targets that are associated with neuronal function and may be involved in the pathogenesis of mental illnesses.
Material and Methods: Human embryonic kidney cells (HEK 293) were used. SIRT1 was induced using resveratrol at a physiological dose (50 uM). A modified ChIP approach was used followed by DNA cloning. Cross-linked protein/DNA complexes were isolated in two parallel but independent approaches, one using a polyclonal, the other a monoclonal antibody directed against SIRT1. After protein elimination, endogenous DNA fragments were ligated to DNA-adapters, amplified by PCR, and transferred into a DNA cloning vector. After bacterial amplification, the cloned DNAs were sequenced and identified with the "Basic Local Alignment Search Tool". SIRT1 DNA targets were verified by PCR.
Results: A DNA target associated with the induction of SIRT1, identified by sequence analysis, was the gene encoding GRP50 (G-receptor protein 50). GRP50, operating through the cell membrane, functions at the melatonin 1 (MT1) receptor. GRP50 dimerizes with MT1 and MT2 receptors and antagonizes the functional response of the MT1 receptor to its native ligand (pineal melatonin hormone). Melatonin and its pathways have been implicated in mood disorders.
Conclusions: Changes in the functional status of MT receptors by GRP50 may be the basis by which receptor-receptor interactions give rise to neuronal function. A deletion mutant of GPR50 appears to be genetically associated with mental disorders. Studies are needed to verify the transcriptional effects of SIRT1 with those of GPR50 and to explore protein interactions involved in brain cell function, protein regulation and gene expression.

♦B9

Blimp1 is Necessary for Drosophila Germline Stem Cell Maintenance

A.R. Sacks, OMS-II[1], G.B. Call, PhD[2]
[1]Midwestern University/AZCOM, Glendale, AZ, [2]Dept. of Pharmacology, Midwestern University/AZCOM, Glendale, AZ

Oogenesis in the fruit fly, *Drosophila melanogaster*, begins with a single germline stem cell (GSC). When the GSC divides in the wild-type ovary, one daughter cell remains a pluripotent GSC while the other continues to divide and differentiate to produce the eventual egg. Blimp1 has recently been shown to play a role in germ cell identity in mice. In this experiment, Blimp1 mutant flies were analyzed for its role in the *Drosophila* GSC. It was hypothesized that Blimp1 mutant GSCs would lose their stem cell identity and be lost from their ovarian niche. Experimental and control flies were heat shocked to induce mitotic recombination between flipase recombination target sites on *Blimp1*-mutant chromosomes. This process yields homozygous mutant GSCs for Blimp1 that are identifiable by the lack of green fluorescent protein expression. Following clonal mutation, ovaries were dissected at weekly intervals and observed with fluorescent microscopy to quantitate wild-type and mutant GSCs. Both groups started with about the same amount of GSC clones. Over a period of three weeks, about 33% of Blimp1 mutant GSCs were lost, while the GSC number in the control group stayed relatively constant. It is well known that other factors also influence GSC maintenance and these might have prevented the mutant GSCs from being completely lost. Another explanation might be the relatively weak nature of the Blimp1 mutant employed, which will be addressed in future experiments. This data supports the hypothesis that Blimp1 is necessary for GSC maintenance.

♦B10

Fractalkine Regulates Rheumatoid Arthritis Fibroblast-like Synoviocyte Production of Monocyte Chemoattractant Protein-1 and Interleukin-6

E. Cruz, OMS-II, K. Klosowska, MS, M.V. Volin, PhD, J.M. Woods, PhD
Dept. of Microbiology and Immunology, Midwestern University/CCOM, Downers Grove, IL

Background: We have shown previously that fractalkine (Fkn) is a proinflammatory chemokine that is overexpressed in the synovium of rheumatoid arthritis (RA) patients. We also have shown that RA fibroblast-like synoviocytes (FLS), which are central players in the pathogenesis of RA, respond to Fkn through its cell surface receptor, CX3CR1. It has recently been demonstrated that all RA FLS express this receptor for Fkn. Here, we examined whether Fkn may regulate RA FLS production of proinflammatory mediators.
Hypothesis: Fkn alters RA FLS cytokine and chemokine secretion.
Materials & Methods: Conditioned media (CM) from RA FLS cultures in the presence and absence of various concentrations of Fkn were analyzed by antibody (Ab) array (Ray Biotech, Atlanta, GA) or ELISA (R&D Systems, Minneapolis, MN) for levels of cytokines and chemokines after 48 hrs.
Results: RA FLS CM were collected from non-stimulated and Fkn-stimulated cultures and analyzed by Ab array as an initial screen. The results suggested that secretion of interleukin (IL)-8 was the only cytokine increased by stimulation with 1 nM Fkn (of 79 screened). In contrast, monocyte chemoattractant protein (MCP)-1, regulated upon activation, normal T cell expressed and secreted (RANTES), vascular endothelial growth factor (VEGF), and oncostatin M all appeared decreased. ELISAs were performed to further confirm some of these initial findings. Fkn-stimulated RA FLS did not significantly alter secretion of IL-8 or the chemokine

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growth related oncogene-alpha when CM from 3 different patients were examined (n=3; $p>0.05$). In contrast, secretion of the potent proinflammatory mediator IL-6 was significantly increased by Fkn (n=3; $p<0.05$). In line with our Ab array data, analysis of CM from RA FLS demonstrated that Fkn-inhibited MCP-1 secretion at physiologically relevant concentrations of 1 and 10 nM (n=6; $p<0.05$).

Conclusions: We have potentially identified two new ways in which Fkn may play roles within the RA synovium through interactions with FLS. Fkn significantly increases the proinflammatory mediator IL-6 while significantly decreasing the potent monocyte chemoattractant, MCP-1.

B11

Lack of PTCH Gene Mutations in Non-NBCCS Basal Cell Carcinoma Susceptibility Patients

A. Bansal, OMS-IV[1], S.S. Fakharzadeh, MD, PhD[2]
[1]UMDNJ-SOM, Stratford, NJ, [2]Dept. of Dermatology, University of Pennsylvania Health System, Philadelphia, PA

Background: With over 1,000,000 new cases per year, basal cell carcinoma is the most common cancer in the U.S. Nevoid basal cell carcinoma syndrome (NBCCS) is a rare hereditary disorder in which patients may develop hundreds of BCCs. In addition, they may manifest other developmental anomalies, including jaw cysts, palmar pitting, intracranial calcification and various skeletal anomalies. NBCCS is caused by germline inactivating mutations in the *PTCH* gene.

We identified 8 patients with numerous BCCs that lacked other clinical manifestations of NBCCS. We hypothesize that they represent a class of patients distinct from those with NBCCS, and that the genetic basis underlying their BCC susceptibility differs from NBCCS patients. To evaluate this, for each subject we performed sequence analysis of the *PTCH* gene and assessed genotype for six single nucleotide polymorphisms (SNPs) within the *p53*, *GSTP1*, and *MC1R* genes that have been previously reported to be associated with BCC susceptibility.

Methods: Patient blood samples were obtained with informed consent in accord with protocols approved by the IRBs at the University of Pennsylvania or Philadelphia VA Medical Center. Genomic leukocytic DNA was extracted and coding sequences for the *PTCH*, *p53*, *GSTP1*, and *MC1R* genes were PCR-amplified using specific primer pairs flanking intron-exon boundaries. PCR products were resolved by agarose gel electrophoresis, extracted, and subjected to direct sequence analysis on an ABI 3730 sequencing apparatus.

Results: No germline inactivating *PTCH* mutations were detected for any of the 8 patients. Similarly, *GSTP1* codon 114 SNP was not observed. Only 1 patient carried the *p53* codon 72 SNP. However, 5 patients were hemizygous for the *GSTP1* Ile105Val SNP. Four of these 5 patients and 2 other patients also carried *MC1R* SNPs.

Conclusions: These findings suggest that these subjects represent a class of patients distinct from those with NBCCS and that the genetic basis for their BCC susceptibility does not involve inactivating coding sequence mutations in the *PTCH* gene. Variants in *MC1R* gene and the *GSTP1* Ile105Val variant were the most commonly observed SNPs. Further studies are required to determine if these polymorphic variants and/or aberrations in other genes may contribute to BCC susceptibility in this class of patients.

♦B12

Determination of the Rate Limiting Step in p-Aminobenzoic Acid Biosynthesis in Escherichia coli

T.W. Roberts, BS, OMS-II, J.M. Green, PhD
Department of Biochemistry, Midwestern University/CCOM, Downers Grove, IL

Background: Folate is an essential vitamin for *Escherichia coli (E. coli)*, and is required for DNA and RNA synthesis. While it is synthesized *de novo* in bacteria, the pathway does not exist in humans, making folate biosynthesis a convenient target for antibiotics. Production of folate building block *p*-aminobenzoic acid (PABA) requires three genes, *pabA*, *pabB*, and *pabC*, and their corresponding gene products. Development of antibiotic resistance has a created a need for new antibiotics. Sulfonamide drugs compete with PABA in the folate biosynthetic pathway. The protein that is rate limiting for PABA biosynthesis would serve as a future antibiotic target.

Hypothesis: Expressing higher amounts of the rate limiting protein will increase cellular resistance to sulfonamide antibiotics, and provides a mechanism of identifying the rate limiting step in PABA biosynthesis.

Material and Methods: The growth of MG1655 was measured with fixed concentrations of a sulfonamide and varying amounts of exogenous PABA. The *pabA*, *pabB*, and *pabC* genes were first amplified using PCR. They were then cloned into the plasmid pACYC184. Each plasmid and the vector control were then transformed into wild type (MG1655) *E. coli*. The cells were then grown with various concentrations of sulfonamide antibiotics. Growth was measured at selected time intervals in several ways, using a spectrophotometer, as well as by measuring the minimum inhibitory concentration (MIC) using a 96 well plate.

Results: Exogenous PABA did increase the ability of *E. coli* to grow in the presence of sulfonamides. All three genes were successfully cloned and transformed into *E. coli*. Cells transformed with the plasmid encoding *pabB* were slightly more resistant to sulfathiazole than controls, indicating that *pabB* might be somewhat limiting. In general, however, data indicated that none of the proteins were significantly rate limiting for PABA biosynthesis.

Conclusion: Elevated levels of exogenous PABA does protect *E. coli* against growth inhibition by sulfonamides. While PabB might be slightly rate limiting for PABA biosynthesis,

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it was not a significant difference. We conclude that any of the three proteins involved in PABA biosynthesis would serve as an appropriate antibiotic target.

♦B13

Neuronal Morphology of the Superior Olivary Complex in the Rodent Model of Autism

R.L. Lukose, MS, OMS-III, R.J. Kulesza, PhD
Lake Erie College of Osteopathic Medicine, Erie, PA

Background:Autism is a complex neurological disorder that affects social development and is associated with auditory deficits including deafness, increased thresholds to tones, intolerance for ordinary sound levels and difficulty hearing in the presence of background noise. A general disorganization in the auditory brainstem nuclei has been described in the medial superior olive in postmortem human autistic specimens. Taken together, these observations provide the foundation for a systematic and thorough evaluation of all the components of the auditory system in a controlled model for autism. Researchers have hypothesized that early gestational injury may provide a starting point for examining the effects of autism and prenatal exposure to valproic acid [VPA] in rodents yields morphological and behavioral changes similar to those observed in autism.

Hypothesis: Components of the brainstem in rats exposed to VPA will differ from a control group in neuronal morphology and number.

Materials and Methods: Our examination has focused on the components of the superior olivary complex (SOC). Specifically, we have examined the medial superior olivary nucleus, the lateral superior olivary nucleus, and the medial nucleus of the trapezoid body. Our morphometric study includes examination of neuron number, neuron size, circularity and orientation. Animal were divided into two groups: prenatal exposure to VPA or control. On embryonic day 12.5, dams were given an injection of VPA or normal saline. Adult rats were anesthetized, brains were dissected, incubated and sectioned at a thickness of 40 μm. Specimens were mounted onto glass slides, and stained for Nissl substance or for myelin and counterstained with neutral red. For morphometric analyses, sections were randomly (but systematically) selected and neurons were sampled throughout the rostro-caudal extent of each nucleus. Cell bodies were traced while focusing with the aide of a camera lucida attachment to a microscope. Grayscale tracings were analyzed using ImageJ software for neuron size, circularity and orientation.

Results: Our preliminary investigations have revealed significant alterations in neuronal morphology (cell body size and shape) in the entire MSO, the caudal half of the MNTB and in the central limb of the LSO.

Conclusion: These results provide some evidence that the VPA rat may be a model for the auditory deficits observed in autistic children.

♦B14

Modulation of Escherichia coli Adherence to Latex by Insulin and Carbohydrates

S. Surapaneni, BS., OMS-II, B.J. Plotkin, PhD
Dept. of Microbiology and Immunology, Midwestern University/CCOM, Downers Grove, IL

Hypothesis: Catheter-associated infections are a significant cause of morbidity and mortality in hospitalized patients. *E. coli* form biofilms on various surfaces including latex, contributing to catheter-associated infections and nosocomial spread. Insulin is a quorum signal for *E. coli* modulating its environmental response by inducing behavior changes. We hypothesize that human insulin, a signal surrogate for microbial insulin, alters the ability of *E. coli* to interact with latex in the presence of various carbohydrates. To test this hypothesis we measured the effect of insulin on E. coli adherence to surgical latex in the presence of various sugars.

Materials and Methods: *E. coli* ATCC 25923 was grown in peptone (1%) yeast nitrogen base broth to either logarithmic or stationary growth phase. Adherence to latex was determined using 6 x 6mm latex squares placed in a suspension of washed cells (10^3 CFU/ml; 30min; 37°C) in buffer containing insulin at 2, 20, and 200 mU mL (Humulin R; Lilly) with and without mannose (10^{-1} ,10^{-2}M), galactose (10^{-3} ,10^{-4} M), fructose (10^{-3} ,10^{-4}M), sorbose (10^{-2} ,10^{-3}M), arabinose (10^{-1} ,10^{-2}M), xylose (10^{-2} ,10^{-3}M), lactose(10^{-3} ,10^{-5}M), maltose (10^{-1} ,10^{-2}M), melibiose (10^{-2} ,10^{-3}M), glucose-6-phosphate (10^{-2} ,10^{-3}M), glucose-1-phosphate (10^{-2} ,10^{-3}M), glucosamine (10^{-1} ,10^{-2}M). The sugar concentrations tested represent the concentrations reported to affect behavioral response. Adherence levels to latex were determined by the press plate method. Controls were media or buffer alone. Glucose (0.1%) served as the positive control.

Results: Overall, stationary phase cells adherence to latex was greater, regardless of test condition, than that measured for logarithmic phase cells. The effect of insulin on adherence to latex was insulin and sugar concentration dependent. Addition of insulin (200 mU mL resulted in significantly ($p<0.05$) increased adherence to latex as compared to sugar alone for 12 of the 13 sugars tested for stationary phase bacteria and 10 of 13 sugars tested for logarithmic phase bacteria. Adherence in response to sorbose was the only sugar tested unaffected by insulin.

Conclusion: These findings show that insulin can enhance *E. coli*'s association with latex containing materials, e.g., gloves, catheters, and potentially contribute to transmittance in the hospital environment.

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♦B15

Determination of the Role of Escherichia coli Gene Products OmpF, OmpC, and PhoE in Cellular Sensitivity to Antibacterial Drugs

N. Rai, BS, OMS-II, J. Green, PhD
Dept of Biochemistry, Midwestern University/CCOM, Downers Grove, IL

Background and Significance: *Escherichia coli (E. coli)* contain an outer membrane that includes OmpC, OmpF, and PhoE. These regulate the passage of materials into the cell, including antibiotics. Studies suggest that mutations in outer membrane proteins can cause resistance to antibiotics.

Hypothesis: Using cells lacking each of three specific outer membrane proteins with known roles in cellular transport, and the isogenic parent strain, we performed a systematic study to investigate resistance to a variety of antibacterial compounds. We hypothesized that the strains lacking OmpC, OmpF, or PhoE would result in either unchanged or increased resistance to some antibiotics compared to the parent.

Materials and Methods: Knockout strains lacking OmpC, OmpF, and PhoE and their isogenic parent were tested for resistance by microdilution growth experiments in Mueller Hinton medium containing varying concentrations of different antibiotics. We measured both the minimum inhibitory concentration (MIC) and the minimum bactericidal concentration (MBC). MIC measures the amount of drug that inhibits growth, while the MBC measures the amount of drug that results in cell death.

Results: Strains lacking OmpC, OmpF, and PhoE, respectively, showed non-significant variations in resistance as compared to the parent strain when MIC values are compared for ampicillin, carbenicillin, bactrim, streptomycin, nalidixic acid, rifampicin, and erythromycin. In contrast, strains lacking OmpC, OmpF, and PhoE, respectively, showed significantly increased MBC values, and increased resistance, for ampicillin, carbenicillin, and bactrim. Interestingly, the strains lacking OmpC, OmpF, or PhoE were all more sensitive to rifampicin than the parent. For streptomycin, nalidixic acid, and erythromycin no significant variation was observed.

Conclusion: While these results showed that lack of OmpC, OmpF or PhoE resulted in no significant variation in MIC values for the antibiotics tested, there was significant increased resistance as measured by MBC values for strains lacking these outer membrane proteins. Mutation in these proteins is likely an importance source of antibiotic resistance, affecting a wide range of drugs. These results will enhance the understanding of bacterial resistance as a result of mutations in outer membrane proteins which results in increased survival of the bacteria and thus susceptibility to recurrence of bacterial infections post antibacterial therapy.

♦B16

The Role and Regulation of Ornithine Decarboxylase in Human Gingival Fibroblasts

J.K. Pomeroy, BS, OMS-III, F. Daghigh, PhD, E. Cho, MS
Dept. of Biochemistry and Molecular Biology, Philadelphia College of Osteopathic Medicine, Philadelphia, PA

Background. Polyamines are naturally occurring compounds in human cells. The category includes putrescine, spermidine, cadaverine and spermine. Although their function is not completely understood, polyamines appear essential to cell proliferation and differentiation. These compounds are derived from ornithine which, via ornithine decarboxylase (ODC), yields putrescine. Availability of certain polyamines during periodontitis, a disease of gingival tissue, may be regulated by ODC activity. Arginine is the metabolic source for ornithine and nitric oxide (NO) through separate pathways. Ornithine is produced from arginine via arginase isoforms ARG I and ARG II and NO from nitric oxide synthase (NOS). ARGI is a component of the urea cycle while ARGII may be involved in tissue repair and collagen synthesis. cAMP and IL-4, have been previously found to up-regulate ARG I in HGF, but the regulation of ODC has yet to be determined. The presence of ODC in human gingival fibroblasts (HGF) may provide a source of polyamines for collagen synthesis and cell proliferation and may be involved in the response to periodontitis.

Materials/Methods. IRB approved. HGF were collected from patients undergoing periodontal surgery under their informed consent. Cells underwent 3-5 passages. HGF were incubated with cytokines mimicking pre-inflammatory and anti-inflammatory conditions: cAMP, TNF, IFN, IL-1, cAMP + IFN, TNF+IFN+IL-1, norvaline, and norvaline + cAMP. Incubation times ranged from 1, 3, 6, 9, 12, 24, and 48 hours. Real-time PCR was used to measure the mRNA levels.

Results. ODC was constitutively expressed in HGF. After 3 hours of incubation with cAMP, mRNA levels of ODC significantly increased when compared to control. Under conditions leading to an increase in NO levels (combination of pro-inflammatory cytokines TNF-α, IL-1-β, and IFN-δ), ODC mRNA levels remained unchanged. IFN-δ seemed to reduce the up-regulation effects of cAMP on ODC mRNA. Other experiments involved effects of anti-inflammatory cytokines and arginase inhibitor, norvaline, on ODC.

Conclusion. ODC may be an important component of the cell proliferation/repair process in HGF. Similar to arginase, ODC up-regulation was enhanced by cAMP. Therefore, arginase and ODC enzymes may work in a concerted anti-inflammatory pathway in HGF.

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♦B17

SIRT1 Transcriptional Regulation of DNA Targets and Neuronal Function

S. Sarwar, OMS-III[1], G. Torres, PhD[1], B. Hallas, PhD[2], J. Leheste, PhD[2]
[1]Dept. of Neuroscience, NYCOM, Old Westbury, NY, [2]NYCOM, Old Westbury, NY

Background:The mammalian protein deacetylase SIRT1 is widely recognized for its link to calorie restriction and longevity. SIRT1 not only modulates the function of protein targets such as p53 or NFkappaB, but it also affects gene transcription by causing hypoacetylation of associated nucleosomal histones. However, the identification of SIRT1-specific DNA targets that confer chromosomal stability and cell longevity have remained elusive. Much of the work on SIRT1 has focused on linking Sirt1-induced protein modification with age-onset diseases. In contrast, the search for specific gene targets, directly affected by SIRT1-induced epigenetic changes of the histone code, has been largely ignored.
Hypothesis: We hypothesize that by using a modified chromatin immunoprecipitation (ChiP) approach, we could identify putative genes that might affect neuronal function *via* SIRT1 regulation.
Materials and Methods: ChIP was performed using the EZ ChIP Kit (Upstate, NY) with human embryonic kidney cells (HEK-293). Monoclonal and polyclonal anti-SIRT antibodies were used to select for the SIRT1/DNA complexes. The DNA fraction was amplified by PCR, transferred into a standard DNA cloning vector, and sequenced. Sequences were identified with the "Basic Local Alignment Search Tool" (BLAST; http://blast.ncbi.nlm.nih.gov/Blast.cgi). Potential DNA targets were verified by gene-specific PCR on unamplified ChIP DNA.
Results: One of the identified DNA sequences corresponds to the gene encoding the neuro-oncological ventral antigen 2 (*nova2*), which regulates the alternative splicing at exon 5 of the neuron-specific sodium channel gene *scn1a*. Of potential interest, this sodium channel is targeted by the pharmacological actions of anti-epileptic drugs.
Conclusion: Using a modified ChIP approach we were able to identify DNA targets of SIRT1. In the case of *nova2*, our findings suggest a possible involvement of SIRT1 function in neuronal function. Further studies will determine the physiological consequences of SIRT1 association with *nova2* on *scn1a* splicing and the importance of this pathway for epilepsy onset.

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♦B18

The Alpha-catenin and GSK-3beta Binding Regions of β-catenin Shape Optic Axonal Paths and Growth Cones Independent of the TCF/LEF Regulatory Domain

A. Pelzer, BS[1], M. Southard, BA[2], A. Shah, BS[2], T. Elul, PhD[2]
[1]Dept. of Basic Sciences, Touro University College of Osteopathic Medicine, Vallejo, CA, [2]Touro University College of Medicine, Vallejo, CA

We over expressed different mutants of the N- and C-terminal domains of beta-catenin in individual optic axons. Over expression of the entire N-terminal domain of beta-catenin that interacts with alpha-catenin dispersed and reduced the directional persistence of optic axons. In contrast, expression of a truncated N-terminal mutant of beta-catenin (betacat107) that regulates interaction with GSK-3beta converged and increased the directional persistence of optic axons. NTERM also collapsed filopodia and enlarged growth cones whereas betacat107 straightened filopodia and compressed lamellipodia of optic axons. Significantly, over expression of the C-termianl domain of beta-catenin that regulates TCF/LEF transcription did not perturb optic axonal paths or growth cones in the optic tract. These data suggest that interactions of beta-catenin with alpha-catenin and GSK-3beta shape optic axonal paths and growth cones independent of regulation of TCF/LEF transcription.

♦B19

Effects of Cadmium (Cd) on Cell Viability and β-catenin Regulated Gene Expression in Mouse Lung

M. Kumar, OMS-I[1], J.R. Edwards, PhD[1], P.C. Lamar, BS[1], J. Liu, PhD[2], M.P. Waalkes, PhD[2], W.C. Prozialeck, Ph.D[1]
[1]Department of Pharmacology, Midwestern University/CCOM, Downers Grove, IL, [2]National Institutes of Health, Research Triangle Park, NC

Objective: Previous studies from our laboratory have shown that Cd-induced pulmonary edema is associated with the disruption of E-cadherin- and VE-cadherin-dependent cell-cell junctions in mouse lung. The objective of the present study was to examine the possible relationship between these Cd-induced changes in cadherin function and alterations in β-catenin-regulated gene expression. We postulated that disruption of cadherin-mediated cell-cell adhesion by Cd would mobilize β-catenin from the intracellular portion of the cadherin and lead to activation of β-catenin-regulated gene expression.
Methods: Male CF-1 mice were anesthetized and treated with 65nmol $CdCl_2$ in 50µl isotonic saline by intratracheal installation at the bronchial bifurcation. After 24 hours of exposure, the mice were again anesthetized and the lungs were removed, weighed and evaluated for evidence of pulmonary edema. Lung tissue was then frozen and later processed for histologic evaluation and analyzed for levels of expression of a panel of genes by real time RT- PCR. Animal protocol was approved by the Midwestern University IACUC (Institutional Animal Care Use Committee).

Results: The acute pneumotoxic effects of Cd were associated with an increase in lung weight, confirming the presence of pulmonary edema. Immunofluorescence labeling studies showed that Cd decreased the amount of E-cadherin at the contacts between the alveolar epithelial cells. RT-PCR analyses showed an increase in the expression of the metal-binding protein metallothionein, and several other genes including IL-1β, iNOS, and CHK1. The Cd-treated animals showed a decrease in expression of E-cadherin, VE-cadherin, and β-catenin. Most significantly, there was either no change or a slight decrease in the expression of a panel of β-catenin-regulated genes including cyclin D-1, matrilysin, c-myc, and c-jun.
Conclusion: These results are consistent with previous findings that Cd alters the localization of E-cadherin in lung and this effect is associated with a decrease in the level of expression of E-cadherin and its associated protein β-catenin. These effects do not lead to the activation of β-catenin-regulated gene expression.
Acknowledgment: Supported by NIH Grant R01 ES006478.

♦B20

Lymphatic Pump Treatment Mobilizes Leukocytes from the Gut Associated Lymphoid Tissue Into Thoracic Duct Lymph

A. Schander, MS, OMS-I[1], M.K. Bearden, BS[2], J.B. Huff, BS, OMS-III[3], A.J. Williams, Jr., BS[4], S.T. Stoll, DO, PhD[3], J.W. Simecka, PhD[2], H.H. King, DO, PhD[3], H.F. Downey, PhD[4] L.M. Hodge, PhD[3]
[1]Dept. of Microbiology and Immunology, UNTHSC, Fort Worth, TX, [2]Dept. of Molecular Biology and Immunology, UNTHSC, Fort Worth, TX, [3]Osteopathic Research Center, UNTHSC, Fort Worth, TX, [4]Dept. of Integrative Physiology, UNTHSC, Fort Worth, TX

Rhythmic compressions on the abdomen during LPT most likely compress the abdominal area, including the spleen and gastrointestinal mucosa, which may facilitate the release of leukocytes from these tissues into circulation. To determine the acute effects of LPT on canine intestinal lymph leukocytes, a catheter was inserted into the large intestinal lymph duct. In a separate set of experiments, the thoracic lymph duct was cannulated and 25-50% of the mesenteric lymph nodes (MLN) were fluorescently labeled *in situ* with carboxyfluorescein diacetate succinimidyl ester (CFSE). The abdominal incision was closed, and thoracic duct lymph was collected at baseline, during 4 min of LPT, and during 10 min following LPT. Leukocytes in both thoracic duct and intestinal duct lymph were enumerated and the percentage of CFSE labeled leukocytes (reflective of cells from the MLN), B cells, T cells, IgA and IgG antibody forming cells were measured by flow cytometry. Within the first 2 min of LPT, leukocytes are mobilized into intestinal and thoracic duct lymph circulation; however, larger increases in thoracic duct leukocytes appear later, in the last 2-4 min of treatment, and stay elevated during recovery while intestinal leukocyte numbers decrease. Flow cytometry and differential cell staining revealed that CD4+ T cells, CD8+ T cells, B cells and IgG antibody forming cells numbers were similarly increased during LPT. Interestingly, the baseline population of IgA forming cells was 6.10 ± 1.80 %, which increased to 8.75 ± 2.62 % during LPT, suggesting that LPT acts preferentially on mucosal-derived cells. Furthermore, LPT increased the percentage of CFSE labeled leukocytes in the thoracic duct lymph from 15% to 22.6%, suggesting that the MLN are a tissue source that LPT can release leukocytes from. Collectively, these data suggest that LPT can mobilize T and B cells from the MLN into the thoracic duct lymph. The gut associated lymphoid tissue (GALT) is an inductive tissue of antigen-specific leukocytes which migrate from GALT into other mucosal associated tissues, such as the lung. Therefore, treatments, such as LPT, that specifically mobilize leukocytes from GALT may increase the numbers of leukocytes that are able to traffic into the lung during pulmonary infection.

♦B21

The Effects of MIST Ultrasound Therapy on Inflammatory Responses of Macrophages

S.E. Kozak, MS-II[1], J. Goral, PhD[2]
[1]Midwestern University/CCOM, Downers Grove, IL, [2]Dept. of Anatomy, Midwestern University/CCOM, Downers Grove, IL

Hypothesis: Mist Therapy (MIST) promotes chronic wound healing by affecting the inflammatory processes occurring in the wound.
Background: Chronic wounds are characterized by a prolonged inflammatory phase. Macrophages, which mediate inflammatory responses, are among the cells participating in wound healing. MIST is a therapeutic, non-contact ultrasound system used to promote chronic wound healing. This study examined the effects of MIST on the inflammatory responses of human macrophages.
Methods: Human macrophage THP-1 cell line was used. The cells were subjected to MIST delivered with an atomized solution of sterile saline or without saline. A nebulizer was used for control treatment. The cell viability was examined immediately and 18 h after procedure. Following the treatments, THP-1 cell populations were stimulated with lipopolysaccharide (LPS, 10 ng/ml). Tumor Necrosis Factor (TNF)α levels, activation of p38 mitogen-activated protein kinase (MAPK) and 27 kD heat shock protein (hsp27) were assessed.
Results: The THP-1 cell viability was not affected by MIST and by nebulizer treatments. MIST significantly reduced TNFα production triggered by LPS (45-60% of untreated or control cells, $p<0.01$). The degree of inhibition was dependent on duration of MIST, and was significantly greater after a longer treatment. In addition, levels of LPS-activated p38 MAPK and hsp27 were lower in MIST than in the control or untreated THP-1 cells.

♦Indicates posters entered in the Student Prize Competition, a judged event that takes place during the Poster Session at the Research Conference.

Conclusions: The results of this study indicate that MIST significantly down-regulates inflammatory responses of THP-1 cells. The mechanism of inhibition involves diminished activation of the p38 MAPK signaling pathway. Since excess of inflammation is a characteristic feature of chronic wounds, the anti-inflammatory effects of MIST may contribute to better healing of such wounds.

♦B22

Performance of a Low or Moderate Intensity Exercise Bout Results in Equivalent Moderation of Glycemia After an Oral Glucose Load in Non-Diabetic Subjects

B. Boesch, OMS-III[1], T. Wong, PhD[2], E. Ip, PharmD[3], N. Philbin, OMS-II[1], B. Boesch, OMS-II[1], N. Muraoka, OMS-II[1], M. McClymont, OMS-II[1], R. Doxey, OMS-II[1], S. Ostrander, OMS-II[1]
[1]Touro University-COM., Vallejo, CA, [2]Dept. of Basic Science, Touro University/CCOM, Vallejo, CA, [3]Dept. of Clinical Sciences, Touro University College of Pharmacy, Vallejo, CA

Hypothesis: ADA guidelines recommend 150 min/wk of moderate intensity aerobic exercise. However, moderate intensity exercise (jogging) can be too rigorous for many diabetics. Although low intensity exercise (walking) is more easily achieved, its effectiveness for hyperglycemia control is unclear. The hypothesis is that low intensity exercise after a glucose load reduces postprandial hyperglycemia as effectively as moderate intensity exercise.

Methods: Non-diabetic subjects were recruited from the campus community (n=9). A non-exercise Oral Glucose Tolerance Test was performed to obtain a glycemia response profile for comparison to the response to low and moderate intensity exercise. After fasting 4-6 hrs, 52-75 gms of glucose (Dex4) was consumed. Glyemia was assayed (TheraSense Freestyle Freedom) at 10-20 min intervals over 130 min while subjects rested. Exercise procedures were identical except glycemia was assayed while subjects performed stationary recumbent cycling (StarTrac Pro). Exercise intensity was based on subject's peak O2 consumption (VO2pk) rate (Korr CardioCoach-PLUS Fitness Assessment): Low = 30%; Mod = 70% VO2pk. Cycling duration was adjusted for isocaloric work output. Data were analyzed for parameters indicative of glycemic exposure.

Results: At rest, plasma glucose rose (151 ±31 mg/dL) within 20 min. after glucose ingestion. As testing progressed, subjects displayed higher than expected glycemia levels, perhaps attributable to the short fasting period. Average values between 40-60 min. exceeded 200 mg/dL (peak: 204 ±32 mg/dL). However, levels declined to near pre-glucose levels by the end of the period (112 ±29 mg/dL). By comparison, exercise resulted in reduced glycemia over the same period. Peak exercise values tended to be lower (30% =174 ±29; 70% =173 ±18 mg/dL). Moreover, values at most points during the period ranged between 5-30% lower than corresponding non-exercise levels, resulting in overall reduced hyperglycemic exposure. Interestingly, although glycemic peak was delayed by moderate vs. low intensity exercise, no other parametric differences were apparent between cycling regimens.

Conclusions: Data supports effectiveness of exercise in reducing postprandial glycemia. Results also suggest that a comparable level of glycemia control may be achieved during low intensity compared to more vigorous moderate intensity exercise.

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♦B23

Acute Versus Chronic Gestational Ethanol Exposure in the Murine Model

T. Ho, MS-I[1], T. Thal, MS[2], Y. Yueh, PhD[2]
[1]Midwestern University/AZCOM, Glendale, AZ, [2]The Translational Genomics Research Institute, Phoenix, AZ

Background: Ethanol is a teratogen that causes a variety of gestational anomalies, including abnormal limb formation. Previous models show that acute ethanol exposure at E9.25 and E9.5 possibly disrupts a positive feedback loop between the apical ectodermal ridge and zone of polarizing activity. Current studies aim to establish the effects of acute versus chronic ethanol exposure on limb development. Plasma ethanol concentrations, soft tissue and skeleton, and expression of Fgf-8, Fgf-10, Sonic hedgehog (Shh), Gremlin and Patched are determined.

Methods: The following experiments were approved by the Midwestern University Research and Animal Care Committee. For the acute model, pregnant females were injected with 0.175mL or 0.020mL 25% ethanol/ g body weight at E10.25 and E10.42. For the chronic model, female mice were acquainted with a control liquid diet for two days, followed by a 5.3% ethanol liquid diet, where mating took place three days after ethanol exposure. Maternal plasma ethanol concentration was determined. Embryos were isolated at E11.25 and stained using in situ hybridization to visualize gene expression in the limb bud, or at E18.0 days for bone and cartilage analysis using alizarin red and alcian blue stains.

Results: The acute model revealed a significant decrease in maternal plasma ethanol at 2.5 hours after the first injection. Skeletal analysis exhibited ectrodactyly for digit 5 on both forelimbs and delay in bone ossification. Fgf-8, Fgf-10, and Shh expressions were down-regulated, while Gremlin and Patched appeared to be up-regulated. Data on the chronic model showed that plasma ethanol concentrations followed a quadratic trend throughout the course of the ethanol-containing liquid diet. In the skeletal analysis, 18 day fetuses revealed missing cartilage and delayed bone ossification. Fgf-8, Shh, and Gremlin expressions were down regulated.

♦Indicates posters entered in the Student Prize Competition, a judged event that takes place during the Poster Session at the Research Conference.

Conclusion: Acute and chronic ethanol exposure produces different trends in plasma ethanol concentrations and limb abnormalities. Future research will focus on the specific molecular mechanisms responsible for the differences observed in our study.

♦B24

The Role of CXCR2 Chemokines in Pathogenesis of Chlamydia Infection

H.Y. Lee, OMS-II, MBS[1], J.H. Schripsema, BS[1], I.M. Sigar, PhD[1], C.M. Murray, BS[1], J.K. Kasimos, DO[2], K.H. Ramsey, PhD[1]
[1]Dept. of Microbiology and Immunology, Midwestern University/CCOM, Downers Grove, IL, [2]Dept. of Pathology, Midwestern University/CCOM, Downers Grove, IL

Background: Pathogenesis of *Chlamydia* female urogenital infections has been studied using a mouse model of infection with *Chlamydia muridarum*. We have previously reported that during ascending infection into the upper urogenital tract, a vigorous acute inflammatory infiltrate composed primarily of polymorphonuclear neutrophils (PMN) ensues. PMN infiltrates are associated with sloughing of epithelial cells and dissolution. Upon chlamydial infection, mouse oviduct epithelial cells have been shown to rapidly release certain so-called ELR CXC motif chemokines. These chemokines are known to bind the CXC receptor-2 (CXCR2) which is found in high density on PMN. Thus, we sought to determine the role of CXCR2 chemokines in pathogenesis of *Chlamydia muridarum* urogenital infection.

Hypothesis: We hypothesized that PMN chemotaxis and subsequent PMN- mediated pathological damage will be mollified in mice genetically deficient in CXCR2.

Materials and Methods: We first infected CXCR2 gene deleted (KO) and wild type CXCR2 sufficient control mice with *Chlamydia muridarum* and monitored the infection course for up to 56 days post-infection by quantitative culture of cervical-vaginal swabs in HeLa 229 monolayers. We assessed blood PMN and band cell counts on Giemsa-stained peripheral blood smears and gross pathology and histopathology upon necropsy of infected mice.

Results: Our results indicated a tendency toward a less intense and slightly more prolonged infection course in CXCR2 KO although this trend did not yield statistical significance. Nonetheless, higher percentages of peripheral blood PMNs were observed in mice genetically deficient in CXCR2 compared to wild type mice ($P<0.05$, two-tailed t test, N=5). Gross pathology revealed 60% reduction in acute pathological damage (pyosalpinx, $P<0.02$, Fisher's Exact Test) and 85% reduction in chronic pathology (hydrosalpinx, $P<0.0001$) in our CXCR2 KO mice when compared to CXCR2 intact wild type mice.

Conclusions: Based on these data, we conclude that CXCR2 is critical to recruitment of PMN to sites of chlamydial infection. In the absence of CXCR2, PMNs are "trapped" within the vascular compartment and are unable to assemble at the site of infection to inflict damage to host tissues. CXCR2-mediated accumulation of PMN in infected tissue had no significant effect on the course of infection but reduced acute and chronic pathological outcomes to include hydrosalpinx which is a surrogate marker of tubal factor infertility.

♦B25

Inflammatory Responses of Macrophages Inhibited by Ethanol are Restored by Vitamin D

B. Hanshaw, OMS-II, J. Goral, PhD
Dept. of Anatomy, Midwestern University/CCOM, Downers Grove, IL

Hypothesis: Ethanol is known to increase susceptibility to infection, at least in part by suppressing macrophage function. This study examined whether 1α, 25-dihydroxyvitamin D3 (1,25D3), the active form of vitamin D3, could restore the ethanol-impaired inflammatory response of the human monocytic cell line THP-1. 1,25D3 is known to increase antimicrobial activity of macrophages and keratinocytes. In addition 1,25D3 promotes monocytes to mature to macrophages and induces expression of CD14. CD14 together with TLR4 and MD-2 participates in the recognition of LPS by macrophages.

Methods: THP-1 cells were cultured in the presence or absence of ethanol (0.3%). Forty eight hr prior to the experiments, culture medium of half of the ethanol-treated and untreated THP-1 cells was supplemented with 1,25D3 (100 nM). The cell populations were then stimulated with LPS (10 ng/ml), and TNFα production and activation of p38 MAPK were assessed.

Results: Ethanol treatment alone reduced TNFa synthesis 3.7 fold ($p<0.05$). 1,25D3 augmented TNFa production in both untreated control and THP-1 cells subjected to ethanol (3.3 and 6.6 fold, respectively, $p<0.05$). This 1,25D3-induced upregulation of TNFα levels was accompanied by an additional increase of p38 activation (2.8 and 2.0 fold in untreated control and ethanol-treated THP-1 cells, respectively).

Conclusion: This study shows that 1,25D3 can significantly augment inflammatory responses of human monocytic THP-1 cells. Moreover, the effect of 1,25D3 on TNFα production in ethanol-treated cells was more pronounced than in untreated control cells, suggesting that vitamin D3 may restore ethanol-induced impairment of inflammatory responses. Future experiments will assess whether 1,25D3 can similarly affect ethanol-impaired inflammatory responses to other pathogen-associated-molecular patterns (PAMPs).

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B26

Upregulation of Cellular glutathione by 3H-1, 2-Dithiole-3-Thione as a Highly Effective Strategy for Protecting Against Acrolein-induced Neurocytotoxicity

H.P. Misra, PhD[1], z. Jia, PhD[2], B.R. Misra, DO[2], H. zhu, MD[2], y. Li, MD, PhD[2]
[1]Dept. of Biomedical Sciences, Edward Via Virginia College of Osteopathic Medicine, Blacksburg, VA, [2]Edward Via Virginia College of Osteopathic Medicine, Blacksburg, VA

Acrolein, an unsaturated aldehydic product of lipid peroxidation, has been implicated in the pathogenesis of various neurodegenerative disorders including Parkinson's disease. A number of cellular factors including glutathione (GSH), GSH S-transferase (GST) and aldose reductase (AR) have been proposed to play an important role in the detoxification of acrolein in target cells. However, whether chemical upregulation of these cellular defenses affords protection against acrolein toxicity in neuronal cells has not been investigated. In this study, we have characterized the inducibility of GSH, GST and AR by 3*H*-1,2-dithiole-3-thione (D3T) and the protective effects of the D3T-elevated cellular defenses on acrolein-mediated toxicity in human neuroblastoma SH-SY5Y cells. Incubation of SH-SY5Y cells with D3T (10-100 μM) resulted in a marked concentration- and time-dependent induction of GSH, but not GST or AR. D3T treatment also led to increased protein and mRNA expression of γ-glutamycysteine ligase (GCL), the key enzyme in GSH biosynthesis. Incubation of SH-SY5Y cells with acrolein for 0.5 and 1 h resulted in a significant depletion of cellular GSH, which preceded the decrease of cell viability, suggesting a critical involvement of GSH in acrolein-induced cytotoxicity. Pretreatment of SH-SY5Y cells with D3T afforded a dramatic protection against acrolein-induced cytotoxicity, as assessed by MTT reduction, lactate dehydrogenase release, as well as morphological changes. To further demonstrate the involvement of GSH in protection against acrolein-induced cytotoxicity, buthionine sulfoximine (BSO) was used to inhibit cellular GSH biosynthesis. Depletion of cellular GSH by BSO dramatically potentiated acrolein-induced cytotoxicity. Cotreatment of SH-SY5Y cells with BSO and D3T was found to prevent the D3T-mediated GSH induction and completely reverse the cytoprotective effects of D3T on acrolein-induced toxicity. In contrast, selective inhibition of either AR or GST failed to potentiate acrolein-induced cytotoxicity. However, when cells were depleted of GSH by BSO, the inhibition of AR by sorbinil potentiated acrolein-induced toxicity. Taken together, this study demonstrates that upregulation of GSH is a predominant mechanism underlying D3T-mediated protection against acrolein-induced neurocytotoxicity.

B27

Alpha-lipoic Acid Potently Inhibits Peroxynitrite-mediated DNA Strand Breakage and Hydroxyl Radical Formation: Implications for the Neuroprotective Effects of Alpha-lipoic Acid

H.P. Misra, PhD[1], z. Jia, PhD[2], H. zhu, MD[2], M. Vitto, MS[3], y. Li, MD, PhD[2]
[1]Dept. of Biomedical Sciences, Edward Via Virginia College of Osteopathic Medicine, Blacksburg, VA, [2]Edward Via Virginia College of Osteopathic Medicine, Blacksburg, VA

Alpha-lipoic acid (LA) has recently been reported to afford protection against neurodegenerative disorders in humans and experimental animals. However, the mechanisms underlying LA-mediated neuroprotection remain an enigma. Because peroxynitrite has been extensively implicated in the pathogenesis of various forms of neurodegenerative disorders, this study was undertaken to investigate the effects of LA in peroxynitrite-induced DNA strand breaks, a critical event leading to peroxynitrite-elicited cytotoxicity. Incubation of φX-174 plasmid DNA with the 3-morpholinosydnonimine (SIN-1), a peroxynitrite generator, led to the formation of both single- and double-stranded DNA breaks in a concentration- and time-dependent fashion. The presence of LA at 100-1600 μM was found to significantly inhibit SIN-1-induced DNA strand breaks in a concentration-dependent manner. The consumption of oxygen induced by 250 μM SIN-1 was found to be decreased in the presence of high concentrations of LA (400-1600 μM), indicating that LA at these concentrations may affect the generation of peroxynitrite from auto-oxidation of SIN-1. It is observed that incubation of the plasmid DNA with authentic peroxynitrite resulted in a significant formation of DNA strand breaks, which could also be dramatically inhibited by the presence of LA (100-1600 μM). EPR spectroscopy in combination with spin-trapping experiments, using 5,5-dimethylpyrroline-*N*-oxide (DMPO) as spin trap, resulted in the formation of DMPO-hydroxyl radical adduct (DMPO-OH) from authentic peroxynitrite and LA at 50-1600 μM inhibited the adduct signal. Taken together, these studies demonstrate for the first time that LA can potently inhibit peroxynitrite-mediated DNA strand breakage and hydroxyl radical formation. In view of the critical involvement of peroxynitrite in the pathogenesis of various neurodegenerative diseases, the inhibition of peroxynitrite-mediated DNA damage by LA may be responsible, at least partially, for its neuroprotective activities.

♦B28

Growth of Osteoblasts on 3-D Collagen

A. Lyons, BA, OMS-II, E. Hays, BS, N. Chandar, PhD
Dept. of Biochemistry, Midwestern University/CCOM, Downers Grove, IL

Hypothesis: Monolayer cultures of normal and transformed cells on plastic surface are suboptimal in simulating the in vivo condition. Therefore, we have developed a three dimen-

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sional (3-D) type 1 collagen gel system to study bone cells in culture with the hypothesis that it would offer a more physiological model system for studying bone cell interaction with its microenvironment. In contrast, we hypothesized that a cell line with a genetic defect in attachment will behave similarly on either surface.

Materials and Methods: We established the 3-D collagen model using rat tail type I collagen and compared growth and differentiation of an osteoblast cell line. We studied the growth of a prostate adenocarcinoma line with propensity to grow in bone and an osteoblast cell line with reduced expression of a signaling protein (PTEN) important for cell attachment. Cells grown on either surface were studied for changes in cell morphology, differentiation markers and mineralization capacity.

Results: We found osteoblasts to grow slower and differentiate faster on collagen when compared to plastic. With the prostate cancer cell line we found better growth on collagen than plastic. In previous studies we observed loss of PTEN to initially decrease the ability of osteoblasts to adhere to plastic and grow. In this study, we found loss of PTEN did not alter this property irrespective of the surface employed for their growth. After a lag period in growth, these cells eventually attached and differentiated well on collagen. Alkaline phosphatase levels were higher and cells were larger when compared to control osteoblasts. Mineral deposition was quantified and revealed that the mineralization of osteoblasts was two fold greater when grown on collagen compared to plastic. Cells with reduced PTEN showed a two fold greater capacity to mineralize when compared to cells with normal PTEN expression.

Conclusions: These findings show that the collagen surface, while offering a more physiological surface to osteoblasts, also allows better growth of cancer cell types that migrate to bone. The loss of PTEN function affects cell attachment to both plastic and collagen, showing that a defect in the genetic pathway cannot be reversed by collagen.

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B29

Prediction of Ligament Length During Wrist Flexion and Extension

R.M. Patterson, PhD[1], N. Yazaki, MD[2], C.R. Andersen, BS[3], N.H. Scott, AA[3], S.F. Viegas, MD[3]
[1]Dept. of Osteopathic Manipulative Medicine, University of North Texas Health Science Center, Fort Worth TX, [2]Nagoya University, Hagoya Aichi, Japan, [3]Dept. of Orthopaedic Surgery and Rehabilitation, University of Texas Medical Branch, Galveston, TX

This project combines high precision motion analysis of the carpal bones, subsequent manual digitization of the ligament attachment regions, and a simulated ligament wrapping model, to generate predictions of carpal ligaments' length and implied strain during wrist motion. Three cadaver upper extremities were studied. Rods were placed into the radius, capitate, scaphoid, lunate, triquetrum, and ulna. A triad pin (TP) was attached to each rod. The TPs have three 5-mm diameter spheres, coated with reflective tape placed in a cruciform arrangement on top. TPs were oriented to assure that they would not come into contact with each other during a full range of motion of the. The flexor and extensors of the wrist were then weighted and the wrist moved passively through a flexion/extension motion. A six camera optical motion system was used to track the reflective markers during motion. Then each wrist was tested in a series of progressive and cumulative disruptions of the intercarpal ligaments. The order of ligament cuts were as follows: 1) middle and palmar portion of the scapholunate interosseous ligament (SLIOL), 2) Dorsal intercarpal (DIC) off the scaphoid, 3) dorsal portion of the SLIOL, 4) DIC off the lunate and 5) lunotriquetral interosseous ligament. CT scans of the specimens were performed and a 3D surface model of each bone and markers was generated. Each specimen was disarticulated, ligament attachment regions identified, and a 3D model created. The 3D models were synchronized with the motion analysis to generate an animation. Simulated ligament fibers were mapped between corresponding attachment regions in the model which included the capability for surface wrapping. Data analysis included the wrist angle in terms of the capitate orientation with regard to the radius as well as predicted ligament length. Ligament strain was estimated as the change in ligament length over entire wrist range of motion. Twenty two ligament segments were modeled. Statistical differences in predicted ligament length occurred most commonly after the dorsal SLIOL was cut. Significant changes occurred after cutting the dorsal portion of the SLIOL. Two major conclusions were found. First, normal motion and function will be restored if an anatomic reduction between the scaphoid and lunate is achieved surgically by repairing the dorsal SLIOL. Second, significant changes in ligament length occur after disruption of the ligaments between the scaphoid and lunate.

♦B30

DDE Abrogates Effects of Testosterone in NZB/W F1 Female Mice

J.R. Mensing, MBS, OMS-III, S. Viselli, PhD
Dept. of Biochemistry, Midwestern University/CCOM, Downers Grove, IL

Background: DDE is a toxic environmental contaminant and known antiandrogen. It has been shown to have pathophysiologic effects on the reproductive and immune systems. In this study we use a mouse model, the female NZB/W F1 hybrid, which develops a disease very similar to human systemic lupus erythematosus (SLE). Testosterone treatment is known to result in improvement of their SLE-

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like symptoms.
Hypothesis: DDE will impact the immune system of ZB/W F1 hybrid mice by decreasing the subpopulation of regulatory T cells thereby abating the positive effect of testosterone on the symptoms of their SLE- like disease. DDE will also decrease the presence of autoimmune disease markers.
Materials & Methods: Female NZB/W F1 hybrid mice were separated into three treatment groups of twelve mice each. All mice were implanted with subcutaneous capsules that were either inert (control) or eluted testosterone over 90 days. Mice also received either DDE in cottonseed oil (200mg/kg) or vehicle control by oral gavage (02 ml). Urine protein concentration was measured as a monitor of kidney function. At 2, 4, 6, and 7 months, mice were sacrificed then spleen, thymus and kidneys were collected. Immune cell populations from spleen and thymus were measured by flow cytometry. In addition, serum samples were collected for analysis of autoantibodies. For this analysis, a proteome array created to identify seroprofiles of the human SLE disease state was utilized.
Results: Urine protein concentration was reduced by testosterone treatment. This effect was attenuated by concurrent DDE administration. Regulatory T cell subpopulations were also increased with testosterone treatment. Again, this effect was attenuated by concurrent DDE administration. Generally, autoantibodies found to be decreased in mice treated with testosterone, as compared to untreated controls with SLE-like disease. Surprisingly, concurrent DDE administration further reduced autoantibodies. A notable exception was autoantibodies directed to the Vimentin antigen.
Conclusions: DDE co-administration with testosterone appears to reduce some beneficial effects of testosterone treatment of the NZB/W F1 mice with a lupus-like disease. However, DDE also appears to alter autoantibody production in these mice.

♦B31

Expression of Cystine-glutamate Transporter SLC7A11 (xCT) Increases Cell Survival in Mesothelioma

C.L. Nguyen, BS, OMS-II, Y. Huang, MD, PhD
WesternU/COMP, Pomona, CA

Malignant mesothelioma is an aggressive and treatment-resistant tumor; the incidence of this tumor is increasing throughout the world. Several studies have shown that the expression of genes encoding antioxidants (e.g. glutathione) are increased in mesothelioma cells and may play an important role their drug resistance. The synthesis of glutathione requires the rate-limiting cellular uptake of cystine via the cystine-glutamate transporter SLC7A11. Our previous studies showed that SLC7A11 overexpression in lung and ovarian cancers conferred chemoresistance to multiple anticancer agents. The present study investigated the expression and activity of SLC7A11 and related genes such as NADP[H] quinine oxidoreductase 1 (NQO1), both of which are positively regulated by the transcriptional factor NRF2 and negatively regulated by the NRF2 suppressor KEAP1. We examined the mRNA and protein levels of SLC7A11, NQO1, NRF2 and KEAP1 in eight mesothelioma cell lines using RT-PCR, Dot Blot, Western Blot and immunocytochemistry techniques. We also inhibited the transport activity of SLC7A11 using glutamate or (S)-4-carboxyphenylglycine and examined their effects on the sensitivity of tumor cells to anticancer drugs geldanamycin and L-alanosine. Our results indicated that SLC7A11 and NQO1 were differentially expressed by the eight mesothelioma cell lines and their expression levels correlated with the drug resistance in these cells: In cell lines with high levels of SLC7A11 expression, SLC7A11 inhibition significantly increased the potency of geldanamycin, while the potency of L-alanosine, an amino acid analog and potential substrate of SLC7A11 was reduced. No somatic mutation in exon-coding regions of the KEAP1 gene was detected in the eight cell lines. These findings indicate a possible role of NRF2-regulated proteins such as SLC7A11 and NQO1 in chemoresistance of mesothelioma. Understanding the function of these proteins will allow more effective pharmacological treatment for this illness.

♦B32

Chlamydophila (Chlamydia) Pneumoniae Promotes AB 1-42 Amyloid Processing in Neuronal Cells: A Pathogenic Trigger for Alzheimer's Disease

E.K. Ruszak, MS[1], K.C. McCarthy, OMS-II[1], M.G. Bell, PhD[1], B.J. Balin, PhD[2], D.M. Appelt, PhD[1]
[1]Dept. of Neuroscience, Pharmacology and Physiology, PCOM, Philadelphia, PA, [2]Dept. of Microbiology, Immunology and Forensic Medicine, PCOM, Philadelphia, PA

Background: Previously, our laboratory identified *Chlamydophila (Chlamydia) pneumoniae* (Cpn) in autopsied sporadic AD brains. Furthermore, we have developed a BALB/c mouse model that demonstrated infection-induced amyloid plaques similar to those found in AD, and demonstrated that Cpn infection of neuronal cells inhibited apoptotic pathways of cell death.
Hypothesis: Our current studies address whether infection with Cpn triggers abnormal cleavage of the beta amyloid precursor protein (▼APP) into A▼1-42, thereby contributing to amyloid plaque formation characteristic of the pathology identified in AD.
Materials and Methods: Human neuroblastoma cells were infected with the respiratory strain AR39 Cpn *in vitro*, then amyloid processing was analyzed and quantitated using immunocytochemistry, Western blotting and ELISA assays.
Results: Cpn was shown to infect neuronal cells and induce intracellular amyloid processing. Cpn infection yielded cytoplasmic labeling of A▼1-42 that was increased relative to uninfected cells. The ELISA assay revealed that in neuronal

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cell lysates, A-1-42 in the infected cells was increased 3 to 16-fold over the uninfected cells, from 24 to 72hr post infection. Western blot analysis confirmed an increase in Aβ1-42 in the infected neuronal cell lysates.

Conclusions: These data suggest that infection of neuronal cells with *Chlamydophila (Chlamydia) pneumoniae* alters the processing of -APP, thereby producing A-1-42. Therefore, these studies and previous research reported by our laboratory support the implication of Cpn as a pathogenic agent in perpetuating the hallmark amyloid plaque formations observed in AD. This concept holds major therapeutic considerations for future studies.

♦B33

Lymphatic Pump Treatment Enhances Immunity and Reduces Pulmonary Disease During Experimental Pneumonia Infection

J.B. Huff, BS, OMS-III[1], A. Schander, MS[2], S.T. Stoll, DO, PhD[1], J.W. Simecka, PhD[2], H.F. Downey, PhD[3], H.H. King, DO, PhD[1], L.M. Hodge, PhD[1]

[1]Osteopathic Research Center, UNTHSC, Fort Worth, TX, [2]Dept. of Molecular Biology and Immunology, UNTHSC, Fort Worth, TX, [3]Dept. of Integrative Physiology, UNTHSC, Fort Worth, TX

Clinical studies have shown that patients given osteopathic lymphatic pump treatment (LPT) during pneumonia have enhanced clearance of the tracheobronchial tissues, shorter duration of cough, and shorter duration of total and intravenous antibiotic treatment and hospitalization. These studies suggest that LPT may reduce pulmonary infection by enhancing immunity; however, the exact mechanisms responsible for the clinical benefits of LPT have not been identified. The purpose of this study was to determine if LPT would enhance immunity and reduce pulmonary disease during chronic pneumonia. To determine if a single LPT would increase blood leukocytes, samples were collected from the jugular vein at baseline, immediately following LPT (n=7) or sham (n=7), and at 10, 20, 30, 45, and 60 minutes post LPT or sham and analyzed for leukocyte concentrations. Consistent with reports in humans, LPT released approximately 4,000,000 more leukocytes into blood circulation 45 minutes after treatment compared to sham ($p<0.01$). Differential analysis revealed these were primarily lymphocytes. In a separate set of experiments, rats were intranasally infected with 5×10^5 colony forming units of *Mycoplasma pulmonis*. Twenty-four hours following infection, rats received either Sham (n=8) or LPT (n=9), under anesthesia, daily for days 1-4, and 7-10 post infection. Fourteen days following infection rats were euthanized, lungs were removed and analyzed for gross lesions and bacterial numbers, and blood samples were analyzed for leukocyte concentrations. During *M. pulmonis* infection, LPT reduced pulmonary bacterial numbers 4-fold, and lung lesions 13% compared to sham ($p<0.05$). Furthermore, LPT increased blood leukocyte numbers compared to sham ($p<0.05$). Specifically, LPT released approximately 1, 000,000 more lymphocytes and 80,000 more monocytes into blood circulation compared to sham. Collectively, these data suggest that during pulmonary infection, LPT increases circulating leukocytes that may traffic into the lung and kill bacteria, thereby reducing lung lesions. Ongoing and future studies will examine if LPT enhances leukocyte activation and recruitment into the lung. These data are essential to identifying the mechanisms by which LPT enhances immunity and clearance of pneumonia, and will provide scientific support for the clinical use of LPT.

♦B34

Comparison of Detection Methods Specific for Chlamydophila pneumoniae in Cell Culture after Infection and in the Brains of BALB/c Mice Following Direct Injection

C. Caruthers, BS[1], C.J. Hammond, MS[1], D.M. Appelt, PhD[2], B.J. Balin, PhD[1], C.S. Little, PhD[1]

[1]Dept. of Pathology, Microbiology, & Immunology, PCOM, Philadelphia, PA, [2]Dept. of Neuroscience, Physiology, and Pharmacology, PCOM, Philadelphia, PA

Background and Hypothesis: Infection with *Chlamydophila pneumoniae* (CP) has been associated with AD and was first reported by Balin et al, identifying CP post-mortem in 17 of 19 AD brains. Additionally, Mahony et al, an independent research laboratory, replicated this study identifying CP in 18 of 21 AD brains. However, other reports have been unable to replicate the findings. Following the identification of CP in AD brain tissue, Little et al identified amyloid deposits, resembling plaques found in AD, in brains of experimentally CP-infected non-transgenic BALB/c mice. Tissue was examined immunohistologically at 1-3 months post-infection. The goal of the current study is to optimize and standardize a protocol that is, both highly sensitive and specific for the detection of CP. This work advances previous studies examining the role of CP in the induction/progression of AD-like pathology in BALB/c mice.

Materials and Methods: The evaluated techniques included PCR, immunohisto/cytochemistry, and recovery of viable organism. Detection techniques were first optimized in cell culture infected with known amounts of CP. These optimized techniques were used to detect CP in experimentally-infected mouse tissues, infected by direct injection of CP into the CNS.

Results and Conclusions: All detection methods analyzed were specific for CP, however PCR was the most sensitive. Furthermore, nested PCR was the most sensitive technique employed. Thus, nested PCR, specific for omp-A, will facilitate the detection of low numbers of CP-infected cells in experimentally-infected mouse tissue in addition to CP in clinical samples.

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♦B35

Effects of Microvascular Amyloid Deposition on the Structural and Functional Integrity of Vascular Smooth Muscle Cells and Blood-Brain Barrier in the Alzheimer's Disease Brain

E. Levin, OMS-III[1], P.M. Clifford, PhD[2], S.B. Zavareh, BS[3], V. Venkataraman, PhD[4], R.G. Nagele, PhD[2]
[1]Institute for Successful Aging, UMDNJ-SOM, Stratford, NJ, [2]New Jersey Institute for Successful Aging, UMDNJ-SOM, Stratford, NJ, [3]Graduate School for Biomedical Sciences, UMDNJ-SOM, Stratford, NJ, [4]Dept. of Cell Biology, UMDNJ-SOM, Stratford, NJ

Background:Deposition of beta-amyloid (Aβ) peptides in human brain blood vessels, referred to as cerebral amyloid angiopathy (CAA), is commonly concurrent with Alzheimer's disease (AD) and vascular cognitive impairment patients. Within blood vessels, Aβ peptide deposition occurs preferentially within vascular smooth muscle cells (VSMCs).

Hypothesis: We have proposed that the source of Aβ peptides that deposit within the microvasculature is the blood, and that Aβ peptide deposition compromises the structure and function of VSMCs leading to breakdown of the blood-brain barrier (BBB).

Materials and Methods: In the present study, we examined the deposition patterns of Aβ40 and Aβ42, within the cerebrovasculature of AD and age-matched controls (IRB protocol 2138-E-01) using immunohistochemistry. Also, we tested for BBB breakdown via detection of leaked plasma components in local brain interstitium.

Results: In early stage AD brains with CAA, both Aβ40 and Aβ42 were abundant in VSMCs, especially those in leptomeningeal arteries and their initial cortical branches; in later stage AD brains this pattern extended into smaller branches. The extent of Aβ peptide deposition in VSMCs was linked to loss of their viability as evidenced by lack of expression of smooth muscle actin and loss of nuclei. Perivascular clouds of Aβ42- and less frequently Aβ40-positive material were associated primarily with arterioles, but also with capillaries and venules in brains with more severe pathology. By contrast, comparable regions of most control brains possessed far fewer perivascular leak clouds and Aβ positive blood vessels. In addition, we demonstrate that VSMCs in brain blood vessels express the α7 nicotinic acetylcholine receptor (α7nAChR), which has high binding affinity for Aβ peptides, especially Aβ42.

Conclusions: Results suggest that the blood and BBB permeability provide a major source of the Aβ peptides in brain VSMCs, and the presence and abundance of the α7nAChR on VSMCs may play a role VSMC selective accumulation of Aβ peptides. Aβ peptides are initially confined to VSMCs in the vessel walls, but loss of function and viability eventually allows them to bypass this secondary barrier, enter and accumulate in the brain tissue. This establishes a link between Aβ peptide deposition within the brain microvasculature and chronic breakdown of the BBB in the Alzheimer's disease brain.

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♦B36

Prostate Cancer Cells Can Cause Osteolytic or Osteoproliferative Lesions in Bone by Differential Gene Induction in Bone Cells

S.U. Shetgeri, MS-II, E. Hays, BS, N. Chandar, PhD
Dept. of Biochemistry, Midwestern University/CCOM, Downers Grove, IL

Hypothesis: DU-145 F3 and DU-145 N3 prostate cancer cells can cause osteolytic or osteoproliferative lesions in bone by induction of differentiation-promoting or proliferation-promoting genes in bone cells. This is studied by the use of three models of cell-cell interaction.

Materials and Methods: The first model was a co-culture where osteoblasts were exposed to cancer cells through a 0.04 μm filter separated the two permitting proteins to pass, but no direct contact. Osteoblast numbers and PCR analysis was done to amplify cell differentiation genes. The second model measured the direct effect of harvested rat femoral bone-marrow cells (osteocytes) on cell-free 2 day old rat calvaria when exposed to either DU-145 F3 or DU-145 N3 cancer cell lines in co-culture. The third model cultured osteoblasts in conditioned media (CM) that was initially used to culture either DU-145 F3 or DU-145 N3 cancer cell lines to show if factors secreted by cancer cells could influence osteoblast behavior without their physical presence. This was compared to effect of untreated differentiation promoting (DP) media on osteoblasts.

Results: DU-145 F3 cancer cell line had a greater direct proliferative effect on osteoblast cell numbers than the DU-145 N3 line. Genes involved in cell differentiation such as Cbfa-1 and Osteocalcin were expressed at higher levels in osteoblasts co-cultured with the DU-145 N3 cancer cell line. Increased pitting was observed in rat calvaria cultured with osteocytes and DU-145 F3 cells than with N3 cells. CM treated osteoblasts proliferated at markedly lower levels than those treated with untreated DP media.

Conclusion: DU-145 F3 prostate cancer cells activate proliferation-responsive genes in osteoblasts and favor osteoproliferation. DU-145 N3 prostate cancer cells induce differentiation-responsive genes more avidly than do DU-145 F3 cells. Factors secreted by DU-145 F3 prostate cancer cells cause increased transformation of osteocytes to osteoclasts, thus causing increased osteolytic lesions in living bone tissue. Proliferative properties of CM are blocked by the differentiation promoting properties of DP media, thus living cancer cells must be present for lesions to occur.

♦B37

Role of Telomere Length and Telomere-mediated Chromosomal End-Fusion in Invitro Aging of Human Umbilical Cord Mesenchymal Stem Cells (MSCs)

E. Levin, OMS-III[1], P.M. Clifford, PhD[1], M. Parisi, BS[2], S.B. Zavareh, BS[2], M.C. Kosciuk, PhD[1], R.G. Nagele, PhD[1]
[1]Institute for Successful Aging, UMDNJ-SOM, Stratford, NJ, [2]Graduate School of Biomedical Sciences, UMDNJ-SOM, Stratford, NJ

Background: Mesenchymal stem cells (MSCs) are rare in the body and thus require extensive *ex vivo* expansion prior to clinical use. Potential negative cellular consequences of *ex vivo* expansion include entrance into a state of replicative senescence, loss of stem cell characteristics, and the appearance of potentially precancerous chromosomally abnormal variants.

Hypothesis: We have proposed that some of the cellular changes mentioned above are accompanied by (and possibly the result of) progressive chromosomal changes that include shortening of telomeres and an increased incidence of telomere-mediated chromosomal end fusions (TMCEFs).

Materials and Methods: MSCs were grown and fixed at selected intervals during expansion. The effects of expansion on telomere length were determined by quantitative image analysis of incorporated telomeric peptide nucleic acid (PNA) probes. We followed individual telomeres to determine if decreased length inversely correlates with cell proliferation rates and is associated with senescence. Telomere length profiles (TLPs) were calculated for individual cells using both interphase nuclei and spreads of mitotic chromosomes.

Results: TLPs confirmed telomere length heterogeneity and proportional shortening of telomere length during aging. TLPs also revealed that some telomeric ends of chromosomes were so closely juxtaposed within interphase nuclei that they appeared as a single spot. These TMCEFs were far more prevalent in slowly dividing MSCs. Interestingly, comparable numbers of TMCEFs were observed in MSC nuclei at each selected cell culture interval. Moreover, interphase TMCEFs were relatively rare in more rapidly cycling MSCs at each interval.

Conclusions: Our results suggest that the number of TMCEFs seen in individual cell nuclei is more dependent on the rate at which cells are cycling than on telomere length, with TMCEFs being most prominent in senescent cells. These observations lead us to propose that TMCEFs may play a role in the generation and/or maintenance of chromosome positional stability within interphase nuclei. This may be required for proper functioning of cells that are transitioning from the stem cell state into a more differentiated state. If this proves true, then the lack of TMCEFs in cells may be useful as an index of "stemness" (i.e., retention of full proliferative and developmental potential).

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B38

Obesity Management: A Potential Therapeutic Role for Carbonic Anhydrase Inhibitors

W.R. Chegwidden, PhD, FRSC[1], I.M. Spencer, PhD[2]
[1]Lake Erie College of Osteopathic Medicine, Erie, PA, [2]Dept. of Biomedical and Biomolecular Sciences, Sheffield Hallam University, Sheffield, S. Yorkshire, England

More than 60% of American adults over the age of 20 are overweight and about one quarter are obese. The prevalence of obesity is increasing worldwide, with a total of obese adults exceeding 300 million. Currently available pharmacotherapy is both limited and less than satisfactory, with significant side effects. *De novo* fat synthesis requires specific provision of bicarbonate, not CO_2, as substrate for both the mitochondrial pyruvate carboxylase reaction (which is essential for the efflux from mitochondria of acetyl CoA substrate) and the cytoplasmic acetyl CoA carboxylase reaction (a controlling step in fatty acid synthesis). Carbonic anhydrase (CA), which catalyses the production of bicarbonate from CO_2, the end product of metabolism, is widespread throughout eukaryotic cells where it is present in a variety of isozyme forms in both of these cellular locations. We tested the hypothesis that CA activity is necessary, in liver and adipose cells, for the production of bicarbonate to sustain significant levels of lipid synthesis. Male Wistar rats were euthanized in accordance with the regulations of Sheffield Hallam University. Cell preparations from liver and epididymal fat pads were produced by collagenase digestion. The rate of lipogenesis was assessed by measuring incorporation of radioactive label from ^{14}C-acetate into total lipid, which was extracted in chloroform/methanol mixture and quantitated by liquid scintillation. Lipid production by both cell types was strongly inhibited by the specific CA inhibitors acetazolamide (DIAMOX), methazolamide (NEPTAZANE) and ethoxzolamide (CARDRASE), and the relative effectiveness of these three sulfonamides in inhibiting lipogenesis correlated with their effectiveness as CA inhibitors. Furthermore, the rate of lipogenesis was enhanced by the addition of bicarbonate, which also reduced the effectiveness of the inhibitors. Obese patients treated with the antiepileptic drug topiramate, which is a CA inhibitor, have been reported to suffer from weight loss, and this effect of topiramate has been substantiated by subsequent placebo-controlled trials. These data suggest that carbonic anhydrase is a potential new target for weight control therapy.

♦Indicates posters entered in the Student Prize Competition, a judged event that takes place during the Poster Session at the Research Conference.

B39

Escherichia coli Insulin Isolation, Purification, and Comparative Function

B.J. Plotkin, PhD[1], N. Patel, BS[1], R. Relwani, BS[1], L. Phouikham, BS[1], J. Green, PhD[2], M. Konaklieva, PhD[3]
[1]Dept. of Microbiology and Immunology, Midwestern University/CCOM, Downers Grove, IL, [2]Dept. of Biochemistry, Midwestern University/CCOM, Downers Grove, IL, [3]Dept. of Chemistry, American University, Washington, D.C.

Hypothesis: We hypothesize that the immuno- and bioactivity of insulin transcends biological taxonomy. Insulin is a highly conserved protein evolutionarily. The historically difficult, low yield isolation and purification process has impeded characterization of *E. coli* insulin's properties.

Materials and Methods: A simplified purification method for *E. coli* insulin was designed and the resultant product tested for bioactivity (biofilm formation). Using a combination of acid extractions (HCl and acetic acid), insulin was extracted from disrupted *E. coli*. The acid extraction was followed by chromatography with C-18 SEP PAK (500mg). Microbial insulin was eluted with 75% ethanol/10mM HCl then concentrated. Affinity chromatography (1.5 x 13cm column) which exploited phylogenetic conservation was done with monoclonal mouse anti-human insulin antibody.

Results: *E. coli* insulin was detected in fractions 10-18 (pH 6) with maximal level measured 0. 2 mg/L human insulin equivalents/800g wet weight *E. coli*. A single protein band was seen on SDS-PAGE gel with an estimated molecular weight of 6kd. The ability of purified *E. coli* insulin to affect biofilm formation as compared to human insulin was determined. *E. coli* (10^3 CFU/ml yeast nitrogen base with 1% peptone) was place in 96 well plates with and without insulin and or glucose (pH7.0 and pH 5.5). *E. coli*'s insulin increased production of biofilm ($p<0.001$) as compared to media alone, microbial insulin alone or media with glucose alone (.01%, 0.05%, 0.1%). Human insulin performed similarly. The optimal pH for *E. coli* insulin activity was pH 5. Human insulin was active at pH 5 and 7.

Conclusion: *E. coli* insulin purified with the streamlined procedure and human insulin exhibit analogous effects on *E. coli* phenotype.

B40

Plasma IGF-1, Nitric Oxide and Ionized Magnesium in Aging Hypertensive Rats

C.A. Standley, PhD, P.R. Standley, PhD
School of Osteopathic Medicine, University of Arizona College of Medicine, Phoenix, AZ

Hypothesis: Production of vascular growth modulators, such as IGF-1 and NO, are regulated by plasma cation concentrations as exemplified by Mg^{2+}-induced activation of NO synthase (NOS). In this study, we hypothesized that since IGF-1 and NO regulate each others secretory profiles and Mg^{2+} regulates NOS, all three will correlate appropriately with the development and worsening of hypertension and associated vascular wall remodeling in aging rats.

Methods: Twenty eight 10-week-old male SHR and WKY rats were purchased from Harlan Laboratories. Three animals per group were allowed to age to 20 weeks. Blood pressures were measured non-invasively utilizing the tail cuffs. Plasma IGF-1 was measured via ELISA, plasma Mg^{2+} via an ion-sensitive electrode and plasma NO fluorometrically via a nitrite/nitrate assay kit. Following euthanasia, aortic tissue was fixed in formalin and architectural changes were determined.

Results: Elevated blood pressures (systolic, diastolic, and mean pressure) were confirmed in the SHR vs. WKY animals at 10 weeks. At 20 weeks, pulse pressure was also found to be elevated in the SHR vs. WKY animals. No significant differences were observed in plasma IGF-1, NO or Mg^{2+} among these animal groups. However, Mg^{2+} levels significantly increased with age in both groups, while IGF-1 levels significantly decreased. Moreover, while plasma IGF-1 levels negatively correlated with pulse pressure in 10 week-old WKY ($r^2 = 0.57$, $p = 0.01$), these variables were positively correlated in the SHR ($r^2 = -0.4$, $p = 0.04$). Plasma NO levels were negatively correlated with both systolic blood pressure ($r^2 = 0.59$, $p = 0.02$) and pulse pressure ($r^2 = 0.05$, $p = 0.03$) in 10 week-old SHR, but no such correlations existed in any other animal group. Aortic wall thickness, wall:lumen ratio, and wall:lumen area were all greater in 10 week-old SHR vs. WKY animals ($p<0.05$). At 20 weeks of age, wall thickness was not different between the strains, however, lumen diameter and lumen area were greater in the SHR vs. WKY.

Conclusion: These data suggest that IGF-1, shown to induce VSMC hyperplasia, may be responsible for a portion of the aortic architectural changes seen in developing SHR, further supporting the argument that IGF-1 sensitivity differences between SHR and WKY may exist system-wide. Further studies are designed to test the causal and interactive roles of IGF-1, NO and Mg^{2+} in mediating vascular wall changes in developing hypertension.

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Medical Education and Health Policy ME-HP1

Use of Ultrasonography in the Preclinical Education of Osteopathic Medical Students: A Pilot Study

V.A. Syperda, DO, EdD, MBA, P.N. Trivedi, OMS-II, L.C. Melo, OMS-II, M.L. Freeman, OMS-II, E.J. Ledermann, MBA, OMS-II, T.M. Smith, OMS-II, J.O. Alben, PhD
Department of Radiology, LECOM-Bradenton, Bradenton, FL

Context: Ultrasonography (US) is a valuable diagnostic tool in the clinical setting, yet medical students have little exposure to this technology. The authors propose that it would be beneficial to introduce US principles and practice to osteopathic medical students (OMS) during preclinical education.

Objective: To evaluate the ability of second-year OMS to use US for identification of anatomic structures and to apply US instruction and self-driven learning to the identification of pathologic conditions.
Design: A self-directed approach that reduced facilitator involvement, encouraging learning that mimicked the Problem-Based Learning program at Lake Erie College of Osteopathic Medicine—Bradenton, Florida.
Methods: Five OMSII were each given 10 hours of instruction in US techniques by three certified ultrasonographers in outpatient and hospital settings. Each student then performed 40 hours of organ-specific US scans on another student in 2-hour sessions over 20 weeks, using methods learned in the previous instruction. Images were archived for evaluation and quality rating by two radiologists and two US technologists. Students were presented with a post-training examination consisting of 35 questions related to 10 contrived case scenarios, each with presenting symptoms, pertinent findings and corresponding US images. Questions were designed to test students' knowledge in three categories associated with the images: anatomic structure, technical skill, and clinical diagnosis.
Results: Results of the post-training examination, expressed as the percent of correct answers for all five participants by category, were as follows: anatomic structure, 70%; technical skill, 70%; clinical diagnosis, 68%. Evaluations of the archived images, which were graded for proper anatomic identification and image clarity, yielded the following scores of "good" or "fair" quality for each anatomic region: abdominal region, 80%; pelvic region (via transabdominal scan), 63%; cardiac region, 73%.
Conclusion: Based on their satisfactory written and image acquisition performances, OMSII are capable of attaining a sufficient degree of proficiency in limited US technique, and they have the ability to successfully apply US principles to clinical situations. These results support the use of ultrasonography as an educational tool in the preclinical education of osteopathic medical students.

ME-HP2

Percentages vs. Numbers: Measuring Program Success

E.G. Bridges, PhD[1], E.K. Soper, PhD[2], G.D. Lovett, PhD[2], R.M. Fisk, PhD[3], H.H. Baker, PhD[4]
[1]Department of Functional Biology, WVSOM, Lewisburg, WV, [2]Office of Assessment and Educational Development, WVSOM, Lewisburg, WV, [3]Department of Structural Biology, WVSOM, Lewisburg, WV, [4]Department of Clinical Sciences, WVSOM, Lewisburg, WV

Background: West Virginia School of Osteopathic Medicine has had both a high percentage and high number of its graduates entering primary care osteopathic medical practice in West Virginia's rural communities WVSOM recently made substantial increases in class size, from 81 Year 1 students in Fall 2002 to 213 in Fall 2007: this increase took place without supplemental state funding. This poster explores the question of whether percentages, or absolute "numbers", should be used in evaluating continued program success. Since outcomes comparisons are not yet available for graduates, admissions surveys are analyzed.
Null Hypotheses: There will be no difference on attitudes regarding rural family practice in WV between WVSOM students entering Fall 2002 and Fall 2007, as measured by a) Number, and b) Percentage.
Methods: IRB approval was obtained for surveys administered during Orientation. Surveys contained multiple items about primary care, rural practice, and practice in WV. Response rate in 2002 was 98%; in 2007, response rate was 94%. The Number and the Percent answering representative items were recorded.
Results: One survey item asked, "In what state do you intend to practice?" In 2002 (before expansion), 47 entering students indicated they planed to practice in WV, while in 2007 (after expansion) 55 students indicated that they planned to practice in WV, a gain of 8 students. However, examining percentages, 59% in 2002 and 28% in 2007 planned WV practice, a loss of 31 percentage points. Similarly, the attitude item, "There is a critical need in this country for more primary care physicians" received ratings of "Strongly agree" or "Agree" from 73 students in 2002 and 187 students in 2007, a gain of 114 students. However, examining percentages, 91% gave this response in 2002 and 89% in 2007, a loss of two percentage points. For the attitude item, "I would like to practice in a rural area" received ratings of "Strongly Agree" or "Agree" from 52 students in 2002 and 88 students in 2007, a gain of 36 students. However, examining percentages, 66% gave this response in 2002 and 44% in 2007, a loss of 22 percentage points. Many other survey items also had increases in absolute numbers but decreases in percentages. Because the class size increase did not increase costs to the taxpayers of WV, authors argue that numbers should be used rather than percentages.

♦ME-HP3

Perceived Health Care by Military Personnel: A Qualitative Analysis of Military Cultural Influences on Health Behaviors and the Patient-Provider Relationship

A.C. Zender-Princeton, OMS-II
Touro University of Nevada-COM, Henderson, NV

Current literature has demonstrated that cultures have a substantial impact upon health behaviors and patient-provider communication. The purpose of this study was to explore the influence of the military subculture upon the health experience of service members in their relationship with their health care providers and their health behaviors. The methods used were based upon the qualitative description approach and the comparative nature of Grounded Theory. Twenty-five male

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members from the army, air force, and navy were asked to describe their health experience in semi-structured, open-ended interviews, narrative statements, and closed surveys. In addition to that, observations were made of the interactions between patients and military doctors in an air force base's health clinic for a period of two months. Two major themes emerged: (1) the greater the patient-physician social distance, the greater the mistrust, and (2) service members desire to be understood by their physicians, not only as people, but in terms of their military professions. These findings correlated with the effects of the military's collectivist, utilitarian, and hierarchical subculture, and the "conflicted medical ethics" of the military providers.

ME-HP4

Student Attitudes towards KCUMB's DOCARE International Medical Mission

G.J. Desai, DO, S. Pyle, PhD
Department of Family Medicine & Medical Affairs, KCUMB-COM, Kansas City, MO

Hypothesis: The investigators conducted a medical mission in February 2008, with DOCARE International, in Guatemala, C.A. Prior missions resulted in impressions that reasons for participation in this rotation were to experience the challenges of health care delivery in a developing country, improve Spanish language skills, and provide care to an underserved population.

Materials & Methods: After IRB approval, an online survey combining qualitative and quantitative questions assessed student perceptions of the DO Care experience before and after the mission. Descriptive statistics were calculated for the quantitative questions and a thematic analysis was conducted on responses to qualitative questions. Participation at post test (n=10) compared to pretest (n=24) limited pre/post statistical comparisons.

Results: When asked "What do you expect to gain from the DO Care experience?", participants reported themes such as (1) increased awareness of the healthcare needs of patients in a developing nation (2) improved Spanish speaking skills (3) increased understanding of international medicine and (4) personal growth. A thematic analysis of the qualitative question "What concerns do you have going into the DOCare experience?" found concerns revolving around (1) safety and (2) communication barriers. One student stated he/she was concerned about "not being fluent in the language and still making an impact." Almost 1/2 of participants reported the possibility of participating in an international rotation had *some* (29%) or *a lot* (17%) of impact on their decision to attend KCUMB. This was the first national/international mission for 58% of participants. Post test, all respondents reported they would *probably* or *definitely* participate in future missions. At post test, when asked "How will the DOCare experience affect how you interact with patients?", common themes were (1) increased compassion and respect for other cultures (2) increased confidence in interacting with Spanish speaking patients.

Conclusions: Students had varying expectations for the mission that ranged from concrete learning experiences to improving cultural competency and personal growth. Concerns were mainly about safety and communication barriers. Continuing to offer opportunities for improving Spanish speaking skills prior to the trip may ease apprehension about the experience. The data will be used to better understand participant needs and provide an empirical basis for pre-mission coursework.

ME-HP5

Using the Health Belief Model (HBM) to Evaluate HIV/AIDS Knowledge Level, Perceived Severity, Perceived Susceptibility, and Behavioral Practices Among 15-39 Year Olds in Six Cities in Sonsonate, El Salvador

S.E. Cates, DO
Virginia College of Osteopathic Medicine, Blacksburg, VA

This descriptive research used the Health Belief Model (HBM) to assess HIV/AIDS knowledge, perceived severity, perceived susceptibility, and behavioral practices within the population throughout the State of Sonsonate, El Salvador. The study population was composed of 15-39 year olds consisting of a total population size of n=1,500 (250 participants from each of the six cities). Institutional Review Board (IRB) approval was sought and obtained from the IRB board of the Virginia College of Osteopathic Medicine (VCOM). Before administration of any questionnaire, a full informed consent was obtained from each participant. An instrument consisting of 65 items including demographics, knowledge, perceived severity, perceived susceptibility, and behavioral practices was used for the general population. The analysis of the data was two-fold using Geographic Information Systems (GIS) mapping and statistical analysis. GIS mapping was used to graphically pinpoint areas of knowledge deficit and misinformation about HIV/AIDS. Results were based on a general population of n=1454. The Knowledge and Behavior sections were aggregated into indexes (k) and (b) respectively to show level of knowledge or frequency of safe behavioral practices. The Perceived Severity and Perceived Susceptibility sections were not aggregated into an index but rather treated as individual variables. An item analysis of the questionnaire found that on average the general population responded correctly to 78% of the knowledge questions. However, a total of 11 questions in the knowledge section had less 75% (n=385) of the general population answering correctly. Another 3 questions in the behavior section were also found to have less than 75% (n=385) indicating safe behavioral practices. Linear regression analyses were performed to explore correlations between the areas of demographics, knowledge level, perceived severity, and perceived susceptibility to safe behavior. Positive and negative correlations were discovered linking aspects of demographic makeup, greater knowledge, heightened perceived severity, and perceived susceptibility with a higher likelihood of engaging in safe behaviors. This research helps to pinpoint

where this population fits within the construct of the Health Belief Model. Continued, better, targeted HIV/AIDS educational efforts are needed in Sonsonate, El Salvador.

ME-HP6

School-Based Health Centers and the Touro University College of Osteopathic Medicine: A Collaboration

J.E. Foy, DO, FACOP[1], K. Hahn, RN, MSN, CPNP[2]
[1]Division of Pediatrics, TUCOM-CA, Vallejo, CA, [2]Department of Student Health Services, TUCOM-CA, Vallejo City, CA

Context: California law requires a recent physical examination upon entry into the first grade. Students that do not meet these requirements may be excluded from school for up to five days. We describe a four year collaborative experience with a school based health center that is supervised by the pediatric faculty of the Touro University College of Osteopathic Medicine, with particular attention to first grade exclusion rates.

Methods: Patient demographics, first grade enrollment statistics, and first grade exclusion rates were analyzed using School District enrollment and exclusion data, billing data, and Child Health Disability Program (CHDP) data during the first four years of the Health Center's operation.

Results: Our school-based health center was opened in August 2004. The trend in first grade exclusion rates throughout the school district was 402 students (2004-2005 school year), 320 students (2005-2006), 254 students (2006-2007) and 104 students (2007-2008). First grade enrollment was relatively static during this time period (2.7% variation). Thus, first grade exclusion rates for failure to meet the mandated physical examination requirement fell 74% over the first four years of the school based health center's operation. Additionally, our data document an ethnically diverse patient population, with the payer source in 99% of patients being the CHDP (income criteria are of less than 200% of the Federal poverty level) or no insurance source. Ninety-one percent of office visits were for well child care and immunizations.

Conclusions: School-based health centers provide services to a population of previously underserved students, and essentially serve as the safety net for the uninsured or underinsured child. Our experience has documented: 1) medical care provision to a student population that is primarily uninsured; and 2) an increased rate of meeting State mandated first grade health care admission requirements, thus reducing rates of student exclusion and funding losses to the school district.

♦ME-HP7

The Veron Community Scabies Education and Eradication Program

J.J. White, DO, PhD
Virginia College of Osteopathic Medicine, Blacksburg, VA

Scabies skin infections are a significant, yet preventable source of morbidity worldwide. While scabies affects all socioeconomic sectors, it is especially prominent in the developing world where crowding, poor hygiene, and limited access to basic health care are commonplace. The Virginia College of Osteopathic Medicine sponsors a public health clinic in Veron, Dominican Republic that reports a high prevalence of scabies infections among its general patient population without any means of direct measurement, proper intervention, or control. The IRB-approved Veron Scabies Eradication and Education Program was designed to address this problem using a novel treatment and education protocol. These two arms were evaluated at various measurement intervals and population means collected for several scabies disease and knowledge markers. These means were then used to test stated program hypotheses. Overall, the program was designed to treat and educate the entire population of Barrio Nuevo, allow subjects to go about daily life, and monitor if these interventions significantly persisted in the population over a 9 month timeline. Following this basic protocol, the following scabies markers were evaluated at baseline: subject demographics, scabies diagnosis and treatment history, baseline treatments with oral Ivermectin or topical Permethrin and reported side effects, and scabies education pre-test results. The following scabies markers were also assessed at baseline and reassessed at 2 weeks, 1 month, 2 months, 8 months, and 9 months: risk and prevention behaviors, symptomatology, skin exam findings, and scabies education post-test results. Overall, there was a statistically significant post-intervention improvement in scabies markers when compared to pre-intervention values ($p<0.05$). This study clearly demonstrated that a scabies program involving large-scale treatment and education can provide rapid and long lasting improvements to the health of a highly endemic population. And like all other mass eradication campaigns using Ivermectin, it was the objective of this program to provide a sustainable, practical, self-sufficient model for improved health outcomes, health behaviors, and health literacy. Indeed, this program has sufficiently demonstrated that community-wide scabies eradication is possible with the appropriate level of structure and support, without significant costs to the health care systems that serve the good people of Veron, Dominican Republic and beyond.

♦ME-HP8

GRO, IL-8, IP-10, and RANTES Expression by Cytokine-Stimulated Human Iris Stromal Cells

P.D. Shah, MS, G.L. Searle, BS, B.W. Zanotti, BS, M.V. Volin, PhD
Midwestern University/CCOM, Downers Grove, IL

Hypothesis: Acute anterior uveitis is characterized by protein buildup and lymphocyte migration into the anterior chamber of the eye. Cytokines play an important role in the pathogenesis of uveitis by increasing vascular permeability, recruiting leukocytes, and importantly, inducing the secre-

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tion of chemokines. Several chemokines are found in increased amounts in the aqueous humor of patients with acute anterior uveitis. We hypothesize that human iris stromal cells are an important source of chemokines in acute anterior uveitis.

Materials and Methods: To test this hypothesis in vitro, we performed experiments with cytokine-stimulated human iris stromal cells in order to determine the expression of chemokines. Human iris stromal cells were isolated and characterized from human donor globes. The human iris stromal cells were stimulated with cytokines TNFα and IFNγ (10ng/ml) for 24 hours. Chemokine expression was detected using reverse transcriptase (RT)-PCR.

Results: RT-PCR showed significantly increased expression of GROγ, IL-8, IP-10, and RANTES in the TNFα-stimulated and TNFα- and IFNγ-costimulated human iris stromal cells compared to non-stimulated cells ($p<0.05$, $n=5$). However, human iris stromal cells stimulated with IFNγ alone showed no significant change. These results confirmed our previous antibody array data which showed that elevated levels of these chemokines were secreted by human iris stromal cell following cytokine-stimulation.

Conclusion: These results show that cytokine-stimulated human iris stromal cells produce a variety of chemokines and therefore may potentially play a role in leukocyte recruitment into the anterior segment of the eye in anterior uveitis. Additionally, this data indicates that TNFα may function as an important cytokine in the pathogenesis of acute anterior uveitis by inducing iris stromal cell chemokine expression.