MIDWESTERN UNIVERSITY

Kenneth A. Suarez Annual Research Day

Chicago College of Osteopathic Medicine
Chicago College of Pharmacy
College of Health Sciences
College of Dental Medicine
MWU/OPTI Downers Grove Campus Region

Sponsored by the Midwestern University Office of Research and Sponsored Programs

Friday May 3, 2013
1:00-5:00 pm
Wellness Center Gymnasium
Kenneth A. Suarez, Ph.D. Professor of Pharmacology and Associate Vice President, Office of Research and Sponsored Programs received his Pharmacy Degree in 1967 and his Ph.D. in Pharmacology from the University of Rhode Island in 1972 before joining the faculty in the Department of Pharmacology at the Chicago College of Osteopathic Medicine. Dr. Suarez spent his early research career studying modifiers of microsomal electron transport on carbon tetrachloride hepatotoxicity and published most of his work in major toxicology journals. He wrote numerous review articles in Pharmacology and served as a book reviewer for the JAOA; he was a member of a number of professional societies both related to pharmacology and research administration. Ken served on many appointed, elected and Ad Hoc Committees during his tenure at Midwestern University. He received two Animal Facility Improvement grants and applied for and received funding for student research programs on campus from various pharmaceutical companies.

In 1982, as an Associate Professor, Dr. Suarez was also appointed to the position of Assistant Director of Research Affairs and rose to the rank of Professor of Pharmacology and was promoted to Associate Vice President of the Office of Research and Sponsored Programs. As Associate VP he was the Institutional Official responsible for ensuring the day to day requirements of the MWU research community were met. Dr. Suarez initiated a number of programs on campus to support student participation in research and The MWU Research Day Program was instituted by him to encourage student interest in academic medicine.

Dr. Suarez was a retired Lt. Col., in the USAR and served in the Medical Service Corp with the 427th Medical Laboratory until retiring from the USAR in 1996. He served in the USAR from 1970 until his retirement in 1996. He was married To Eileen and had one daughter, Christina. In his spare time he enjoyed bike riding and antiquing.

Midwestern University’s Annual Research Day is named in memory of Dr. Kenneth A. Suarez, whose leadership guided the Office of Research and Sponsored Programs for 25 years from 1982-2007. Dr. Suarez was instrumental in conceptualizing and implementing a number of MWU research-related policies and procedures, including Research Day.
MIDWESTERN UNIVERSITY
KENNETH A. SUAREZ, PH.D.
RESEARCH DAY

Friday May 3, 2013
1:00-5:00 p.m. – Wellness Center Gym

PROGRAM

12:00-1:00 p.m. Poster set up

1:00-4:30 p.m. Viewing and Preliminary Judging

4:30-5:00 Announcement of Research Day Awards
James M. Woods, Ph.D.
Director, Office of Research & Sponsored Programs

--RECEPTION--
Judges 2013

Lauren Alt, M.B.S. (Pharmacology)
Bryan Bjork, Ph.D. (Biochemistry)
Seema Briyal, Ph.D. (Pharmaceutical Sciences)
Mae Ciancio, Ph.D. (Biomedical Science)
Karyn DiNardo, B.S. (Physiology)
Chris Evans, Ph.D. (Physical Therapy)
Michael Fay, Ph.D. (Pharmacology) - alternate
Michele Fornaro, Ph.D. (Anatomy)
Julie Fusco, Pharm.D. (Pharmacy Practice)
Joshua Gasiorowski, Ph.D. (Biomedical Sciences)
Joanna Goral, Ph.D. (Anatomy)
Jacalyn Green, Ph.D. (Biochemistry)
Mary Hall, B.D. (Pharmacology)
Timothy Hanke, PT, Ph.D. (Physical Therapy)
Emily Hays, B.S. (Biochemistry)
Janet Helminski, PT, Ph.D. (Physical Therapy)
Kyle Henderson, Ph.D. (Physiology)
Tudy Hodgman, Pharm.D. (Pharmacy Practice) alternate
Medha Joshi, Ph.D. (Pharmaceutical Sciences)
Kolla Kristjansdottir, Ph.D. (Biomedical Sciences)
Mary Ann Kliethermes, Pharm.D. (Pharmacy Practice)
Lisa Knecht-Sabres (OT) alternate
Nate Krumdick, PhD (Behavioral Medicine)
Jeff Kwak, MBS (Biomedical Sciences)
Pete Lamar, B.S. (Pharmacology)
Sophie La Salle, Ph.D. (Biochemistry)
Michelle Lee, Ph.D. (Behavioral Medicine)
Kathy LePard, Ph.D. (Physiology)
Latha M. Malaiyandi, Ph.D. (Anatomy)
Michelle Swanson-Mungerson, Ph.D. (Microbiology & Immunology)
Gwendolyn Pais, Ph.D. (Pharmaceutical Sciences)
Jacob Peuler, Ph.D. (Pharmacology)
Maura Porta, Ph.D. (Physiology)
Ana Quinones-Boex, Ph.D. (Pharmacy Practice)
Madhu Reniguntala, Ph.D. (Pharmaceutical Sciences)
Michelle Singleton, Ph.D. (Anatomy) alternate
Vaibhav Tiwari, Ph.D. (Microbiology & Immunology)
Natarajan Venkatesan, Ph.D. (Pharmaceutical Sciences)
Michael Volin, Ph.D. (Microbiology & Immunology)
Sheila Wang, Pharm.D. (Pharmacy Practice)
MWU PROPOSALS IN STUDENT COMPETITION

CCOM STUDENTS

Kristen Alley and Annette Gilchrist (Department of Pharmacy Practice)
Assessment of CCR/1CCR5 internalization in response to CCL3 using human multiple myeloma cells

Yousuf Bahrami, Christopher Ackerman and Josh Edwards (Department of Pharmacology)
Cadmium causes injury to pancreatic islets that is associated with caspase-3-labeling

John Baldwin, Brian Zanotti, Erika Maus, Michael V. Volin, and Vaibhav Tiwari (Department of Microbiology & Immunology)
Susceptibility of human iris stromal cells to herpes simplex virus 1 (HSV-1) entry

M. Campigotto, J. Fajiculay, G. Park, M. Joshi and A. Gilchrist (Department of Pharmaceutical Sciences)
Does bortezomib sensitivity require the anti-apoptotic p-Akt pathway?

Kevin Chandrasena, Mary L Hall and Alejandro M.S. Mayer (Department of Pharmacology)
The mechanism of the marine β-carboline thromboxane B₂ inhibitor Manzamine A: possible involvement of rat brain microglia p 90 ribosomal S6 kinase 1

Matthew Eaton and Igor Altman (Department of Surgery, University of Illinois Medical Center)
Antiphospholipid syndrome and cutaneous necrosis: A wound care and tissue healing perspective

M. Green, S. Inouye and N. Fanter (Department of Anatomy)
Evaluation of cannulated stainless steel screw fixation of fifth metatarsal Jones fracture

Thomas O'Grady, Jed Robinson, Marc Bjurlin, Naveen Divakaruni, Chicago, IL, Matthew Houlihan, Downers Grove, Il, Sand Muktar Emhmed Ali, Andrew Drago and Courtney Hollowell, Chicago, IL
Presentation of high grade prostate cancer in the underinsured

Margaret Huynh, Maura Porta and Rafael Mejia-Alvarez (Department of Physiology)
Dantrolene effects on sarcoplasmic reticulum Cl⁻ channels from adult rat heart

Elizabeth Ince, Alice Meyer, Leah Dion and Joanna Goral (Anatomy Department)
Effect of inflammatory response and ethanol exposure on hsp27 and hsp32 in microglial cells
Neeti Kambale and Susan Viselli (Department of Biochemistry)
The long term impact of perinatal exposure to DDE on immune function of adult offspring of Swiss ICR mice

Karolina Kill, Rebecca Rossi, Robert Murphy and Kathleen O’Hagan (Department of Physiology)
Effects of pregnancy on voluntary wheel running activity in rats

T. Kusper, O. Couture, L. Alt, M. Fay and N. Chandar (Departments of Biochemistry and Biomedical Sciences)
P53 Regulated miRNA expression during in vitro osteoblast differentiation

Amber Lautzenheiser, Rajiv Verma, John Hohner, Stuart Marcotte, Justine Parker, Jane Gelfand and Liya Milgram (Department of Osteopathic Manipulative Medicine)
Examiner fatigue as a factor in grade variability during high stakes psychomotor testing

Daniel Lawler, Karyn DiNovo and Paul McCulloch (Department of Physiology)
Colocalization of NMDA glutamate receptor subunits in trigeminal neurons activated during voluntary diving in rats

Bartosz Leszczynski Swati Ratkal, Srikanth Manam and Ashlesh Murthy (Department of Pathology)
Temporal characterization of uterine horn pathological sequelae following genital Chlamydia muridarum infection

Erin Little, Matthew Keeler, Bryan King and John Graneto (Department of Emergency Medicine)
Defining postictal duration for pediatric simple febrile seizures

Alfred Liu, Maura Porta and Rafael Mejia-Alvarez (Department of Physiology)
Low noise recording of fast gating kinetics from cardiac Ca^{2+} channels

Areej Mazhar and Annette Gilchrist (Department of Pharmaceutical Sciences)
Development of a PCR assay for the rapid detection of Pseudomonas Aeruginosa

Vishnu Mudrakola, Paul McCulloch and Karyn DiNovo (Department of Physiology)
Receptor physiology in the MDH responsible for the diving reflex

Robert Myers, April McClish, Brian Zanotti and Michael Volin (Department of Microbiology & Immunology)
Immune response to lymph mobilization in rats with collagen induced autoimmune arthritis

Vijeta Pamudurthy, Carl Cassel, Cyrus Haselby and Glenn Nordehn (Department of Internal Medicine)
Improving auscultation accuracy through developing a new cardiac murmur classification system
Assessment of candidate PRDM16 transcriptional target genes in mouse embryonic craniofacial and brain tissues

Catherine Pinkston, Ryan Incrocci, Annette Gilchrist and Michelle Swanson-Mungerson (Departments of Microbiology & Immunology and Pharmaceutical Sciences)
New insights into the mechanisms by which Epstein-Barr virus may promote Hodgkin’s Lymphoma Development

Trenton Place and Frederick Domann (Molecular and Cellular Biology and Radiation Oncology – University of Iowa)
Actin proline hydroxylation: Discovery of a novel actin post-translational modification and implications for the effects of hypoxia on tumor metastasis

Shannon Powers, Sandra. Inouye and Nathan Fanter (Department of Anatomy)
Evaluation of the osteochondral autograft transplantation system for the talus

Puneet Ralhan, Anil Gulati and Medha Joshi (Department of Pharmaceutical Sciences)
Nanocarrier based formulation of ETB receptor agonist, IRL-1620, for the treatment of cerebral ischemia

Rebecca Rossi, Karolina Kill, Robert Murphy and Kathleen O’Hagan (Department of Physiology)
A case study: Uterine artery vasoconstrictor response to exercise in the rat during paced versus voluntary exercise

Benny Rummani and Balbina Plotkin (Department of Microbiology & Immunology)
The effects of urinary catheter composition on Escherichia coli biofilm formation in a model for type 2 diabetes

Carlyn Sainvil, Justin Schripsema and Kyle Ramsey (Department of Microbiology & Immunology)
Selection of virulence from within Chlamydia trachomatis, serovar E

Jesse Serrins, David Green, Amy Martiny, Phillipp Gunz (Department of Anatomy)
Geometric morphometrics of hominoid infraspinous fossa shape

Cortney Shepard, Seema Briyal and Anil Gulati (Department of Pharmaceutical Sciences)
Endothelin B receptor agonist, IRL-1620, prevents beta amyloid (Aβ) induced oxidative stress and cognitive impairments in normal and diabetic rats

Jeffrey Singh and Susan Viselli (Department of Biochemistry)
Effects of diet change and weight loss on DDE-induced immune alterations

Dejan Slavnic, Cassandra Larimer and Jacalyn Green (Department of Biochemistry)
Comparison of substrate specificity of Escherichia coli p-Aminobenzoylglutamate hydrolase with Pseudomonas carboxypeptidase G
Rachel Troester, Ashley Shah, Emily Hays and Sophie LaSalle (Department of Biochemistry)
Expression of SPATTA22 in mouse models of infertility

Ensi Voshtina, Zhong Zhang and Anil Gulati (Department of Pharmaceutical Sciences)
Alpha adrenergic receptors mediate resuscitative effect of centhaquin in hemorrhaged rats

Rohit Vuppuluri, Laura Bach, Robert Murphy, and Kyle Henderson (Department of Physiology)
Fetal deiodinase increases in a rodent model of myocardial infarction

Cassandra Wasson and Balbina Plotkin (Department of Microbiology & Immunology)
Effect of insulin on Staphylococcus aureus growth and biofilm formation

Nicholas Wilczynski, Karolina Klosowska and James Woods (Department of Microbiology and Immunology)
Low concentrations of dimethyl sulfoxide stimulate MAP kinases in rheumatoid arthritis fibroblast-like synoviocyte: Inhibition by Manzamine A

Dara Wise, Oliver Couture and Nalini Chandar (Department of Biochemistry)
Telomerase associated immortalization of primary cells affects p53 function

CCP STUDENTS

M. Renee Advincula, Milena McLaughlin, Michael Malczynski, Chao Qi, and Marc H. Scheetz (Department of Pharmacy Practice)
Assessing the clinical virulence of KPC (+) Klebsiella pneumonia blood stream infections at a large tertiary academic hospital

Josephine Aranda, Catherine Palladino, Aamna Khan, Ryan LeWan, Weronika Flis, Helga Brake and Kristine Gleason
Meaningful medication reconciliation: the single source of truth

Joshua Artilip, Thomas Dorn, Loreto Lobosco, Veeral Vyas and Thomas Reutzel (Department of Pharmacy Practice)
Obesity: High school students’ knowledge levels and opinions

Christina Bonanno, Robin Zavod and Ana Quiñones-Boex (Departments of Pharmaceutical Sciences and Pharmacy Practice)
Student pharmacists’ knowledge and self-efficacy levels in recommending commonly used over-the-counter vitamin supplements

Alexis Bonnema, Courtney Linhart and Thomas Reutzel (Department of Pharmacy Practice)
The knowledge levels and attitudes of pharmacy students regarding immunizations

Kristen Dabkey, Jennifer Phillips and Sally Arif (Department of Pharmacy Practice)
A survey of Australian pharmacists on job responsibilities and satisfaction
Jenan Dailey, Christina Choi, Yen Duong, and Deborah Rehder (Department of Pharmacy Practice)
Stepwise implementation of total pharmacy medication reconciliation

Ankanksha Dudeja, Sonali Kshatriya, Klodiana Myftari, Susan Winkler, Ana Quiñones-Boex and Thomas Reutzel (Department of Pharmacy Practice)
The impact of an educational program on pharmacist behaviors, confidence and knowledge of probiotic recommendations in a grocery store chain pharmacy

Jay Fajiculay, Zane Elfessi, Gabriel Park, Medha Joshi and Annette Gilchrist (Department of Pharmaceutical Sciences)
Differential effects of bortezomib on osteoblastic and osteosarcoma cell lines suggest resistance may be through anti-apoptotic Akt pathway

Weronika Flis, Rachel Ralph, Michael Fotis, William Budris and Paul Greenberger
Indications and outcomes of epinephrine auto-injector use at a major urban hospital

Mallory Fowler, Jae Chang, Jean Patel and Michael Postelnick (Department of Pharmacy Practice)
Adherence to empiric guidelines for the treatment of community acquired pneumonia in a hospital setting

Amina Ghalyoun, Ray Wang, Annette Gilchrist (Department of Pharmaceutical Sciences)
Development of a health and wellness promoters program for secondary schools facilitated by PharmD students

Marlee Grabiel, Thomas Reutzel, Sheila Wang, Rochelle Rubin, Vinvia Leung, Adrienne Ordonez, Maggie Wong and Emily Jordan (Department of Pharmacy Practice)
HPV and HPV vaccines: The knowledge levels, opinions, and behavior of parents

S. Sam, J. Clark, A. Greenberg, C. Sincak (Department of Pharmacy Practice)
Relationship between varying daptomycin MICs and outcomes in enterococcal bacteremia

Connie Lam, Jen Phillips and Lisa Mackowski (Department of Pharmacy Practice)
Analysis of the completeness and accuracy of dietary supplement information in Wikipedia

Benjamin Lee, Rachel Ralph and William Budris
Evaluation of transmucosal immediate release fentanyl (TIRF) use and implications under risk evaluation mitigation strategy (REMS)

Hyaera Lee, Shridhar Andurkar, Anil Gulati and Medha Joshi (Department of Pharmaceutical Sciences)
Formulations of Centhaquin loaded nanocarriers for targeted delivery to the brain
Vinvia Leung, Brandon Chiu, Sheila Wang and Hong Liu (Department of Pharmacy Practice)
Asian Community Health Education Initiative: Students and faculty bridging gaps in healthcare disparities

Beth Lubecke, Milena McLaughlin, Chastity Franklin, and Raymond Black II Monitoring medication waste and developing strategies to reduce medication expenditures at a tertiary academic medical center

Stephen Ly, Ayesha Abrar, Natarajan Venkatesan and Guru Betageri (Department of Pharmaceutical Sciences)
Development of an enteric coating composition resistant to alcohol

Troy McLouth, Nabiha Mahood and Sheri Strensland (Department of Pharmacy Practice)
Impact of the career explorers program on college preparation

Nabila Mirza, Luke Jackson, Huzefa Master and Sean Mirk (Department of Pharmacy Practice)
Pharmacy involvement to improve admission medication histories

Daniel Barone, Archana Nath, Sonia Nevrekar, Stephanie Kliethermes, Amy Pavell, Sheron Mui, Carrie Sincak and Sheila Wang (Department of Pharmacy Practice)
Identification of clinical predictors of elevated creatinine phosphokinase during daptomycin use: a matched case-control study

Gabriel Park, Annette Gilchrist and Medha Joshi (Department of Pharmaceutical Sciences)
Encapsulation in ceramide lipid nanoparticles enhances bortezomib-induced effects on metabolic activity

Zachary Pentoney, Erik Skoglund, Milena McLaughlin and Marc Scheetz (Department of Pharmacy Practice)
Navigating antimicrobial drug shortages: where are we one year later?

Marianne Pop, Amisha Mehta, Mary Ann Kliethermes, Kathleen Vest, and Nicole Rockey (Department of Pharmacy Practice)
Establishment of a quality evaluation program for a pharmacist led medication therapy management (MTM) clinic in a physician office

Marianne Pop, Hilary Sheridan, Jessica Johnson, Sally Arif and Thomas Reutzel (Department of Pharmacy Practice)
Impact of an international experience in Guatemala on the attitudes of healthcare professional students

Daniel Pyen and Annette Gilchrist (Department of Pharmaceutical Sciences)
Evaluation of pyrrolidine derivatives as CCR1 antagonist for in vitro inhibition of multiple myeloma
**Erik Skoglund**, Zachary Pentoney, Milena McLaughlin and Marc Scheetz (Department of Pharmacy Practice)
Tracking patient harm due to antimicrobial shortages: how bad is it?

**Sandra Tooley** and Robin Zavod (Department of Pharmaceutical Sciences)
Changes in lecture handout role and value as the professional curriculum evolves

**Cortney Valela**, Jennifer Phillips and Meghana Aruru (Department of Pharmacy Practice)
Labeling accuracy of weight loss dietary supplements

**Sara Vander Ploeg** and Mary Ann Kliethermes (Department of Pharmacy Practice)
Pharmacist provided medication therapy management in ambulatory care and the impact on adverse drug events

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**CHS STUDENTS**

**Biomedical Sciences**

**Christopher Ackerman**, Walter Prozialeck, Peter Lamar and Joshua Edwards (Department of Pharmacology)
Evaluation of early-stage biomarkers of cadmium nephrotoxicity

**Megan Andrzejak** and Jacalyn Green (Department of Biochemistry)
Characterization of the role of manganese on structure and function of *Escherichia coli* p-Aminobenzoylglutamate hydrolase

**Jonathan Bardahl**, Ryan Incrocci and Michelle Swanson-Mungerson (Department of Microbiology & Immunology)
Epstein-Barr virus LMP2A enhances MIP-1α expression in a B cell lymphoma by utilizing Syk tyrosine kinase and p38 MAPK pathway

**Levi Barse**, Ryan Incrocci and Michelle Swanson-Mungerson (Department of Microbiology & Immunology)
Analysis of the signal transduction pathway required for LMP2A-mediated increases in interleukin-10 production

**Jill Chotiyanonta**, Karyn Di Novo and Paul McCulloch (Department of Physiology)
Bilateral sectioning of the anterior ethmoidal nerves does not eliminate the diving response in voluntarily diving rats

**Aseel Dabbagh**, Srikanth Manam, Natarajan Venkatesan, Mark Sanders and Ashlesh Murthy (Departments of Pathology, Pharmaceutical Sciences and Family Medicine)
Graviola fruit extract reduces TLR2 and TLR4-induced TNF-alpha production in J774 mouse macrophages
Sehar Dadani, Oliver Couture and Nalini Chandar (Department of Biochemistry)
Role of the retinoblastoma gene in the regulation of osteoblast differentiation

Terry Fokakis and Susan Viselli (Department of Biochemistry)
Immune effects of DDE in a mouse model of weight loss

Lauren Furlan, Brock Nelson, Lenore Pitstick and Bryan Bjork (Department of Biochemistry)
Molecular and phenotypic consequences of loss of Prdm16 during embryonic mandible development using a novel conditional gene trap null allele of Prdm16 (Prdm16GT)

Karolina Kata, Seema Briyal and Anil Gulati (Department of Pharmaceutical Sciences)
Efficacy of centhaquin and selective serotonin reuptake inhibitors on behavior and oxidative stress in a rodent model of autism

Komal Kenkare, Thomas Walsh, Jeff Kwak, Christian Evans, Kathy LePard and Mae Ciancio (Department of Biomedical Sciences)
Exercise improves glucose sensitivity in a mouse model of diet induced obesity: Role of glucose transporters

Jessica Landaiche, Emily Hays and Sophie La Salle (Department of Biochemistry)
Characterization of SPATA22, a novel mammalian protein required for meiotic progression in mouse germ cells

Joseph Lorenz, Steven Klotz and Sean Lynch (Department of Biochemistry)
Comparison of HDL antioxidant and paraoxonase enzyme activities

David MacAdam, Mary L. Hall, Domonkos Feher, Philip Williams and Alejandro M.S. Mayer (Department of Pharmacology)
Cyanobacterium Anabaena sp. Lipopolysaccharide (LPS) elicits release of matrix metalloproteinase-9 from rat brain microglia

Allison Maladore, Joshua Thomas, Srikanth Manam and Ashlesh Murthy (Department of Pathology)
TNFR 2 on CD8+ T cells mediate to upper genital tract pathology in Chlamydia muridarum infected mice

Nora Mulloy, Gwendolyn Pais, Zhong Zhang and Anil Gulati (department of Pharmaceutical Sciences)
Resuscitative efficacy of centhaquin in a rabbit model of uncontrolled hemorrhagic shock with tissue injury

Brock Nelson, Lauren Furlan, Lenore Pitstick and Bryan Bjork (Department of biochemistry)
Molecular and phenotypic consequences of loss of Prdm16 in a conditional gene trap null allele of Prdm16 during palate development

Shivang Shah, Oliver Couture and Nalini Chandar (Department of Biochemistry)
Effect of overexpression of miR-34b and miR-140 on p53-dependent osteoblast differentiation
Joshua Thomas, Srikanth Manam, Justin Schripsema, Kyle Ramsey and Ashlesh Murthy (Departments of Pathology and Microbiology & Immunology)
TNF-α receptors 1 and 2 contribute to the development of upper genital tract pathology following primary genital chlamydia muridarum infection in mice

Stacey Tinkoff, K. LePard and J. Cellini (Department of Biomedical Sciences)
Gastric regional differences in nerve-stimulated contractions and relaxations contribute to delayed gastric emptying in type 2 diabetic mice

Matthew Wu, Brian Zanotti and Michael Volin (Department of Microbiology & Immunology)
Mucin 3 (MUC3) decreases apoptosis in rheumatoid arthritis synovial fibroblasts

Mark Zafiratos, Srikanth Manam, Kyle Henderson and Ashlesh Murthy (Departments of Pathology and Physiology)
CD8+ T cells and TNF-alpha contribute to the development of atherosclerotic pathology following primary pulmonary Chlamydia pneumoniae infection in mice

**Occupational Therapy**

Shane Allen, Kelly Hayn, Megan Rowland and Kimberly Bryze (Occupational Therapy)
The effects of scuba diving on occupational performance in individuals with autism spectrum disorders

Lindsey Askins, Dagmara Szewerniak, Brittany Diasio and Susan Cahill (Occupational Therapy)
Children with developmental disabilities and their motivation to play

Prerna Basnet, Cheryl Bathan, Ashley Mcgaughy and Mark Kovic (Occupational Therapy)
The contribution of occupational therapy for unmet life skill needs of children in the foster care system

Cara Bredeson, Natalie Cramarosso, Chelsey Straight and Emily Simpson (Occupational Therapy)
Experiences of role and responsibility changes in transitionally housed single mothers

Corrine Breskovich, Vanessa Niland, Marie Therese Smith and Kimberly Bryze (Occupational Therapy)
Young adults’ perspective on parental cancer: A mixed methods study on resilience, coping and occupational identity

Jacqueline Cummings, Lana Lobdell, Sarah Shivley and Mark Kovic (Occupational Therapy)
Key determinants to clinical reasoning for use of electrical stimulation with persons with stroke
Kathryn Dragich, Erin Mangin, Shannon Yorke and Brad Egan (Occupational Therapy)
Occupational therapy practitioners’ comfort level addressing driving with youth who experience difficulty learning

Brooke Dudley, Brianne Heiland, Elizabeth Kohler-Rausch and Mark Kovic (Occupational Therapy)
Education and technology used to improve the quality of life for people with diabetes mellitus type 2

Brenna Duffy, Nathan Hebda and Kimberly Bryze (Occupational Therapy)
Facilitating leisure time physical activity for American veterans with traumatic brain injury and posttraumatic stress disorder

Sonia Hammond, Katherine Petersen, Noelle Warren and Mark Kovic (Occupational Therapy)
Traumatic Brain Injury: Caregiver Education in a Community Based Program for Adults with a TBI

Debbie Morey and Kimberly Bryze (Occupational Therapy)
Improving adaptation in adults with acquired disability: Using narratives to support identity reconstruction – A systematic review

Nikki Neumann and Emily Simpson (Occupational Therapy)
Ex-offenders in transitional housing: Needs for successful community reintegration

Allison Porschakin and Mark Kovic (Occupational Therapy)
Impact of cancer diagnosis on adolescents and young adults: Systematic review

Alex Robinson, Kiley Rich and Emily Simpson (Occupational Therapy)
Occupational therapists’ perceptions of best practice for Parkinson’s disease

Jamie Rotter, Kara Lyons, Antonina Marrone and Susan Cahill (Occupational Therapy)
Survivors of brain injury: The narrative experiences of undergraduate students

Rebecca Yelle and Emily Simpson (Occupational Therapy)
Occupational therapy interventions with cancer patients: A systematic review of outcomes-based literature

Behavioral Medicine

Krista Escamillo, Diana Semmelhack (Department of Behavioral Medicine)
Implementation of an animal assisted therapy group for severely mentally ill clients residing in a long term care facility
**CDMI STUDENTS**

*Lama Alghanem, Hector Trevino, Bilal Alnahass, Katie Riesenber, Emily Carley, Raj Darji, Corry Grathwol, Ryan Kuebler and Matthew Manious*

Benefits of sutureless woundhealing in third molar extractions

*Cody Boals and Jacalyn Green (Department of Biochemistry)*

Cloning, purification and partial characterization of Escherichia coli transcriptional regulator AbgR

*Gregory Brown and Michelle Singleton (Department of Anatomy)*

Developmental simulation of facial growth restriction in the rhesus macaque (Macaca mulatta)

*Joseph Dougherty, Samantha Laskowski, Jeff Kwak, Mae Ciancio and Christian Evans (Department of Biomedical Sciences)*

Phylogenic alterations of gastrointestinal bacteria as a result of high fat diet and exercise

*Seunghyan Jae, Oliver Couture and Nalini Chandar (Department of Biochemistry)*

Understanding the functions of tumor suppressor gene Rb in maintaining normal osteoblast hemostasis

*Antonio Rossi and Bruno Jham (Dentistry)*

Expression of angiopoietin-2 in oral Kaposi’s sarcomas

**CCP Residents and Postdoctoral Fellows**

*Courtney Ammons, Elizabeth Gozdziak, Susan Winkler and Megan Wagner (Department of Pharmacy Practice)*

Assessment of pharmacists’ knowledge necessary to provide community-based pharmacogenomics interventions

*Akanksha Dudeja, Sonali Kshatriya, Klodiana Myftari, Susan Winkler, Ana Quiñones-Boex and Thomas Reutzel (Department of Pharmacy Practice)*

The impact of an educational program on pharmacist behaviors, confidence and knowledge of probiotic recommendations in a grocery store chain pharmacy

*Olabisi Falana and Gourang Patel (Department of Pharmacy Practice)*

Efficacy and safety of tranexamic acid versus ε-aminocaproic acid in cardiovascular surgery

*Brittany Hoffmann, Amir Masood, Megan Wagner and Susan Winkler (Department of Pharmacy Practice)*

Impact of a diabetes intervention tool on the frequency of recommendations made by pharmacists during a comprehensive medication review
Sharlene Huang, Kasey Greathouse, Sonia Nevrekar and Sheila Wang (Department of Pharmacy Practice)
Dexmedetomidine use and associated fever of unknown origin: impact of drug substitution during the propofol shortage

Mindy Joseph, Kimberly Ackerbauer (Department of Pharmacy Practice)
Incidence of adverse bleeding events in patients on dabigatran or rivaroxaban for stroke prevention in patients with atrial fibrillation

Lisa Mackowski, Kathleen Vest and Jennifer D’Souza (Department of Pharmacy Practice)
Comparing patients’ and fourth year professional pharmacy students’ perceptions of communication and confidence in the ambulatory care setting

Milena McLaughlin, Maria Renee Advincula, Michael Malczynski, Grace Barajas, Chao Qi, and Marc Scheetz (Department of Pharmacy Practice)
Quantifying the magnitude of clinical virulence of KPC through translational study

Nabila Mirza, Luke Jackson, Huzefa Master and Sean Mirk (Department of Pharmacy Practice)
Pharmacy involvement to improve admission medication histories

Sonia Nevrekar, N. James Rhodes, Sheila Wang, Marc Scheetz Amy Pavell and Christopher Crank (Department of Pharmacy Practice)
Evaluation of treatment outcomes of Cefazolin versus Oxacillin for MSSA bloodstream infections – A multi-center observational study

N. James Rhodes, Sonia Nevrekar, Milena McLaughlin, Sheila Wang, Christopher Crank, Chao Qi, and Marc Scheetz (Department of Pharmacy Practice)
Evaluation of clinical outcomes in patients with gram negative bloodstream infections according to Cefepime MIC

Elizabeth Short, Nikki Cool, Amy Wilson, Travis Abicht, and Patrick McCarthy (Department of Pharmacy Practice)
Colchicine for prevention of post-operative atrial fibrillation

Ryan Van Engel, Nikki Cool, Amy Wilson, Andrew Sauer and Karen Meehan (Department of Pharmacy Practice)
Evaluation of sildenafil use in pulmonary hypertension patients with left ventricular assist devices prior to orthotopic heart transplant

Nicole Wegrzyn and Sean Mirk (Department of Pharmacy Practice)
Evaluation of patient interest in mobile Apps for health related education

Rebecca Zaworski and Kelly Lempicki (Department of Pharmacy Practice)
Evaluating men’s health education in US pharmacy practice curriculum
Other MWU Posters on Display

MWU OPTI/Residents

Ugne Adikevicuie and Keri Robertson (Emergency Medicine)
Basilar artery aneurysm rupture in a pediatric patient

April Brill, Ryan Misiek, Ashley Debarba, Katherine Nonweiler, Robert Long, Lauren Fontana, Alecia Clary and Erik Frost (Emergency Medicine)
Does insurance status affect the rate of psychiatric bouncebacks to the emergency department?

Thomas Brozek and Steven Vucovic (Emergency Medicine)
Emergent TPA administration for acute PE

Daniel De Feo, Christopher Colbert, Thomas Olmstead and Saisha Mangla (Department of Emergency Medicine)
Combined Osteopathic physicians’ careers after residency (COPCAR)

Michele Finkle and Ashlee Bergin (Obstetrics & Gynecology)
Obstetricians and educating women about breastfeeding, Is there a role?

Katie Gualandri and Steven Bujewski (Obstetrics and Obstetrics and Gynecology)
Changing how we care: Bolivia

J. Schriefer and E. Chapman-Davis (Obstetrics and Gynecology)
Surgical management of elderly women with endometrial cancer in a community setting

Christy Short and Jennifer Ron (Emergency Medicine)
When back pain is more than just back pain

Christy Short and Tom Green (Emergency Medicine)
Ectopic Pregnancy

Michelle VonDielingen Quinn, Midwestern University/OPTI, Elena Trukhacheva and Teresa Hubka (Department of Obstetrics and Gynecology)
Demographic characteristics predicting deficiencies in women’s knowledge of heart disease and cancer
MWU Faculty Abstracts

Joseph Cellini and Kathy LePard (Department of Physiology)
Age-related increase in Glut4 and cleaved caspase-3 expression in gastric vagal neurons of insulin resistant mice

Oliver Couture, Eric Lombardi, Kendra Davis, Emily Hays and Nalini Chandar
(Department of biochemistry)
Gene expression profiles resulting from stable and transient loss of p53 mirrors its role in tissue differentiation

Shaifali Bhalla, Mary Leonard, Seema Briyal and Anil Gulati (Department of Pharmaceutical Sciences)
Alteration in the brain ET<sub>B</sub> receptor binding characteristics following cerebral ischemia

Shaifali Bhalla, Izna Ali, Shridhar Andurkar and Anil Gulati (Department of Pharmaceutical Sciences)
Centhaquin antinociception in mice is mediated by α<sub>2A</sub> and α<sub>2B</sub> but not α<sub>2C</sub> adrenergic receptors

Mary Leonard and Anil Gulati (Department of Pharmaceutical Sciences)
Endothelin B receptor agonist, IRL-1620, enhances angiogenesis and neurogenesis following cerebral ischemia in rats

Srikanth Manam, Sophie La Salle, Yong Zhang, Michael Holtzman, Bruce Nicholson and Ashlesh Murthy (Departments of Pathology and Biochemistry)
Gap junction protein connexin 43 contributes to upper genital tract pathology following Chlamydial infection

Sean M. Mirk, Jen Phillips and Huzefa Master (Department of Pharmacy Practice)
Evaluating the effectiveness and student perceptions of on-line interactive learning lectures

Gwendolyn Pais, Nora Mulloy, Zhong Zhang and Anil Gulati (Department of Pharmaceutical Sciences)
Effect of centhaquin resuscitation on coagulation in a rabbit model of uncontrolled hemorrhagic shock

J. Toljanic, R. Baer, K. Ekstrand and A. Thor (Dental Medicine)
Immediate loading of implants in the atrophic edentulous maxilla without bone augmentation: 5-year clinical outcomes
The goal of this study was to evaluate the ability of CCR1 antagonists to modulate internalization of the receptor via flow cytometry. Previous research has suggested that human myeloma cells contain several different types of chemokine receptors, including CCR1 and CCR5, which may be involved in cell migration to the bone marrow. Preliminary work indicated that CCR1 antagonists showed variations in their ability to inhibit β-arrestin translocation. We measured CCL3-induced internalization of CCR1 and CCR5 by flow cytometry. We used RPMI 8226 cells which are a human multiple myeloma cell line that endogenously express both chemokine receptors. For these studies, cells were simultaneously mixed with varying concentrations of CCR1 antagonists as well as a single dose of agonist (CCL3) and incubated for two hours before being mixed with PE conjugated anti-CCR1 antibody and FITC conjugated anti-CCR5 antibody. CCL3 is known to serve as an agonist for both CCR1 and CCR5. If the ligand induces receptor internalization, surface expression would be expected to decrease. We predicted that the presence of CCR1 antagonists would alter surface expression of this receptor only. Finally, we hoped that the effects of the antagonists on CCR1 internalization could be correlated with our previous results with β-arrestin translocation, a process that often mirrors receptor internalization.
Cadmiun causes injury to pancreatic islets that is associated with caspase-3 labeling

Yousuf Bahrami, Christopher Ackerman and Josh Edwards, Ph.D.

Pharmacology Department, Midwestern University, Downers Grove, IL 60515

Diabetes is a growing worldwide epidemic. There is increasing interest in how environmental contaminants can contribute to the onset of type II diabetes. Impaired insulin release is a hallmark of type I diabetes and is key in the progression of type II diabetes. Multiple epidemiological and experimental studies show that exposure to the metal cadmium (Cd), is associated with diabetes and reduced serum insulin. To examine the cytotoxic effects of Cd within pancreatic islets, male Sprague Dawley rats were injected subcutaneously with either saline (control) or Cd (0.6 mg Cd/kg/day, 5 days per week). After 6, 9 and 12 weeks of Cd treatment, pancreatic tissue samples were removed then fixed in formalin. Pancreata were sectioned and H&E stained to identify islets then examined for changes in islet histology. A trained veterinary pathologist scored each sample for cytoplasmic vacuolization and signs of necrosis and apoptosis. All pancreata from Cd treated animals had elevated scores for signs of vacuolization, apoptosis and necrosis. However, these changes in cell viability did not appear to change with longer Cd exposure times. In another study using the same pancreas samples, tissue was labeled for the apoptosis indicator, active caspase 3. In this study, pancreatic samples were counter stained with hemotoxylin so that immuno-labeled islets could be identified. This study resulted in similar findings. Islets from Cd-treated animals had greater caspase-3 labeling and as before, the intensity of labeling appeared to be time independent. These preliminary results show that Cd acts to injury pancreatic islets which may result in diminished insulin release.
Susceptibility of human iris stromal cells to herpes simplex virus 1 (HSV-1) entry

John Baldwin, Brian Zanotti, Erika Maus, Michael V. Volin, Vaibhav Tiwari
Department of Microbiology & Immunology, Midwestern University, Downers Grove, IL 60515

Abstract

Herpes simplex virus type-1 (HSV-1) is a significant ocular pathogen affecting multiple regions including the iris. The iris, a specialized eye tissue, is affected in various inflammatory ophthalmic conditions. For instance, inflammation of the iris following HSV-1 infection may be associated with elevated intraocular pressure, ultimately resulting in glaucoma. In addition, the iris has been shown to have histopathologic involvement in HSV-1 infection of the corneal stroma, herpetic stromal keratitis (HSK). Inflammation of the iris is also seen in herpetic anterior uveitis, a condition that often presents as an inflammation of the iris and ciliary body (iridocyclitis) and is the leading cause of infectious anterior uveitis worldwide. Here we use human iris stroma cells as a novel in vitro model to demonstrate HSV-1 entry and the upregulated cytokines observed in this study provide a new understanding of the intrinsic immune mechanisms that can contribute to the onset of iritis. This model may also serve as a platform to test for potential therapeutics that may help against HSV-1 induced iritis.

This research project was supported by Midwestern University (Downers Grove, IL) sponsored Kenneth A. Suarez Summer Research Fellowship (10-2014-8172) to JB.
Differential effects of bortezomib resistance to osteosarcoma and osteoblastic cell lines suggests down regulation of anti-apoptotic p-Akt pathway as mechanism of action

Campigotto, M., Fajiculay, J., Park, G., Joshi, M., Gilchrist, A.

Department of Pharmaceutical Sciences, Midwestern University, Downers Grove, Illinois

Bortezomib is a proteasome inhibitor that has been clinically approved for the treatment of multiple myeloma. Akt, also known as protein kinase B, is a serine/threonine-specific protein kinase that plays an important part in inhibiting apoptotic pathways in its active form. Osteosarcomas are highly aggressive and metastatic primary bone tumors of osteoblastic origin, which primarily affect adolescents. In order to test the effects of bortezomib in on Akt activity in osteoblastic and osteosarcoma the following cell lines were examined by using western blotting:

MC3T3, an osteoblast precursor cell line derived from mouse calvaria; ROS 17/2.8, a rat osteosarcoma cell line; and U2OS, a human osteosarcoma cell line. The cell lines were differentiated for 7 days and then treated with 1nM bortezomib and lysed at 0, 24, and 48 hours. Protein concentrations were then determined using Precision Red protein assay. The samples were then blotted and labeled with antibodies for the active p-Akt or inactive Akt. Next the samples were examined using electrochemiluminescence viewed with a charge-coupled device (CCD) camera. Densitometric Analysis performed using the images J software demonstrated bortezomib down-regulated p-Akt in a dose- and time-dependent manner in MC3T3 and U2OS cells, whereas no alteration in p-Akt was observed in ROS 17/2.8. Bortezomib was the first approved proteasome inhibitor. It is used for multiple myeloma but has potential benefits against other cancer types. Several explanations have been presented for the antitumor properties of bortezomib, including NF-Kb inhibition, stabilization of p53, and down regulation of p-Akt. We found that the ROS 17/2.8 cell line was resistant to bortezomib, and showed no alteration in p-Akt levels. Our results are consistent with the hypothesis that Akt signaling is important in bortezomib-resistant ROS 17/2.8 cells and suggest that targeting Akt signaling may provide approach for combinational therapy to overcome drug resistance to bortezomib.

This research was supported in part by the Kenneth A. Suarez research fellowship
The mechanism of the marine β-carboline thromboxane B₂ inhibitor Manzamine A: possible involvement of rat brain microglia p90 ribosomal S6 kinase 1

Kevin Chandrasena¹, Mary L. Hall¹ and Alejandro M.S. Mayer¹

Department of Pharmacology¹, CCOM, Midwestern University, Downers Grove, Illinois

Manzamine A (MZA) inhibited LPS-treated rat microglia (BMD) TXB₂ (IC₅₀<0.016 µM) and O₂⁻ (IC₅₀=0.1 µM) generation, (BMC Pharmacology 5(1) 6, 2005), LPS-treated human BMD TXB₂ (apparent IC₅₀<0.7 µM) (Inflammation 53(S3): S217, 2004) and rat p90 ribosomal S6 kinase 1 (RSK1) (IC₅₀ =15.01 µM) (Program 545.5, Society of Neuroscience, 2009). RSK1 is expressed in LPS-treated rat microglia (BMD) (J. Neurosci. 26: 1124, 2012). The RSK (90kDa ribosomal S6 kinase) family are serine/threonine kinases that regulate several cellular processes, including cell growth, proliferation and motility. In vertebrates, this family includes several isoforms, (e.g., RSK1, RSK2) which are downstream effectors of the Ras/ERK (extracellular-signal-regulated kinase) signaling pathway. We hypothesized that in BMD MZA might inhibit RSK1 phosphorylation induced at residue S380 by kinases activated by PKC. In order to test our hypothesis, we determined the presence of constitutive and phosphorylated RSK1 proteins in rat BV-2 BMD cell line. Briefly, we prepared protein extracts from untreated, LPS (100 ng/mL)-treated, and LPS + PMA, a PKC activator, (1µM)-treated BV-2 BMD in the presence or absence of DMSO and MZA (3, 10 and 30 µM), and probed by western blot analysis using constitutive RSK1 (Cell Signaling) and phosphorylated RSK1 (pRSK1) antibodies against S380 (Epitomics). Results: 1) Constitutive RSK1 and pRSK1 proteins were present in all BV-2 BMD extracts tested; 2) PMA enhanced pRSK1 protein in LPS-treated BV-2 BMD; 3) MZA did not inhibit pRSK1 protein on S380 in LPS + PMA-treated BV-2 BMD. Future studies will determine 1) whether RSK1 in primary rat microglia show a similar response to MZA, and 2) evaluate the effect of MZA on phosphorylation of RSK1 at several additional residues required for activation of this enzyme in vivo.

Kevin Chandrasena was supported by a Kenneth A. Suarez CCOM Student Summer Research Award. The research was funded in part by the Office of Research and Sponsored Programs, Midwestern University.
Antiphospholipid Syndrome and Cutaneous Necrosis: A Wound Care and Tissue Healing Perspective

Matthew A. Eaton, MPH, OMS-III and Igor Altman, DO, MBA

Midwestern University Chicago College of Osteopathic Medicine. Downers Grove, IL
University of Illinois at Chicago. Department of Surgery. Division of Wound Care and Tissue Healing. University of Illinois Medical Center. Chicago, IL

ABSTRACT
Cutaneous manifestations occur as the presenting symptom in up to 50% of patients with antiphospholipid syndrome (APS). In particular, livedo reticularis, cutaneous necrosis, distal ulceration and digital ischemia have been associated with this medical condition. Many case reports emphasize the difficulty in diagnosing APS and outline the prophylactic medical management. Few, however, describe the process of wound care and cutaneous healing. Because certain mechanisms of APS are not fully known, treatment recommendations from a wound care standpoint are difficult to define. The importance of prophylaxis with anti-thrombotic agents like warfarin and strict anticoagulation monitoring has been well established in preventing cutaneous events in APS. However, the literature is lacking specific wound care recommendations after cutaneous events have already occurred. We reviewed journal articles and case reports that mentioned wound care management. This article will outline treatments that have previously been described in the literature. We also present a case of APS in a 22-year-old male with bilateral lower extremity cutaneous ischemia and necrosis. Multiple treatment modalities, both medical and surgical, were used throughout his hospital course. We provide a thorough account of wound care methods and interventions used in a case of widespread cutaneous necrosis and digital ischemia.
Evaluation of Cannulated Stainless Steel Screw Fixation of Fifth Metatarsal Jones Fracture

M. J. Green¹, S.E. Inouye, Ph.D.¹,², and N.J. Fanter, D.O.³
1. Chicago College of Osteopathic Medicine, 2. Department of Anatomy, 3. Hinsdale Orthopaedics

A Jones fracture is a fracture of the proximal fifth metatarsal just distal to the tuberosity, at the junction of the metaphysis and diaphysis. Chronic stress is a common cause of a Jones fracture, especially for athletes. There are several approaches for treatment of a Jones fracture, but intramedullary screw fixation has become a popular surgical treatment for athletes due to the rapid bony union rates and decreased recovery time. However, this treatment is controversial and challenging for the surgeon due to the variation in lateral bowing of the intramedullary cavity, cortical thickness along the diaphysis, and intramedullary cavity diameter along the diaphysis of the fifth metatarsal. Due to these anatomical challenges, cannulated stainless steel screw fixation is purported to contribute to high rates of delayed bony union and nonunion as well as refracture of the metatarsal in active individual.

The purpose of this study is to examine the surgical protocol for treatment of a Jones fracture via cannulated stainless steel screw fixation. A thorough understanding of the consequences of this surgical treatment on the fifth metatarsal and its potential effect on the lateral tarsometatarsal joint will assist the surgeon in proper insertion of the screw into the medullary cavity of the metatarsal.

The right and left fifth metatarsals of 23 adult male and female cadavers were sectioned at 80% and 60% of the total length, respectively, and 4mm diameter stainless steel screws were threaded in retrograde fashion through the medullary cavities. The screws were allowed to self-center in the medullary cavity in order to determine the best path for insertion of the screw and thus reduce compromising the integrity of the diaphysis. We evaluated whether or not the screw penetrated the lateral tarsometatarsal joint and whether or not the screw would penetrate the tendon of the fibularis brevis muscle.

For the total sample, 83% of the right and 46% of the left lateral articular tarsometatarsal joint surfaces were penetrated by the cannulated screws. For males, 73% and 46% of the right and left lateral articular tarsometatarsal joints respectively were penetrated by the cannulated screw. In comparison, 92% of the right and 50% of the left lateral articular tarsometatarsal joints in females were penetrated by the cannulated screws. For the total sample, 87% of the right and 96% of the left fibularis brevis tendon would be compromised by the cannulated screw. In males, 91% of the right and 100% of the left fibularis brevis tendon would be compromised. Whereas in females, 83% of the right and 92% of the left fibularis brevis tendon would be compromised. Our data demonstrate that in order to properly insert and thread a cannulated screw into the fifth metatarsal, it would require penetration of the fibularis brevis tendon and lateral tarsometatarsal joint for a large proportion of patients.

The authors would like to thank Midwestern University and the Kenneth A. Suarez CCOM Research Fellowship for support of this project.
Presentation of High Grade Prostate Cancer in the Underinsured

Thomas O'Grady, Jed Robinson, Marc Bjurlin, Naveen Divakaruni, Chicago, IL, Matthew Houlihan, Downers Grove, IL, Saad Muktar Emhmed Ali, Andrew Drago, Courtney Hollowell, Chicago, IL

INTRODUCTION AND OBJECTIVES: A major barrier to preventive healthcare maintenance and cancer screening is low socioeconomic status and being underinsured. Previous studies have demonstrated that patients who may benefit most from prostate cancer screening are those with risk factors such as African American race and low socioeconomic status. In order to investigate the presentation and disease burden of unscreened men, specifically those with high grade prostate cancer, we assessed the prostate cancer screening status and clinical presentation of underinsured men with Gleason 8-10 prostate cancer at our institution.

METHODS: We performed a retrospective cohort study of men diagnosed with Gleason 8-10 prostate cancer from 2002-2011 at our institution and analyzed by race, age, presenting prostate specific antigen (PSA), and previous PSA screening status. Clinical TNM staging was determined by chart review, with locally advanced disease defined as clinical stage T3 and higher and nodal and bone metastasis by suspicion on radiographic imaging.

RESULTS: A total of 1,402 men were diagnosed with prostate cancer at our institution from 2002-2011, with 238 (16.9%) men having Gleason 8-10 pathology, which were evaluated in our study. Racial distribution was predominantly minorities: 67% were African American, 14% White, 13% Hispanic, and 5% Asian. All patients were uninsured or publically insured. The mean age at diagnosis was 64 years and the mean PSA at diagnosis was 386 ng/mL (median 62.7 ng/mL). Nearly all (97%) of the cohort had no previous PSA screening before their diagnostic PSA, and PSA levels at diagnosis exceeded 10 ng/mL in 89% of patients. Nearly a quarter (21%) presented with locally advanced disease, a third (31%) presented with radiographic evidence of nodal metastasis, and a half (46%) presented with bone metastasis, all of which are significantly higher than historically reported screened cohorts of prostate cancer.

CONCLUSIONS: Our underinsured, predominantly minority patient population, the vast majority of whom are without previous prostate cancer screening, present with a significant disease burden, specifically high grade, locally advanced, and metastatic disease. While much attention focuses on potential overdiagnosis and overtreatment of men with screen detected prostate cancer, our findings suggest that for the uninsured, underscreening is a significant concern. Future efforts should be focused on overcoming the barriers of access to PSA screening in this population.

Source of Funding: None
Malignant hyperthermia (MH), a subclinical myopathy usually triggered by general anesthetics, induces a hypercatabolic state that causes high body temperature, increased respiratory and heart rates that eventually leads to death if not treated quickly. Dantrolene is the most effective treatment for this condition. It is believed that dantrolene reduces Ca\textsuperscript{2+} release from the sarcoplasmic reticulum (SR) by affecting directly the activity of the Ca\textsuperscript{2+} release channels (known as ryanodine receptors; RyRs); however, the results addressing this assumption are contradicting and non-conclusive, thus the mechanism of action of dantrolene remains poorly understood. It has recently been reported that dantrolene blocks a surface anion channel (PSAC) present in red blood cells infected with *Plasmodium falciparum* (a protozoan that produces malaria in humans). Consequently, we hypothesize that dantrolene decreases SR Ca\textsuperscript{2+} release by directly blocking SR Cl\textsuperscript{−} channels, which in turn, would reduce the counterion mechanism that prolongs SR Ca\textsuperscript{2+} release through RyRs. To test this assumption, we have used native SR membranes from rat heart, enriched with SR Cl\textsuperscript{−} channels and incorporated into artificial planar lipid bilayers. After Cl\textsuperscript{−} channel activity was stably reconstituted, unitary currents were recorded with continuous voltage ramps (from -50 to +50 mV, during 5 s) before and after addition of 10 µM dantrolene (dissolved in DMSO-ethanol at final concentration of 1%) to the Cis side of the bilayer. Our preliminary results suggested that dantrolene reduced the open probability of Cl\textsuperscript{−} channels, without affecting its permeation properties (i.e. unitary conductance and ion selectivity). Our goal in this work was to confirm this preliminary observation with a more rigorous experimental approach. To this end, dantrolene effect was evaluated at different concentrations (from 1-10 µM) and at different steady-state membrane potentials maintained for prolonged periods of time (at least 3 min). Our recording solutions were designed to selectively record Cl\textsuperscript{−} channels without the interference of other ion channels present in the SR membrane (namely, RyRs and K\textsuperscript{+} channels). The ionic composition of these solutions was (Cis/Trans, in mM): 500/500 mM CsCl, 0.01/0.001 CaCl\textsubscript{2}, 1/1 MgCl\textsubscript{2}, 10/10 HEPES-Cs, 10/0 EGTA, pH = 7.3, at room temperature (~70 °F). Our results indicate that under these conditions addition of dantrolene did not exhibit consistent effects on the open probability and/or ion-permeation properties of the channel. These negative results may reflect the fact that in our study a low-affinity form of dantrolene was used, instead of the high-affinity dantrolene derivatives NPF-1 and NPF-2 that have been previously used for the referred effects on PSAC. (Work supported by K. Suarez fellowship to N.H.).
Effect of inflammatory response and ethanol exposure on hsp27 and hsp32 in microglial cells.

Elizabeth Ince¹, Alice Meyer², Leah Dion³, and Joanna Goral²

Chicago College of Osteopathic Medicine¹, Department of Anatomy², Department of Biomedical Sciences³, Midwestern University, Downers Grove, Illinois

Rationale and methods: Ethanol is a known modifier of both innate and adaptive immune responses. Heat Shock Proteins (hsp) are proteins that are elevated in cells after exposure to stress, such as extreme temperatures, radiation, or toxins. In this study we investigated whether inflammatory responses and exposure to ethanol could induce phosphorylation of hsp27 (phsp27) and synthesis of hsp32 in mouse microglial BV2 cells. We also examined whether ethanol could modify heat shock response to inflammatory agents in BV2 cells. The cells were stimulated with LPS (100 and 1000 ng/mL) with or without ethanol (100 mM) for 24 h. In addition, we examined the effect of heat shock on phsp27 and hsp32 levels in BV2 cells. The cells were incubated at 42° C for 20 minutes, and allowed to recover for either 2 or 18 h at 37°C. The levels of phsp27 and hsp32 in BV2 cells were assessed by western blot. Results: Both LPS and ethanol induced hsp32 but did not affect phsp27 levels in BV2 cells. Ethanol further augmented LPS-induced hsp32 levels in BV2 cells. Heat shock induced both phsp27 and hsp32 in BV2 cells with maximum protein levels at 18 h after the treatment. These results demonstrate that in BV2 microglia both hsp27 and hsp32 could be induced, however only hsp32 synthesis was stimulated by LPS and ethanol.

This research was supported in part by the CHS Biomedical Sciences Program funds. Elizabeth Ince was supported by the Midwestern University Kenneth A. Suarez Summer Fellowship Program.
The Long Term Impact of Perinatal Exposure to DDE on Immune Function of Adult Offspring of Swiss ICR Mice.

Neeti P. Kambale, and Susan Viselli

Department of Biochemistry, Department of Biomedical Sciences, Midwestern University, Downers Grove, Illinois

DDT was a widely used pesticide, banned due to adverse environmental effects. DDE, its major metabolite, has a long half life and acts as an anti-androgen. It is transferred via the placenta, breast milk and food. We assessed immune effects in year-old offspring of mice treated during pregnancy or lactation. Since autoimmunity may develop when androgenic signals are interrupted, we assessed autoimmune markers and immune organs. Thymus weights of male offspring treated during lactation were greater (82.5 mg vs. 38.4 mg, p<0.05). Male offspring of mice given DDE during pregnancy had higher thymus cell counts (9.4 mg vs. 5.8 mg, p<0.05). More CD3+ thymocytes were found in female offspring treated in utero compared to controls (66.2% vs. 40.4%, p<0.05). CD4+ thymocytes were higher in male offspring treated during lactation (29.2% vs. 13.6%, p<0.01) and CD8+ thymocytes were lower in female offspring treated during lactation (4.40% vs. 9.40%, p<0.05). Fewer CD4+CD8+ T cells were observed in thymuses of male offspring treated during lactation (29.6% vs. 61.9%, p<0.001). While we saw no changes in spleen weights or cell numbers, total spleen T and B cells percentages were affected. More CD3+ splenocytes were found in male offspring treated during lactation (18.3% vs. 12.0 %, p<0.05). But, fewer CD3+ splenocytes were seen in male offspring treated in utero (11.7% vs. 22.1%, p<0.05). More B220+ B cells were found in male (40.6% vs. 17.0%, p<0.05) and female (39.6% vs. 18.9%, p<0.05) offspring treated during lactation. Kidneys were assessed for their expression of autoimmune-related proteins MCP-1 and OPN. Kidney weights of male offspring treated during lactation were greater (468.5 mg vs. 363.6 mg, p<0.001). Both MCP-1 and OPN had increased renal expression in all DDE-treated mice. C1q expression and IL-17 expression was increased in the male offspring of mice treated during pregnancy and during lactation. C1q and IL-17 expression was noted to be increased in female offspring of mice treated during pregnancy. C1q expression alone was found to be increased in female offspring of mice that were treated during lactation. Based on preliminary studies in mice models, further research is needed to conclude the link between DDE and autoimmune diseases in humans.
Effects of Pregnancy on Voluntary Wheel Running Activity in Rats

Karolina A. Kill, Rebecca Rossi, Robert J. Murphy and Kathleen P. O’Hagan

Department of Physiology, CCOM, Midwestern University, Downers Grove, Illinois

Pregnancy is associated with physiological alterations in the function of maternal organ systems to meet the increasing metabolic needs of the developing fetus. During pregnancy resting blood flow to the uterus increases throughout the gestational period to supply oxygen and nutrients to the developing fetus, which greatly impacts fetoplacental growth. The long term goal is to understand how voluntary physical activity affects the control of uterine blood flow during normal and compromised pregnancy states that affect fetoplacental growth, such as hypertension and diabetes. To accomplish this goal, it is necessary to establish the pattern (velocity, duration and distance) of voluntary physical activity in rats allowed 24/7 access to a cage running wheel in the nonpregnant state, during gestation and after parturition. We hypothesized that the volume of voluntary physical activity would decrease as gestation advanced, continue to be at least partially suppressed during nursing and rebound after weaning of the pups. The cage wheel physical activity was monitored daily with a bike computer, from which was derived average velocity (m/min), distance (m) and duration (minutes). Ten Sprague-Dawley female rats were studied. After a 4-6 week run-in period, physical activity data was collected for one week in 10 non-pregnant (NP) Sprague Dawley female rats. Subsequently, 5 rats were bred (pregnant, P) and followed through gestation and 5 rats were followed in parallel as time controls (TC) (3 consecutive weeks). In a subgroup of 4 age-matched rats monitored in parallel, 2 P rats were followed through nursing (3 weeks) and weaning (2 weeks) accompanied by 2 TC rats. Values are mean[SD]. One way ANOVA with repeated measures was employed to evaluate group and time period effects. NP rats (N=10) averaged 13977 [8953] m/day, 226[70] min/day and 58[24] m/min. Pregnancy resulted in a considerable decrease in run distance (gestational week 3 = 669 [96] m/day, -Δ95% [20]) compared to the time controls (8568 [2718] m/day, - Δ21% [18], interaction term P<0.01), which was primarily due to a decrease in run time (gestational week 3 P,17 [3] vs TC, 172 [ 65] min/day or -Δ92% [3] vs. -Δ16% [15], interaction term P<0.001) with a trend toward a decrease in average velocity (interaction term, P=0.07). The decreases in distance (P, -Δ70% [11] vs TC, -Δ18% [18]) and time (P, -Δ68% [11] vs TC, -Δ13% [15]) were evident (P<0.001) during the first week of gestation. In the subgroup of 2 rats, the suppression of wheel running activity continued during the 3 week nursing phase, but rebounded towards pre-gestation levels immediately after pup weaning. We speculate that the rapid decline in voluntary physical activity with pregnancy in the rat reflects adoption of an energy conservation strategy prior to a significant fetal metabolic demand. Peripheral feedback signals, likely associated with the hormonal response to implantation and early fetal development, may initially signal the brain to reduce voluntary physical activity. Additional feedback signals may contribute to the suppression of physical activity during the nursing phase.

Supported by the CCOM Summer Research Fellowship Program (KAK and RR) and Midwestern University (RJM, KPO).
Osteoblastic differentiation is a complex process and proceeds through steps of proliferation, extracellular matrix deposition and mineralization. The p53 tumor suppressor gene is a transcription factor that plays an important role in this process, by influencing the expression of important bone specific proteins. Several recent studies have identified non-coding microRNAs (miRNAs) that function as post-transcriptional regulators of gene expression and play important role in bone formation. The objective of the present study was to analyze the miRNA expression in undifferentiated and differentiated MC3T3 p53 wild-type and p53 knocked-down (KD) murine pre-osteoblast cells and to investigate how p53 status affects their expression. Osteoblasts were subjected to differentiation promoting (DP) media for different lengths of time and miRNA was extracted using the mirVana miRNA isolation kit and analyzed using a murine microRNA LC Sciences Microarray. P53 levels were initially monitored in MC3T3 cells and we chose to compare Day 4 DP treated cells when p53 levels were the highest to p53 KD cells treated similarly. There was a differentiation related modulation in expression of several miRNAs. Among these miRNAs the ones that showed p53 dependency were further analyzed. MiR-199a, 34b, 21, 140 and 206 showed a 2-6 fold reduction in expression in p53 deficient cells. Differentially expressed miRNAs were confirmed using real-time Taqman and SYBR Green PCR. For further analyses we chose to study miR-34b and miR-140. These miRNAs were also transiently overexpressed in osteoblasts to determine their effect on key bone specific transcription factors Cbfa1 and osterix. Overexpression of miR 140 produced a significant increase in Cbfa1 activity while overexpression of both miR 34b and 140 produced a reduction in osterix activity. These results indicate that p53 can function through miRNAs to affect bone specific gene expression.
Examiner Fatigue as a Factor in Grade Variability During High Stakes Psychomotor Testing

Amber Lautzenheiser OMS II, Rajiv Verma OMS II John Hohner D.O, Stuart Marcotte OMS V, Justine Parker OMSV, Jane Gelfand OMS IV, Liya Milgram OMS IV

Department of Osteopathic Manipulative Medicine, Chicago College of Osteopathic Medicine, Midwestern University, Downers Grove, Illinois

The current method of examining medical students’ clinical ability in the Chicago College of Osteopathic Medicine Department of Manipulative Medicine is via a practical examination. For Osteopathic Manipulative Medicine, first and second year students are evaluated six times per year to assess their ability to complete the skills learned in class. The students are given a specific time of day for which they are required to be present for their practical, during which they are paired and evaluated on their ability to perform diagnostic and treatment maneuvers. The time of day and partner are each determined at random and change with each practical exam, so that no student is always taking his or her exam toward the beginning or end of the test day or with the same partner.

Students evaluate each other in pairs, looking for somatic dysfunction. After the initial evaluation, the students’ diagnoses are evaluated by a faculty member and their grade for that specific station is recorded. The student pair then moves to the second station, where they are required to perform a diagnostic or treatment technique while being observed by a different faculty member. Another grade is given at this time. Finally, the student pair moves to the third station. Here they perform a treatment technique and are again observed and graded by a third faculty member. Depending on the lay out and difficulty of the practical exam, each faculty member completes these high level decisions with 30-60 students per exam.

The goal of the research was to assess whether or not faculty showed variance in the output of their decision-making process as the exam day progressed, given the possibility of fatigue or frustration. The methodology was to collate the scores for each physician over a four hour testing block, over the course of 25 – 30 exams and analyze for variance, from the beginning to the end of each four hour exam block, in a repeatable pattern.

The study population was first and second year osteopathic medical students at the Chicago College of Osteopathic Medicine, and the faculty within the department. Data from practical examinations, given to the first and second year medical students 2-6 times per academic year, from the years 2006-2012 were entered into a Microsoft Excel spread sheet. 5,411 exam forms, each including three separate testing encounters, were examined for 16 variables for each encounter. Individual student identifiers were removed from the data. The same collection of examiners was in place for this entire time. Variables that were assessed included, but were not limited to, time of day test was taken, order of student examinee, year in medical school, age of faculty, sex of faculty, sex of student, and years of teaching experience. The data has been submitted to a psychometrician in Arizona. Five examiners thus far been analyzed and there are 32 examiners remaining. Of the five examiners completed, two display a trend toward higher grades over the four hour time, two show a trend toward lower grades over the four hour time and one stayed level throughout. The total analysis is pending.
Colocalization of NMDA glutamate receptor subunits in trigeminal neurons activated during voluntary diving in rats

Daniel Lawler2, Karyn DiNovo1, and Paul F. McCulloch1,2

Department of Physiology1, Chicago College of Osteopathic Medicine2, Midwestern University, Downers Grove, Illinois

The mammalian diving response is an important physiological mechanism that is exhibited in all mammals. Upon stimulation of the upper respiratory tract with cold water (or in some instances air-borne chemicals: ammonia, ether, formaldehyde, benzene, or carbon dioxide), mammalian subjects will respond with sympathetic peripheral vasoconstriction combined with parasympathetic bradycardia and apnea. The exposure of the face to water is relayed to the brain mainly via the anterior ethmoidal nerve (AEN), a branch of the ophthalmic division of the trigeminal nerve. The role of the AEN in this response has been verified by measuring Fos, a marker of neuronal activation, within the trigeminal nucleus. Also, sectioning of the AEN results in a largely diminished response to nasal stimulation. These gross neuronal signals are mediated by the release of glutamate by the central terminals within the trigeminal nucleus caudalis, also known as the medullary dorsal horn (MDH). To help determine the specific secondary signal responsible for the synaptic actions within the MDH, we performed Fos and Substance P receptor immunohistochemical labeling. Sections of brain tissue obtained from rats trained in repetitive voluntary underwater diving were labeled with anti-Fos and anti-Substance P receptor antibodies, and co-localization was counted via fluorescent microscopy. Substance P receptor and Fos co-localization was not limited to the superficial lamina of the MDH, but rather was present in both superficial and deep laminae in greater quantities than the co-localization observed in the paratrigeminal nucleus. Our data suggests that diving causes release of Substance P by the central terminals of the AEN. The secondary neurons within the MDH expressing the Substance P receptor Neurokinin-1 then propagate the nociceptive afferent signal to other brainstem areas that are involved in the efferent aspect of this response. The activation of MDH neurons that co-express Substance P receptors suggests that either nociception, or activation of nociceptive circuitry, may be involved in the voluntary diving response of rats.

This research was supported by the Dr. Kenneth A. Suarez Summer Research program, 2012
Temporal Characterization of Uterine Horn Pathological Sequelae Following Genital Chlamydia muridarum Infection

Bartosz Leszczynski1,*, Swati Ratkal1,*, Srikanth Manam1, Ashlesh K. Murthy1

1Department of Pathology, Midwestern University, Downers Grove, IL 60515

Genital chlamydial infection in mice closely mimics many aspects of infection in women. Typically, mice naturally resolve the infection within 4 weeks, but similarly to human infection, they may develop complications such as fluid-filled dilatation of oviducts (hydrosalpinx) followed by infertility. Previous studies have reported extensive characterization of infiltration of acute (PMN), and chronic (lymphocytes and plasma cells) inflammatory cells, fibrosis, and oviduct dilatation in wild type BALB/c mice. Over the last several years, wild type C57BL/6 mice have been used for studies of pathogenesis due to the availability of various gene knockout strains in this background. Following intravaginal Chlamydia muridarum infection, C57BL/6 mice develop uterine horn dilatation in addition to oviduct dilatation. Our group had previously reported that mice deficient in B cells (B cell KO mice) develop significantly greater uterine horn pathologies, but comparable oviduct pathology, compared to wild type mice, suggesting that pathogenic mechanisms may be different at these two anatomic sites. While fibrotic blockade of lumen has been suggested to underlie oviduct pathologies, the mechanistic basis of uterine horn pathologies have not been characterized in detail within the mouse model. Therefore, wild-type BL6 mice and B cell KO mice were infected with Chlamydia muridarum and pathology evaluated after days 6, 18, 36, 60, and 80. Infiltration of acute and chronic inflammatory cells, fibrosis, and cell density in the lamina propria were semi-quantitatively scored under 10 high-power (40x) microscopic fields. Acute inflammation was highest at day 6 and progressively declined, reaching lowest levels at day 80. Chronic inflammation was lowest initially at day 6; it progressively increased and peaked at days 36 and 60 and approached to initial levels by day 80. B cell KO mice generally showed higher levels of acute and chronic inflammatory infiltrates compared to C57BL/6 mice. Fibrosis was minimal at days 6 and 18, and was low and comparable at days 36, 60, and 80 in both groups of mice. The uterine wall cell density was observed to be highest at day 6, before it declined progressively and reached lowest levels at day 60, and demonstrated modest cellular recovery by day 80. B cell KO mice displayed a significant reduction in cell density compared to C57BL/6 mice. Taken together, these results suggest that acute and chronic inflammatory cells may contribute to uterine horn pathology. However, the reduction in uterine wall cell density, rather than luminal fibrosis, may underlie uterine horn pathologies following genital chlamydial infections in C57BL/6 mice.

This work was supported by Midwestern University Faculty Start-up Fund and NIH Grant 1R03AI088342 to AKM, and MWU OSRP Research Fund to BL. *BL and SR contributed equally.
Defining Postictal Duration for Pediatric Simple Febrile Seizures
Erin Little, OMS2, Matthew Keeler, D.O., Bryan King, D.O., John Graneto, D.O.
Emergency Medicine-Swedish Covenant Hospital, Department of Integrative Medicine

Objective: The objective of the study is to provide a defined duration of the postictal period in simple febrile seizures. The current definition of simple febrile seizures includes a postictal period described as being brief. The implications of determining the mean postictal duration will be to further clarify the definition of a simple febrile seizure.

Introduction: Simple febrile seizures occur in children between the ages of six months and five years and are distinguished from complex seizures with specific criteria. Some of the distinguishing criteria include lack of intracranial infection, metabolic disturbance, or history of afebrile seizures. Simple febrile seizures are further defined as those that last for less than 15 minutes, are generalized (do not have a focal component), and occur only once in a 24 hour period. The management of simple febrile seizures in the Emergency Department differs from complex seizures. The mean postictal period for a child presenting with a simple febrile seizure, as determined by this study, will help guide management in the Emergency Department.

Methods: After obtaining Institutional Review Board (IRB) approval, a retrospective chart review was conducted of 306 children treated for seizures in a general Emergency Department in Chicago. Of those patients, 150 were found to fit the American Academy of Pediatrics (AAP) diagnostic criteria for a simple febrile seizure. The average postictal time was calculated for these 150 patients. Variables such as height of temperature (Tmax), length of stay, and mode of arrival were compared.

Results: The postictal durations for febrile seizures ranged from zero to 33 minutes, with the average being 8.8 minutes. The most frequently represented duration reported for this data set was zero minutes. Using two standard deviations to eliminate outliers, the range was found to be zero to 27.6 minutes. The duration of the postictal period was also compared with length of stay in the emergency department as well as the Tmax. The average length of stay in the Emergency Department was 99 minutes. Ambulance arrival patients had an average postictal duration that was 3.1 minutes longer than the average for walk in patients (Ambulance 9.5min., Walk in 6.4min.). Patients with a Tmax greater than 103 degrees Fahrenheit had an average postictal duration that was 1.1 minutes less than patients with a Tmax less than 103 degrees (Tmax>103 = 8.3mins, Tmax<103 = 9.4mins).

Discussion: The purpose of the study was to further define the postictal period associated with a simple febrile seizure. Patients with a postictal duration outside the brief range now determined in this study (zero to 27.6 minutes) that otherwise fulfill the diagnostic criteria for simple febrile seizures may need to be carefully evaluated for further ED workup. An unexpected finding in the remainder of the study showed lower fevers correlated with longer postictal periods. This seems counterintuitive and may be a source for further study.
In heart, L-type Ca\textsuperscript{2+} channel (LTCC) is one of the most important membrane proteins because it triggers excitation–contraction coupling (ECC), determines the action potential shape, and is involved in numerous arrhythmogenic mechanisms. Although the functional properties of cardiac LTCC have been thoroughly described at the whole-cell level, detailed description of its biophysical profile at the single-channel level and under physiological conditions is scarce. The main reason for this paucity of information is that LTCC is predominantly located in a membranous system formed by narrow invaginations, called T-tubes. Thus, direct access to record LTCC with standard patch-clamp techniques is not possible without disrupting its natural environment. What is known about LTCC unitary properties has been defined by reconstituting T-tube membrane microsomes into artificial planar lipid bilayers (PLB). A unitary conductance of \(~25\) pS (in 100 mM Ba\textsuperscript{2+}) and a mean open time of \(<1\) ms have been measured with this technique. However, with the high-frequency thermal noise associated to large capacitance values (\(~200\) pF) that characterize traditional PLB (mainly due to their large surface area) these functional properties result in a very poor signal-to-noise ratio. Thus, the use of traditional PLB cannot be applied to the study of LTCC under physiological conditions (i.e. with 2 mM extracellular Ca\textsuperscript{2+} and in the absence of pharmacological agonists, like [-]Bay K) because unitary currents are literally engulfed by the bilayer noise. Similarly, traditional PLB cannot be used to define the temporal attributes of LTCC gating kinetics that occur in the microsecond domain. The novel glass nanomembrane (GNM)-based system, recently engineered by Dr. Geoffrey Barrall (Electronic BioSciences, CA), offers a unique possibility to overcome the experimental hurdles associated to traditional PLB, yet maintaining the ability to record ion-channel activity at the molecular level. The main features of the GNM system are that lipid bilayers are built on the tip of quartz glass pipettes, whose tip size can range from nanometers to few micrometers of diameter (thereby reducing the capacitance-associated thermal noise). Because of these intrinsically low noise properties, the GNM system allows the recording of extremely small currents with channel opening events extremely brief (in the microsecond range). These properties are precisely the characteristics of LTCC unitary currents (small currents through brief openings). Still, the GNM system can offer even lower noise levels (RMS of \(~200\) fA @ 10 kHz) when a capacitor is used as feedback element in the voltage-current converter. This configuration yields such a high temporal resolution that allows to accurately define the LTCC typical dwell times (of hundreds of millisecond) and very importantly, under physiological conditions. To test this GNM, we used in this study native LTCC-containing sarcolemma vesicles from adult rat heart. Once channel activity was stably reconstituted, unitary currents were recorded at different steady-state membrane potentials (from -20 to +20 mV), held constantly for at least 3 min. Our results indicate that cardiac ion channels can be incorporated into GNM and their unitary current recorded with very high signal-to-noise ratio. Nevertheless, the low rate of successful incorporation indicates that with such a small bilayer area the probability of microsomes fusion and their consequent ion channel incorporation is extremely reduced. We therefore conclude that the utility of this promising system would greatly increase with the use of larger-size quartz pipettes. Additionally, working with purified channels reconstituted into artificial liposomes may also improve the likelihood of successful incorporation. (Work supported by K. Suarez fellowship to A.L.).
Development of a PCR assay for the rapid detection of *Pseudomonas Aeruginosa*

Areej Mazhar and Annette Gilchrist

*Department of Pharmacology, Chicago College of Osteopathic Medicine, Midwestern University, Downers Grove, IL*

The detection of bloodstream pathogens currently relies on blood cultures, a procedure that can take 3-7 days to identify the underlying infective agent. An alternative approach using molecular biology tools such as the polymerase chain reaction (PCR) was utilized, with the underlying goal being to look only for those organisms meriting a change in therapy, such as *Pseudomonas aeruginosa*. To this end, the isolation and PCR methods were optimized through the use of different primers, different annealing temperatures, and varying the number of cycles to determine whether such an approach might serve as a diagnostic tool. Given our promising results, it is hoped that in the near future, patient blood samples will be used to test whether our simple and affordable PCR method for detecting *Pseudomonas aeruginosa* will provide not only a means for early detection but also a diagnostic tool that can ultimately improve patient outcomes.
The mammalian diving reflex is a response to underwater submersion that result in apnea, reduced heart rate, and altered blood flow to maintain perfusion of the heart and brain. This reflex is present in decerebrated animals, demonstrating that the neural mechanisms responsible for the reflex occur at the level of the brainstem and are not dependent on cortical output.

Submergence of the nose stimulates free nerve endings supplied by the anterior ethmoidal nerve (AEN). The AEN then carries the afferent signal to the medullary dorsal horn (MDH). The main goal of our lab is to determine how the MDH relays this information to other brainstem locations to initiate the efferent aspects of diving. Prior studies have demonstrated that an intact glutamatergic pathway within the MDH is needed to generate the cardiac response induced by diving. Additionally, ammonia vapor stimulation of the nasal passages in anesthetized animals, which mimics the diving response, activates neurons in MDH. These MDH neurons express glutamate receptor subunits, specifically AMPA receptor subunits GluR2/3.

We hypothesized that voluntary diving in rats would activate neurons within the superficial lamina of the MDH and that these neurons would express GluR2/3 subunits. Rats were trained to repetitively dive through a 5m long underwater maze every 5 minutes for 2 hours. Following pentobarbital overdose and left ventricular exsanguination, rats were perfused with 4% paraformaldehyde. Brainstem tissue was cut at 50 um, and serial sections were stained for Fos (as a measure of neuronal activation) and the GluR2/3 subunit. Our results demonstrate significantly greater Fos expression with co-localization of GluR2/3 in the MDH compared to adjacent brain structures (one way ANOVA; tukey post-hoc, P<0.05). Staining between the superficial and deep lamina within the MDH were not statistically different. The increased activation of the deeper MDH lamina in conscious voluntarily diving rats, as compared to ammonia stimulation in anesthetized animals, may be due to other stimuli (noise, grooming, tactile information) and additional trigeminal activation due to diving. Our data demonstrate that a significant fraction of MDH neurons containing the AMPA subunit GluR2/3 are activated during diving. Future studies will focus on selective receptor activation to elucidate how sensory information is processed and relayed in the diving reflex.

This research was made possible thanks to Dr. McCulloch and Ms. DiNovo, the physiology department of MWU, and was supported by funds from the MWU Kenneth A. Suarez Summer Research Program.
Immune response to lymph mobilization in rats with collagen induced autoimmune arthritis.

Robert C Myers², April M McClish², Brian Zanotti¹, and Michael Volin¹

Department of Microbiology¹, Chicago College of Osteopathic Medicine², Midwestern University, Downers Grove, Illinois

Purpose: Rheumatoid Arthritis (RA) is an inflammatory joint disease affecting many people in the United States. RA development is understood to involve inflammatory cytokines, antibodies, and structurally damaging enzymes. Clinically, lymphatic pump treatment (LPT) is used to increase lymphatic return, reduce edema, and assist in the movement of antigens circulating throughout the body. The goal of our research was to show LPT can alter inflammation in ankles of rats with collagen induced arthritis (CIA), through quantifying differences in the number of T-cells in and the amount of swelling of affected joints between non-treated control and LPT ankles. Another goal was to compare the rat CIA model to the rat adjuvant induced arthritis model (AIA) which Volin, et. al. had conducted previously. Methods: 20 rats were subcutaneously injected with porcine collagen. After onset of arthritis, rat weight and ankle grades were recorded daily while ankle measurements were taken three times per week. Sham and LPT were performed daily after onset of arthritis. After nine days of treatment the animals were euthanized at which time blood was collected for flow cytometry experiments to determine changes in circulating leukocyte populations. Results: The previous rat AIA model showed a similar degree of joint inflammation compared to the rat CIA model as determined by ankle circumferences and ankle grades. AIA rat ankle circumferences plateaued around day 15 at approximately 50 mm while in CIA rats the ankle circumferences peaked around day 18 at approximately 56 mm. Changes in ankle measurements and inflammation grades started at day 10 in the rat AIA model and day 13 in the rat CIA model. Previously, LPT of AIA rats showed trends of reduced swelling and inflammation. However, in this trial run of LPT on CIA rats we did not see a reduction of swelling or inflammation. Conclusion: Our research shows that the rat CIA model has a very similar inflammatory time course to the previously used rat AIA model. Both the timing and extent of inflammation are very similar in each model. In this preliminary experiment using rat CIA, LPT failed to reduce inflammation or alter the number of circulating T-cells. Further studies utilizing different LPT protocols will need to be performed to determine the efficacy of LPT on rats with CIA.

This research was supported in part by a Midwestern University Kenneth A. Suarez research Fellowship (RCM).
Improving Auscultation Accuracy through Developing a New Cardiac Murmur Classification System

Vijeta Pamudurthy, Carl Cassel, Cyrus Haselby, and Glenn Nordehn, DO, FACOI

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

Cardiac murmurs are a common finding on physical exam. Physicians judge the significance using a system developed in 1933 by Freeman and Levine that assigns murmurs grades (1-to-6). Grade 1- faint, 2- soft, 3- mild, 4- loud, 5- very loud, and 6- the loudest. The American College of Cardiology recommends murmurs greater than grade 2 have further evaluation with echocardiogram. The recommendation assumes physicians can accurately grade murmurs. On a more basic level, the recommendation assumes humans can distinguish between murmur variations. However, this classification ability is suboptimal. The result: unnecessary numbers of echocardiograms ordered resulting in significantly wasted health-care dollars. We aim to test the most basic assumption; humans can distinguish between varied murmurs through our hypothesis that, a set of varied heart murmurs and normal sounds, when judged for similarity by naïve auscultators form clusters. Method: naïve auscultators will do a one-to-one comparison of 14 varied murmurs. To prepare for the study: develop software allowing study participation and automatic analytics in order to perform comparison testing of the hypothesis. The present work placed all 14 murmurs pairs in a secured location on the web and developed automated data collection. Future work: obtain IRB approval to proceed with the comparisons. Analysis: a DBSCAN (density-based spatial clustering of applications with noise) data clustering algorithm will be used to determine whether clustering occurs. Additionally, social network analysis using IBM-Many-Eyes software will determine whether clustering occurs. We will consider the hypotheses proven if consistent inter- and intra-subject clustering occurs.
Assessment of candidate PRDM16 transcriptional target genes in mouse embryonic craniofacial and brain tissues.

Paulina Pawluczuk, Lenore Pitstick, Bryan Bjork

Department of Biochemistry, Midwestern University, Downers Grove, Illinois

Craniofacial malformations, including the common disorders of cleft lip and palate and rarely, Pierre Robin Syndrome, represent a significant human health concern with physical, psychological and financial implications. Many gene mutations have been identified in mouse mutants with clefting and have provided inroads into the developmental, genetic and biochemical pathways critical to mouse and human craniofacial development. Loss of function mutations in the Prdm16 Zinc finger transcription factor gene result in cleft secondary palate among multiple additional phenotypic anomalies. We proposed to screen and validate candidate genes whose expression may be directly regulated by the PRDM16 transcription factor during mouse embryonic craniofacial development. Candidate genes were identified via experimental determination of direct target DNA-binding motif sequences for PRDM16 zinc finger DNA-binding domains and subsequent informatics search for the incidence of these motifs within close proximity to gene transcriptional start sites. We report the optimization of novel qPCR expression assays and preliminary studies toward the search for downstream targets of PRDM16 transcriptional regulation. These studies utilize a novel conditional gene trap null allele of Prdm16 (Prdm16\(^{GT}\)) to assess gene expression of these candidate genes in wild type and homozygous mutant craniofacial and forebrain tissues using quantitative PCR (qPCR). The identification of PRDM16 target genes will help us gain a more complete understanding of the role for Prdm16 during craniofacial development and provide novel candidate genes to be examined for etiologic contributions to human craniofacial disease.

This research was supported in part by Kenneth A. Suarez Research Program.
New Insights into the Mechanisms By Which Epstein-Barr Virus May Promote Hodgkin’s Lymphoma Development

Catherine Pinkston\textsuperscript{2}, Ryan Incrocci\textsuperscript{1}, Annette Gilchrist\textsuperscript{3} and Michelle Swanson-Mungerson\textsuperscript{1,2}

\textit{Department of Microbiology\textsuperscript{1}, Chicago College of Osteopathic Medicine\textsuperscript{2}, Chicago College of Pharmacy\textsuperscript{3}, Midwestern University, Downers Grove, Illinois}

The majority of people worldwide are infected with Epstein-Barr virus (EBV), which has been implicated in the development of Hodgkin’s lymphoma (HL). However, the exact mechanism regarding how EBV contributes to the development of HL is unclear. HL is a unique lymphoma in that the bulk of the tumor mass is from lymphocytes and monocytes that are recruited by the malignant tumor cells. The recruitment of the tumor mass is predominantly achieved by the production of proteins called chemokines by the malignant tumor cells. Preliminary data from a chemokine micro-array indicated that a B cell lymphoma BJAB cell line expressing the EBV protein LMP2A increases expression of the chemokine RANTES over LMP2A-negative cells. The goal of this project was to confirm that RANTES expression was increased in BJAB-LMP2A positive cells using ELISA and to determine if RANTES or other factors in the cell supernatant increased chemotaxis of the monocytic cell line, THP-1. An ELISA was performed on supernatants from three different LMP2A-negative or –positive B cell lines: BJAB, RV, and Ramos. Supernatants from LMP2A-positive RV and Ramos cell lines trended toward increased RANTES expression both with and without LPS. However, the results were inconsistent, as the LMP2A-positive BJAB cell line did not show increased RANTES. Despite the lack of a LMP2A-mediated increase in RANTES production, we wanted to determine if LMP2A increases the production of a substance that promotes chemotaxis. Therefore, we initially established conditions for the chemotaxis assay by optimizing FBS concentration, supernatant concentration, incubation time, and cell number. Preliminary data trends toward increased THP-1 chemotaxis when THP-1 cells were incubated with supernatant obtained from BJAB LMP2A-positive cells in comparison to supernatants from LMP2A-negative cell lines. Future studies are planned to identify the altered chemokine in the supernatants from LMP2A-positive cell lines that are responsible for this increase in THP-1 chemotaxis. These data suggest that in EBV-associated Hodgkin’s lymphoma, the EBV protein LMP2A may promote tumor development and survival by increasing the recruitment of monocytes and lymphocytes to the tumor. By identifying novel functions of LMP2A, we can learn of possible targets for future pharmacological intervention for people suffering from EBV-associated lymphomas.

\textit{This research was supported in part by Midwestern University intramural funds and the National Institutes of Health Grant: 1R15CA14969-01.}
Actin Proline Hydroxylation: Discovery of a Novel Actin Post-Translational Modification and Implications for the Effects of Hypoxia on Tumor Metastasis

Trenton L. Place and Frederick E. Domann

The University of Iowa Molecular and Cellular Biology Program and The University of Iowa Department of Radiation Oncology

Tumor metastasis is a complex process requiring reorganization of the actin cytoskeleton to facilitate cell migration. One stimulus thought to initiate the process of metastasis is low oxygen levels (hypoxia) found within primary tumors. However, little is known about the precise mechanisms involved. We previously found that the expression of an oxygen-dependent proline (prolyl)-hydroxylase (PHD3), that targets proteins for prolyl-hydroxylation at L/IXXLAP motifs, is downregulated in MB-435 metastatic melanoma cells. We hypothesized that PHD3 downregulation could be found in samples from metastatic melanomas, and that PHD3 may target a component of the cytoskeleton that contains an I/LXXLAP motif.

Using the Oncomine tumor gene expression database, we discovered PHD3 was downregulated 2.59 fold in malignant melanomas compared to samples of benign melanocytic nevi (p=7.5E-7), and was further downregulated as a function of melanoma invasion depth (r²=0.64). In our search for PHD3-targets that could explain these results, we found that actin contains a highly conserved IXXLAP hydroxylation motif. LC-MS/MS analysis demonstrated that approximately 10% of cellular F-actin is hydroxylated at this proline, whereas no other prolines were detected to have this hydroxyl modification.

These data suggest that actin may be a target for prolyl-hydroxylation by PHD3. Although it is unclear what the precise function of actin hydroxylation may be, our data suggest that loss of hydroxylation following PHD3 downregulation, or in hypoxic regions of tumors, may promote tumor metastasis. We are working to further characterize the function of actin hydroxylation, and hope that this research may further elucidate the role of hypoxia in tumor metastasis.
An osteochondral defect or lesion (bone & cartilage breakdown) of the talus (ankle bone) is a common condition which causes localized joint damage and pain. This type of lesion frequently arises due to trauma, such as a severe ankle sprain. A common site of osteochondral defects is the medial region of the talus. A fairly new procedure that is being performed to treat these defects is an arthroscopic approach called osteochondral autograft transplantation system (OATS). The procedure begins with removal of a cartilage core from an articular cartilage donor site. After a socket has been created in the damaged region of the recipient bone, the donor cartilage is transferred to this site. The transplanted core will result in growth of new cartilage, which will heal the osteochondral lesion. Multiple donor cartilage cores can be inserted into the talus, either from the anterior, middle, or posterior region of the talus to enhance cartilage growth.

The purpose of this study was to determine the maximum depth and spacing of multiple core insertions into the talus without compromising its integrity. We compared adult males and females to see if there was any significant difference in core insertion lengths between the sexes. The ultimate goal of the study is to suggest guidelines to improve the OATS procedure while reducing potential negative outcomes for patients, such as a wedge fracture.

The measurements obtained of the tali were used to calculate the use of 5 mm diameter cartilage cores. Using a trigonometric function, we determined the average maximum insertion depth of two 5 mm cartilage cores without compromising the integrity of the talus. Paired comparisons of the three cores were made in order to determine which combination of core pairs best reduced the chances of wedge fracture.

On average, longer cartilage cores could be inserted into the tali of adult males before wedge fracturing occurred than compared to the core lengths inserted into the tali of adult females. Additionally, it was noted that the combination of core insertions in the middle and anterior regions would result in a wedge fracture at a shorter core depth than in the combinations of anterior and posterior cores and middle and posterior cores.

The authors would like to thank Midwestern University and the Kenneth A. Suarez CCOM Research Fellowship for support of this project.
Nanocarrier formulation of ET\(_B\) receptor agonist, IRL-1620, for the treatment of cerebral ischemia

Puneet Ralhan\(^1\), Anil Gulati\(^2\), Medha Joshi\(^2\)

Chicago College of Osteopathic Medicine\(^1\), Chicago College of Pharmacy- Department of Pharmaceutical Sciences\(^2\), Midwestern University, Downers Grove IL

Stroke remains to be a serious and debilitating neurological disorder, making it the third leading cause of death in the US. Statistical analysis demonstrates that 87% of all strokes are ischemic in nature indicating the presence of thrombosis, embolism, or systemic hypoperfusion which results in reduced oxygen and glucose delivered to the brain. Within minutes of interrupted blood flow, mitochondria are deprived of a substrate, which prevents adenosine triphosphate (ATP) generation and results in membrane depolarization. This leads to increased intracellular calcium and sodium concentrations followed by generation of free radicals and initiation of apoptosis. Despite the severity of this condition, the only currently available FDA approved pharmacological treatment for ischemic stroke is recombinant tissue plasminogen activator (rtPA), which dissolves the clot and restores blood flow to the brain. This treatment is complicated by the relatively short window of time between infarct and treatment (3-4 hrs) and the increased risk for subarachnoid hemorrhage. A neuroprotective agent IRL-1620 which is an endothelin receptor B (ET\(_B\)) agonist has shown promise in previous research aimed at stopping or slowing the secondary damage associated with ischemic cascade following stroke (Leonard et al., 2011). Clinically however, there is a need to improve efficacy of delivery of IRL-1620 to the brain due to the characteristics of the blood brain barrier and the small window of opportunity available for its responsiveness following a cerebral ischemic incident. IRL-1620 being water soluble has less chances of crossing the blood brain barrier (BBB). Liposomal nanocarriers of IRL-1620 that can cross BBB were formulated in this study. PEGylated liposomal nanocarriers were prepared using the dry film evaporation method. The particle size and zeta potential were measured using Zetasizer Nano ZS via 25°C. Liposomes of about 50 nm with polydispersity index (PDI) of 0.14 were prepared with a zeta potential of -7.96 mV indicating stability. The encapsulation efficiency was analyzed with Agilent 1200 HPLC and was found to be 67%. Liposomal uptake into mouse brain endothelial bEND3 cell line was visualized using confocal microscopy with localization of the liposomes mostly in the nucleus. The stability profile of the liposomes showed complete degradation of the encapsulated liposomes by the 7th day. This may be attributed to the low stability of peptides in aqueous solutions. Stability was enhanced in this study by changing from the IRL-1620 made in 5% ammonia solution in water to the preparation in a water solution with neutral pH. Further measures are being evaluated to improve the stability such as freeze drying.

This research was supported by funds from the Kenneth A. Suarez Summer Research Program at Midwestern University.

A Case Study: Uterine artery vasoconstrictor response to exercise in the rat during paced versus voluntary exercise

Rebecca Rossi, Karolina A. Kill, Robert J. Murphy, Kathleen P. O’Hagan

Department of Physiology, CCOM, Midwestern University, Downers Grove, Illinois

We have previously observed that treadmill exercise provokes a 40-70% decrease in uterine artery conductance in non-pregnant rabbits and rats. However, treadmill exercise is involuntary, paced physical activity for a rat compared to spontaneous exercise on a cage running wheel, and thus the vasoconstrictor response on the treadmill may reflect a behavioral stress response in addition to the physiologic response to physical activity. In this case study, we evaluated the feasibility of performing exercise studies on a motorized treadmill and a metal cage wheel using a wireless implantable radiofrequency blood pressure transmitter in rats. Second, we hypothesized that the uterine artery vasoconstrictor response to exercise in the non-pregnant state is greater during paced exercise (treadmill) compared to voluntary exercise (cage wheel) in which velocity and duration are controlled by the rat.

Initially, 5 female Sprague-Dawley rats were acclimated to treadmill exercise and then underwent surgery to implant a Transonic flowprobe around the right uterine artery and a Telemetry Research wireless blood pressure catheter directly into the abdominal aorta. The radiofrequency blood pressure (BP) signals (wireless) and uterine blood flow (UtBF) signals (wired) were recorded during exercise on motorized treadmill and during spontaneous exercise on a metal running cage wheel. Uterine artery conductance (UtC) was calculated (UtBF/BP); changes in UtC reflect the vasoconstrictor response. In one rat with a functioning flowprobe and BP transmitter, we were able to collect usable data on 8 wheel running bouts (range 12-52 m/minute) and 6 treadmill runs (@7(2x), 13, 20 (2x), and 30 m/min) over 2 experimental sessions separated by 10 days. Values are mean [SD]. One way ANOVA was utilized to compare exercise modes. During treadmill exercise, the relative change in UtBF(-10%[12]) and UtC(-15%[12]) were greater compared to wheel bouts (UtBF, 6%[10], P=0.03 and UtC, 2%[10] P =0.008). The average exercise BP (treadmill 124[5], wheel 126[4] mmHg) and heart rate (HR) (treadmill 499[13], wheel 502[23] bpm) were not affected by exercise modality (P>0.05). This preliminary data suggest that involuntary, paced exercise on the treadmill elicits a uterine artery vasoconstrictor response that is greater than the uterine artery vasoconstrictor response during spontaneous wheel running exercise over a similar absolute workload, as indicated by comparable average exercise HR, BP, and running velocities. This difference may reflect an additional behavioral stress with involuntary paced exercise, which is also associated with extra investigator handling of the rats, compared to the voluntary initiation of activity and self-selected workload with cage wheel running.

This research was supported by Kenneth A Suarez Chicago College of Osteopathic Medicine Summer Research Fellowships to Rebecca Rossi and Karolina Kill and Midwestern University funds.
Hypothesis: Urinary catheter composition affects catheter-associated biofilm formation in diabetic patients.

Overview: Biofilm formation is essential for the survival and growth of *Escherichia coli* in catheter-associated infections. Individuals with type 2 diabetes have an increased incidence of urinary tract infections. Pre-diabetic individuals and individuals with poorly controlled or undiagnosed diabetes can excrete insulin, a quorum-signaling compound that induces increased biofilm formation in the presence of glucose. The focus of this study was to determine if the composition of Foley catheter material, which would be used in this patient population, affects biofilm formation by *E. coli* in a model system for diabetes.

Materials and methods: Rubber (lubricious-coated), silicon-coated, silver-coated and nitrofurazone-coated catheter segments (5mm; n=6) were tested. An overnight culture of *E. coli* ATCC25922 (Muller Hinton) was added (10^4 CFU/ml, final concentration) to artificial urine alone, or with insulin (40µU/ml) and/or glucose (0.1%). After incubation (18h, 37°C, in air and anaerobically) the catheter segments were washed extensively in PBS, then stained with crystal violet (3 ml). After removal of excess stain by washing, biofilm-associated crystal violet was eluted with absolute ethanol (3ml) and quantified spectrophotometrically (Abs550nm). Statistical analysis was done by ANOVA (InStat, GraphPad) with post-hoc analysis (Tukey).

Results: With the sole exception of silver-coated catheters grown under aerobic conditions, for all other catheters and growth conditions tested the presence of insulin and glucose significantly (p<0.05) increased levels of catheter-associated biofilm by 11-30%. The highest level of biofilm was measured for rubber catheter incubated aerobically. Biofilm levels upon growth aerobically or anaerobically in the presence of insulin alone or glucose alone were similar to that measured for the media alone control.

Conclusion: Regardless of catheter composition, with the sole exception of silver-coated catheters in the presence of oxygen, the combined presence of insulin and glucose enhanced biofilm formation by *E. coli*. This finding indicates patient compliance, with regards to insulin use and glycemic control, should result in fewer complications associated with biofouling of urinary catheters.

Benny Rummani was supported by the Midwestern University Summer Fellowship Program. Balbina J. Plotkin was supported by Midwestern University intramural funds through ORSP.
Selection of Virulence from Within Chlamydia trachomatis, serovar E

Carlyn K. Sainvil², Justin Schripsema¹, and Dr. Kyle Ramsey¹,²

Department of Microbiology & Immunology¹, Chicago College of Osteopathic Medicine², Midwestern University

This study was conducted to test the following hypothesis: a chlamydial inoculum of a specific serovar will contain variant populations that individually display varying biological properties, such as growth rate, and hence varying degrees of virulence for a given host. We tested this by doing the following: (1) developing a standard growth curve for Chlamydia trachomatis, serovar E/Bour (stock-E), (2) selecting, isolating, and expanding viable elementary bodies at 22 hours post-infection, then verifying it is a faster growing strain by comparing subsequent growth curves. The results showed that the isolate (22-fast-E) caused the shedding of greater than 3 log₁₀ IFUs more than the stock from which it was derived from. Upon initial review, our data supported the hypothesis. However, after PCR analysis and DNA sequencing it was confirmed that our isolate was actually a contaminant of Chlamydia muridarum introduced at some unknown point in our experimentation. Although the finding of the contaminant rendered this particular investigation unsuccessful, our data demonstrated significant results that could be used in future studies.
The study of primate skeletal morphology is a central concern of paleoanthropology, largely due to the fact that the preserved remains of ancestral humans and other primate species are osteological in nature. However, the details of skeletal variation represent complex and incompletely understood interactions between genetics and behavior. For this reason, osteology can help to illuminate phylogenetic relationships between existing primates and the fossil remains of extinct taxa. Additionally, the study of osteology may allow one to glean insights into the role of epigenetic factors in skeletal ontogeny. Of particular interest to physical anthropologists is the role of locomotor behavior in determining skeletal structure, for such insights can aid in the reconstruction of the behavioral tendencies of extinct species. Scapular morphology is an especially rich area for consideration – the scapula plays a central role in a range of locomotor modalities and is employed to very different ends depending on how an animal gets around. Additionally, it has been demonstrated that normal scapular development depends on the physical stresses applied through behavior as well as inherent genetic signals. Most significantly, changes in behavior have been shown to result in altered scapular morphology.

The infraspinous fossa is the region of the scapula inferior to the scapular spine; it is the site of origin for the infraspinatus muscle, which is situated within the infraspinous fossa. In this study, we focused specifically on the morphology of the infraspinous fossa of the scapula to more thoroughly assess shape variation as it relates to function among adult representatives of humans (Homo sapiens), chimpanzees (Pan troglodytes), orangutans (Pongo pygmaeus), gorillas (Gorilla gorilla), and gibbons (Hylobates sp.). In addition to traditional considerations of scapular shape and size (i.e., two-dimensional distance and angle measurements) we also utilized two more in-depth geometric morphometric methods. These methods rely on a technique known as Procrustes superimposition, which evaluates shape differences between individuals to create unique variables to compare individuals and groups (i.e., species). The first of these methods employed five homologous landmarks to construct a wireframe representation of the infraspinous fossa, and the second used sliding semilandmarks along the entire border of the fossa. In this way we were able to directly evaluate interspecific shape variation, while simultaneously considering the methodological value of adding progressively more detailed information about the shape of the scapula into the analysis.

The sliding semilandmark approach represents a far higher-resolution view of infraspinous shape than the two-dimensional and wireframe techniques. The initial conclusions of the two-dimensional approach were confirmed by both the wireframe and sliding semilandmark analyses. However, the more detailed shape assessment enabled by the semilandmark approach afforded greater refinement of interspecific infraspinous shape variation, and accordingly, more specific functional interpretations of the morphology. In particular, the sliding semilandmark approach provided the clearest picture of the morphological divergence of Homo relative to the other extant ape species, as well as the status of Pongo as morphologically intermediate between Homo and the other apes. We hypothesize that, in the case of the non-human primates, the infraspinous fossa is configured to allow the infraspinatus muscle to better stabilize the glenohumeral joint during suspensory activities and postures. Pongo’s intermediate morphology therefore may reflect the fact that its arboreal locomotion differs in style from the other suspensory apes. Meanwhile, Homo’s morphological divergence may correlate with an entirely non-arboreal lifestyle and the repurposing of the modern human upper limb for a range of behaviors distinct from our arboreal relatives.
Endothelin B receptor agonist, IRL-1620, prevents beta amyloid (Aβ) induced oxidative stress and cognitive impairment in normal and diabetic rats

Cortney Shepard1, Seema Briyal2 and Anil Gulati2

Chicago College of Osteopathic Medicine1 and Department of Pharmaceutical Sciences, Chicago College of Pharmacy2, Midwestern University, Downers Grove, IL 60515, USA

Background: Alzheimer’s disease (AD) is a progressive brain disorder leading to impairment of learning and memory. Amyloid β (Aβ)-peptide induced oxidative stress causes the initiation and progression of AD. Endothelin and its receptors have been considered as therapeutic targets in the treatment of AD. Recent studies indicate that stimulation of ETB receptors may provide neuroprotection.

Objective: The purpose of this study was to determine the effect of selectively activating the ETB receptors following Aβ-induced cognitive impairment and oxidative stress in non-diabetic and diabetic rats. IRL-1620, a highly selective ETB agonist, was used alone and in conjunction with BQ788, an ETB antagonist, to determine the role of ETB receptors in AD.

Methods: Adult male Sprague-Dawley rats were treated with Aβ1-40 (20 µg in 3 equally divided doses) in the lateral cerebral ventricles using stereotaxically implanted cannulas. Aβ was administered on day 1, 7 and 14 and all experiments were performed on day 15. The rats were treated chronically with ETB agonist (IRL-1620) and antagonist (BQ788) for 14 days. Oxidative stress markers assessed were malondialdehyde (MDA), glutathione (GSH) and superoxide dismutase (SOD). Learning and memory behavior was assessed using the Morris water maze.

Results: Aβ treatment in non-diabetic and diabetic rats produced a significant (p<0.0001) increase in malondialdehyde (MDA) levels (516.13 ± 14.02 and 531.58 ± 10.21 nmol/g wet tissue, respectively) compared to sham group (112.1 ± 1.82 and 114.31 ± 2.05 nmol/g wet tissue, respectively). Antioxidants (superoxide dismutase and reduced glutathione) decreased following Aβ treatment compared to sham group. Treatment with IRL-1620 reversed these effects, indicating that ETB receptor activation reduces oxidative stress injury following Aβ treatment. Animals pretreated with BQ788 showed similar oxidative stress damage compared to vehicle group. In Morris swim task, Aβ treated rats showed a significant impairment in spatial memory. Rats treated with ETB agonist, IRL-1620, significantly reduced the cognitive impairment induced by Aβ. However, Blockade of ETB receptors by BQ788 followed by either vehicle or IRL-1620 treatment resulted in cognitive impairment similar to those of rats treated with vehicle alone. BQ788 blocked IRL-1620 induced improvement in cognition and oxidative damage.

Conclusion: Results of the present study demonstrate that IRL-1620 administration prevents cognitive impairment and oxidative stress induced by Aβ suggesting that ETB receptor stimulation may be useful in neurodegenerative diseases.

Acknowledgement: Funding for this study was provided by Alzheimer’s Drug Discovery Foundation – www.alzdiscovery.org.
Effects of Diet Change and Weight Loss on DDE-Induced Immune Alterations

Jeffrey Singh and Susan Viselli

Department of Biochemistry, Midwestern University, Downers Grove, Illinois

DDT (dichloro-diphenyl-trichloroethane) is an organopesticide that has been used all around the world. DDT was popularly used in the United States until 1972, when the Food and Drug Administration banned DDT as a pesticide due to its toxic effects. However, in other parts of the world such as India, China and North Korea, DDT is still being produced and used today. Even in countries like the United States where DDT was banned years ago, its long-term health effects may still be occurring today. In the body, DDT is broken down into its metabolite, DDE (dichlorodiphenyldichloroethylene). DDE is fat-soluble and therefore is present in high amounts in adipose tissue. How DDE affects the immune system is not well understood. This project was designed to better understand DDE mediated effects on the immune system, and more specifically, how a reduction in body weight may play a role in these changes. Theoretically, in mice that are fed a high-fat diet, and thus develop more adipose tissue, more DDE may be stored. If these mice are then taken off the high-fat diet and put on a regular rodent chow diet (much lower in fat), the amount of adipose tissue in their bodies will decrease over time. We hypothesized that when the high-fat diet mice switch to the regular fat diet, the DDE originally stored in this fat will be released into the blood, which may exacerbate any DDE mediated effects on the immune system. For our study, mice were fed either a high-fat diet (60% kcal from fat) or a regular rodent chow diet (10% kcal from fat) for three months. The mice then received either DDE or the cottonseed control at a dose of 200 mg/kg. After dosing, all of the mice returned to the regular rodent chow diet for an additional two months of feeding. In order to examine the effects on the immune system, mice were then sacrificed and immune cell subpopulations were quantified. Specifically, CD3+, CD4+, and CD8+ populations in the spleen and the thymus were measured. Results demonstrated that regardless of treatment, mice fed the high-fat diet had a significantly lower number of CD3+ thymocytes, which are the most mature thymocytes, compared to mice fed the regular diet (p≤.0326). In addition, this study showed that regardless of diet, treatment with DDE significantly decreases the number of T-Helper CD4+ splenocytes compared to the mice treated with cottonseed oil (p≤.0167). Interestingly, in the mice that were fed the high-fat diet, DDE significantly increased the number of Cytotoxic CD8+ splenocytes (p≤.040). Lastly, in the group of mice that received the cottonseed vehicle, the mice that were initially fed the high-fat diet displayed a trending decrease in the amount of CD8+ splenocytes (p≤.061). Therefore, the results from this study show that DDE does mediate effects on the immune system, specifically on CD3+, CD4+ and CD8+ populations, and these changes may be influenced by mobilization of DDE following weight loss.
Comparison of Substrate Specificity of *Escherichia coli* p-Aminobenzoylglutamate Hydrolase with *Pseudomonas* Carboxypeptidase G

Dejan Slavnic, OMS-II, Cassandra Larimer, and Jacalyn Green, Department of Biochemistry, CCOM, Midwestern University, 555 31st Street, Downers Grove, IL 60515

Methotrexate (MTX) is a potent chemotherapy drug used in the treatment of various cancers, rheumatoid arthritis, and psoriasis. When patients accumulate toxic levels of MTX, they are treated with intravenous Glucarpidase (carboxypeptidase G2), an enzyme isolated from *Pseudomonas*. Although efficient at cleaving MTX and aminopterin, Glucarpidase also markedly breaks down endogenous folates, which are important for human health. We compared *Escherichia coli* p-aminobenzoylglutamate hydrolase (PGH) to *Pseudomonas* Carboxypeptidase G (CPG) in enzyme assays measuring cleavage of folate, MTX, aminopterin, leucovorin (5-formyltetrahydrofolate, an alternative treatment for MTX overdose), and 5-methyltetrahydrofolate, the circulating form of folate in humans. CPG is a close relative of CPG2 that is readily available. We isolated PGH from *Escherichia coli* (E. coli) cells transformed with a plasmid which expressed high levels of PGH. We then performed kinetic assays on a spectrophotometer to study the rate of enzymatic degradation of a variety of folates and anti-folates. The rate of cleavage was monitored using wavelengths and extinction coefficients obtained from the literature. Our results indicated that the ability of PGH to cleave glutamate from MTX and aminopterin was lower than that of CPG; in addition, while assay limitations made measurement of K_m values impossible, the K_m values for PGH were much higher than those of CPG, as we were unable to saturate PGH for folate and anti-folate substrates. PGH demonstrated no ability to cleave reduced folates, in sharp contrast to CPG. In conclusion, PGH is potentially a useful enzyme in that it would preserve leucovorin and 5-methyltetrahydrofolate while cleaving MTX and aminopterin. However, due its low affinity for the substrates, PGH would need to be genetically modified to increase its efficiency before being considered for use in clinical practice.

*This research has been supported by funds from Midwestern University and R15 GM085760 from the National Institute of General Medical Sciences.*
Expression of SPATA22 in mouse models of infertility
Rachel Troester, Ashley Shah, Emily Hays, and Sophie La Salle. Midwestern University, Department of Biochemistry, Downers Grove, IL, USA.

Approximately 15% of human couples worldwide are infertile. In most cases the cause remains unknown, but meiotic failure is often part of the etiology. Meiosis is critical to the production of haploid gametes capable of supporting embryonic development. A better understanding of the genes involved in meiosis could therefore give insight into the causes of infertility and provide novel therapeutic avenues to explore. We have previously characterized the ENU-induced mouse mutation repro42, which causes both male and female infertility due to meiotic arrest. Characterization of the mutation using positional cloning and sequencing determined that repro42 was a nonsense mutation in spermatogenesis associated 22 (Spata22), an uncharacterized gene. Work conducted previously focused on phenotype analysis and expression of SPATA22 in the repro42 mouse model. To expand our understanding of the role played by this protein, we set out to characterize its expression in two other mouse models: a model carrying a different targeted mutation in Spata22 (Spata22komp), and mice deficient in the meiosis-specific DNA repair gene Dmc1, another mouse model of meiotic arrest. PCR genotyping of genomic DNA was performed to determine the genotype of mice used for experiments. Since the fertility of mice carrying the Spata22komp allele had not been previously assessed, we first set up reciprocal matings using wild-type and mutant mice of both sexes. Spata22komp mutant males never sired any litters, while mutant females never gave birth to offspring. Mating behavior was not affected in mutant mice of either sex. These preliminary results suggest that the phenotype of Spata22komp mutant mice is very similar to the one of repro42 mutant mice. Next, we assessed expression of the SPATA22 protein in whole testis protein extracts prepared from wild-type, heterozygous- and homozygous- Spata22komp males. Immunoblotting analysis allowed detection of SPATA22 in both wild-type and heterozygous testis samples, but not in homozygous mutant extracts. Finally, we wondered if expression of SPATA22 would be compromised in the absence of DMC1 (a protein involved in meiotic recombination), since mice deficient in this protein present a very similar phenotype of meiotic arrest to repro42 mutant mice. Interestingly, SPATA22 was detected in both wild-type and mutant Dmc1 testis protein extracts, suggesting that its expression does not depend on the presence of DMC1. Taken together, analysis of SPATA22 expression dynamics in other mouse models of infertility provides further insight into the function and regulation of Spata22.

This work was supported in part by startup funds provided by Midwestern University and by funds from the Office of Research and Sponsored Programs.
Alpha adrenergic receptors mediate resuscitative effect of centhaquin in hemorrhaged rats

Ensi Voshtina\textsuperscript{1}, Zhong Zhang\textsuperscript{2} and Anil Gulati\textsuperscript{2}

Chicago College of Osteopathic Medicine\textsuperscript{1} and Department of Pharmaceutical Sciences\textsuperscript{2},
Chicago College of Pharmacy, Midwestern University, Downers Grove, IL 60515

Introduction: Centhaquin is being developed as a small volume hypotensive resuscitative agent. It has significant resuscitative effect and improves the survival of hemorrhaged rats. However, its mechanism of action is not known.

Hypothesis: Centhaquin will be an effective resuscitative agent which acts through a unique mechanism of action mediated through $\alpha_2$ adrenergic receptors.

Methods: Rats were anaesthetized with urethane and the femoral vein and artery were isolated and cannulated. A pressure transducer (SPR-320) and pressure-volume (P-V) transducer (SPR-869) were placed into the femoral artery and left ventricle, respectively. P-V loop data were acquired using PowerLab 16/30 data acquisition system (AD Instruments) and analyzed using LabChart-7.00 and PVAN program (Millar Instruments). After completion of surgery, induction of hemorrhage was initiated by withdrawing blood from the right femoral artery to maintain the mean arterial pressure (MAP) at 35 mmHg for 30 minutes. Arterial blood pO\textsubscript{2}, pCO\textsubscript{2}, pH, glucose, and lactate were measured using a pH/blood gas analyzer (GEM Premier 3000). We determined the involvement of $\alpha_2$ adrenergic receptors in the resuscitative effect of centhaquin using specific $\alpha_2$ adrenergic antagonists, yohimbine and atipamezole.

Results: Hematocrit decreased by about 30 to 35\% in all the groups following hemorrhage. Centhaquin (0.05 mg/kg) reduced blood lactate, improved cardiac output and blood pressure of hemorrhaged rats. The time for blood pressure to fall back to 35 mmHg was increased by three folds in centhaquin treated rats compared to vehicle. Centhaquin significantly decreased blood lactate levels (mmol/L) from 10.1 \pm 0.7 at hemorrhage to 4.5 \pm 0.4 at 60 min following resuscitation. However, in yohimbine treated rats blood lactate levels were 10.3 \pm 1.5 at hemorrhage, and 8.4 \pm 0.8 at 60 min following resuscitation; while in atipamezole treated rats blood lactate levels were 10.8 \pm 0.4 at hemorrhage, and 7.7 \pm 1.0 at 60 min following resuscitation.

Conclusions: Centhaquin is an effective resuscitative agent and both yohimbine and atipamezole antagonized the resuscitative effect of centhaquin indicating that $\alpha_2$ adrenergic receptors are involved in the resuscitative effect of centhaquin.
Fetal Deiodinase Increases in a Rodent Model of Myocardial Infarction

Rohit Vuppuluri, Laura Bach, Robert Murphy, and Kyle K. Henderson
Department of Physiology, Midwestern University, Downers Grove, Illinois

Rationale: Thyroid hormone (T3) has been shown to play a critical role in myocardial vascular homeostasis. Importantly, patients with congestive heart failure frequently have reduced serum T3 concentrations which may induce vascular rarefaction and/or limit angiogenesis during left ventricular remodeling. One possible mechanism for reducing T3 concentration is the reactivation of Type III deiodinase. Type III deiodinase (D3) is a fetal enzyme that inactivates thyroxine as well as T3.

Objective: Determine whether enzymes regulating myocardial thyroid hormone concentration are altered after a myocardial infarction.

Hypothesis: Myocardial D3 protein levels will increase in a rodent model of myocardial infarction, and immediate T3 supplementation will augment angiogenesis and adaptive left ventricular remodeling.

Methods and Results: The left anterior descending coronary artery was ligated in adult male Sprague Dawley rats with controls undergoing identical procedures without ligation. Osmotic mini-pumps were immediately implanted subcutaneously to deliver saline or T3 (10ug/kg/day). One week post-surgery, hearts were removed and subdivided into ischemic, border-zone, and non-infarcted/posterior wall. Results show that Type II deiodinase (D2) protein levels were increased in the ischemic zone of infarcted hearts (D2 is normally expressed in the heart and converts thyroxine into T3). D3 protein levels were also increased in the ischemic zone of MI-hearts. Importantly, the D2 to D3 ratio was reduced by ~60% suggesting T3 concentrations could be reduced in the ischemic regions of the heart. Additionally, D3 dimers were only present in the ischemic region of the MI heart. Because dimerization is thought to be required for enzymatic activity, ischemic areas of the heart may have regional hypothyroidism. Overall, these findings support the hypothesis that myocardial D3 protein levels are increased 7-days after a myocardial infarction.

Conclusion: The increase in dimerized D3 protein levels in the ischemic region of the heart may reduce local T3 concentrations and contribute to mal-adaptive left ventricular remodeling.

This research was supported by the American Heart Association: 10SDG2640219
Effect of Insulin on *Staphylococcus aureus* Growth and Biofilm Formation
Cassandra Wasson, OMS2 and Balbina Plotkin, Ph.D.
*Department of Microbiology and Immunology, Midwestern University, Downers Grove*

**Hypothesis.** Biofilm formation by *Staphylococcus aureus* is modulated by physiological conditions present in the host including hormone levels and fermentable substrates.

**Overview.** The ability by *S. aureus* to form biofilms is essential in its establishment and maintenance of infectious processes, e.g. foot ulcers in individuals with type 2 diabetes. *S. aureus* growth and biofilm formation during the course of infection in individuals with uncontrolled type 2 diabetes occurs in the presence of insulin and glucose. The focus of this study was to determine the effects of insulin and/or glucose on *S. aureus* growth and biofilm formation.

**Materials and Methods.** *S. aureus* ATCC25923 and global regulator deletion strains *agr*, *sarA* and *agr*/*sarA* as well as their parent strain 8325-4 were tested. Strains were grown in Luria-Broth (LB) with and without glucose (0.1% and 0.2%) and/or insulin (2 µU/mL, 20 µU/mL, and 200 µU/mL). Various media combinations, inoculated with 10^5 CFU/mL, were placed in 100 well honeycomb plates (200µl/well). Growth curves were measured using the Bioscreen C (GrowthCurves, Inc) (24hr, 37°C, continuous shaking). Biofilm levels, after growth, were determined by measuring the amount of crystal violet staining (Abs580nm).

**Results:** Overall, addition of glucose (0.1% and 0.2%) resulted in monophasic growth as compared to biphasic growth in medium with and without insulin, regardless of strain tested. In addition, glucose, regardless of concentration tested, suppressed the second phase of growth so that the total levels of growth in the absence of glucose were approximately twice that of LB with glucose. Although insulin but had no effect on rate of growth or total amount of growth, for the wild type ATCC isolate the presence of 20 µU/ml and 200 µU/ml insulin increased biofilm formation as compared to medium alone. A similar pattern was observed for strain 8325-4 with respect to insulin effects on growth. However, insulin enhanced biofilm formation in the presence and absence of glucose (0.2%) in a manner that was concentration specific (20 µU/ml and 200 µU/ml insulin, respectively). In the absence of *sarA* and *agr*, global regulator genes, there was a marked suppression of biofilm levels in the presence of insulin as compared to media with glucose alone, regardless of sugar and hormone concentrations tested.

**Conclusion:** These findings show that insulin modulates the response of *S. aureus* to glucose. In addition, biofilm formation appears to be regulated, in part, by *sarA* and *agr*. Taken together, these findings indicate that insulin is an interkingdom quorum signaling compound in *S. aureus* that plays a role in modulating biofilm formation, an essential component in pathogenesis.

*Cassandra Wasson was supported by the Midwestern University Summer Fellowship Program. Balbina J. Plotkin was supported by Midwestern University intramural funds through ORSP.*
Low Concentrations of Dimethyl Sulfoxide stimulate MAP Kinases in Rheumatoid Arthritis Fibroblast-Like Synoviocyte: Inhibition by Manzamine A.

Nicholas Wilczynski, Karolina Klosowska and James M. Woods

Midwestern University, Chicago College of Osteopathic Medicine, Downers Grove, IL 60515

INTRODUCTION: Many *in vitro* studies have used 0.1% dimethyl sulfoxide (DMSO) as a vehicle control, due to its solubility properties. Previous studies in our lab utilized 0.1% DMSO to dissolve Manzamine A (MZA), an alkaloid extracted from a marine sponge, and suggested that this popular concentration of vehicle control may stimulate the phosphorylation of mitogen-activated protein (MAP) kinases. Here, we studied the effect of 0.1% DMSO on phosphorylation of Erk 1/2 and c-Jun N-terminal kinase (JNK) in rheumatoid arthritis (RA) fibroblast-like synoviocytes (FLS), and determined whether MZA could inhibit the effects of DMSO.

METHODS: Cell culture, Western blotting and gel electrophoresis were used in conjunction with phospho-specific antibodies.

RESULTS: 0.1% DMSO consistently induced phosphorylation of Erk 1/2 and JNK. However, MZA’s ability to inhibit DMSO-induced MAP kinase phosphorylation varied with RA FLS derived from different patients. CONCLUSIONS: Our results call into question the wide-spread use of 0.1% DMSO as a vehicle control for *in vitro* studies. While MZA appears capable of inhibiting DMSO-induced MAP kinase phosphorylation in RA FLS from some patients, its overall effect was variable.
Telomerase associated immortalization of primary cells affects p53 function.

Dara Wise², Oliver Couture¹, and Nalini Chandar¹,²

Department of Biochemistry¹, Chicago College of Osteopathic Medicine², Midwestern University, Downers Grove, Illinois

Immortalization with human telomerase reverse transcriptase (hTERT) is commonly used as a way of extending the life span of primary cells and is considered superior to the use of viruses. Even though a relationship exists between p53 and telomere erosion the effect of immortalization on p53 activity has not been investigated. Our lab has shown a requirement of p53 for advanced osteoblast differentiation. In this study we characterized two telomerase immortalized cell lines to study the differentiation capacity of these cells towards osteoblasts. In one case, a mouse osteoblast cell line with and without connexin 43 was investigated for its p53 status and differentiation capability. In the second case, a telomerase immortalized human mesenchymal cell line was induced to differentiate into myoblasts, osteoblasts, or adipocytes, and their gene expression profiles were studied. In the case of the mouse osteoblasts we found that an increased level of hTERT activity was associated with an increase in p53 levels. This was confirmed both at the transcript level as well as functionally using a luciferase assay. Regarding the human mesenchymal line, we found the cells were capable of differentiation to three different lineages. Their gene expression profiles were specific for their cell type. These studies will be discussed in relation to p53 and osteoblast specific differentiation.

This research was supported by the Kenneth A. Suarez Summer Research Program.
Title: Assessing the clinical virulence of KPC (+) Klebsiella pneumoniae blood stream infections at a large tertiary academic hospital

M. Renee Advincula, Milena McLaughlin, Michael Malczynski, Chao Qi, Marc H. Scheetz
Department of Pharmacy Practice, Chicago College of Pharmacy

Background: Klebsiella pneumoniae producing carbapenemase (KPC) Klebsiella pneumoniae has become an increasing problem in hospitals and may cause poor patient outcomes. There is controversy in the literature regarding the reasons for these poor patient outcomes. Variables such as time to active therapy, resistance of the organism itself and patient comorbidities have been implicated. The purpose of this study is to determine the clinical virulence of KPC (+) Klebsiella pneumoniae blood stream infections by comparing KPC (+) to KPC (-) infections while controlling for confounding variables with standard clinical data modeling techniques.

Methods: Men and women at least 18 years old with a blood stream infection will be included in the study if they have at least one blood culture confirming Klebsiella pneumoniae from March 2010 through December 2011. KPC positive or negative status will be verified via PCR with common primers. Only the first bacteremia per patient will be included in the study. KPC (+) patients will be matched on a 1:4 basis with KPC (-) patients. Pertinent patient and clinical variables will be collected. Variables will be analyzed with Stata 11.1. Continuous variables will be assessed with Student’s t-test and Wilcoxon Rank Sum tests where appropriate. Nominal variables will be assessed with Chi-square and Fisher’s Exact tests where appropriate.

Results and Conclusions: Do not fill out per abstract guidelines.

School / Affiliation for all authors involved:

Milena: Midwestern University / Northwestern Memorial Hospital (milgriff@nmh.org)
Marc: Midwestern University / Northwestern Memorial Hospital (mscheetz@nmh.org)
Chao: Northwestern Memorial Hospital / Northwestern University (cqi451@northwestern.edu)
Mike: Northwestern Memorial Hospital (mmalczyn@nmh.org)

Conflicts of Interest: No relevant conflicts of interest from any of the authors exists

Acknowledgements: This research was made possible through a Midwestern University Chicago College of Pharmacy summer research grant.
Meaningful medication reconciliation: the single source of truth

Josephine Aranda1, Catherine Palladino2, Aamna Khan1, Ryan LeWan1, Weronika Flis1, Helga Brake, PharmD3, and Kristine Gleason, RPh, MPH3

Midwestern University1, Downers Grove, Illinois, University of Illinois at Chicago2, Chicago, Illinois, and Northwestern Memorial Hospital3, Chicago, Illinois

Medication reconciliation, the process of reviewing patient medication lists at every care transition point, has been recognized as a national patient safety goal by The Joint Commission. To fulfill this goal and meet Medicare and Medicaid Electronic Medical Record (EMR) Meaningful Use incentive programs, hospitals must thoughtfully integrate the medication reconciliation process into the EMR. The purpose of this quality improvement pilot study was to identify the types and frequencies of unintended discrepancies found at medication history, admission and discharge reconciliations, and to evaluate the effectiveness of using a standardized medication reconciliation tool versus free text notes in the EMR. This pilot study at Northwestern Memorial Hospital in Chicago, Illinois was approved by the hospital’s Medication Safety Subcommittee of the Pharmacy and Therapeutics Committee as a quality improvement project. It involved medication histories from patient interviews collected by student pharmacists (considered gold standard for this study) the day after patient admission. Patient selection included a convenience sample of hospitalized medical and surgical patients, and excluded patients in the intensive care, obstetrics, and psychiatry units. The patient’s home medication list obtained by student pharmacist interview was compared to the home medication list documented in the EMR medication reconciliation tool and in the physician’s history and physical note documented on admission. Next, the patient’s home medication list was compared to the admission medication orders. Lastly, the patient’s final inpatient medication orders on day of discharge were compared to the home medication lists in both the EMR medication reconciliation tool and in the patient’s discharge instructions. Unintended discrepancies were identified and collectively evaluated during the admission and discharge care transitions described above. A total of 67 patients were reviewed to have a total of 376 unintended discrepancies: 230 during the medication history, 50 at admission, and 96 at discharge. Throughout all three reconciliation stages, omission was the most common unintended discrepancy. The drug class most involved with discrepancies was cardiovascular agents. Unintended discrepancies occurred more frequently with incomplete use of the standardized medication reconciliation tool at admission and discharge, but occurred less during medication history. More thorough efforts with medication reconciliation must be made at all three care transition stages to prevent omissions and other unintended medication discrepancies. Utilization of a standardized medication reconciliation tool may facilitate this process and reduce the frequency of discrepancies.

This research was supported in part by Federal Work Study funds.
Obesity: High school students’ knowledge levels and opinions

Joshua Artlip, Thomas Dorn, Loreto Lobosco, Veeral Vyas, and Thomas Reutzel

*Department of Pharmacy Practice, Midwestern University Chicago College of Pharmacy, Downers Grove, Illinois*

Obesity is one of the leading causes of death in the world, more so than starvation. Obese youth are at a much greater risk for having preventable health conditions as they age. Some of these include heart disease, stroke, type 2 diabetes, and several types of cancer. The objective of this research was to assess high school student’s knowledge levels and opinions related to the obesity epidemic as well as how this epidemic affects their daily life. Between October 1, 2012, and February 28, 2013, questionnaires were distributed to four local area high schools (a convenience sample). The survey was reviewed for face validity by College of Pharmacy social science and clinical faculty members. This research was approved by the Midwestern University Institutional Review Board, and school names are not included in the results (rather, the terms, School 1, 2, 3, and 4, are used). 1490 usable surveys were obtained. The mean age of subjects was 15 years old, (range = 13-19). Eighty-four percent of subjects said they received obesity information from the media, 57% from their teachers, 50% from health care practitioner(s), 45% from family, and 35% of subjects viewed their friends as a source of obesity information. The vast majority of subjects (78.7%) reported knowing an obese person. The mean score on a 20-item knowledge test regarding the obesity epidemic was 50% (range = 0%-90%). Caucasian and Asian populations scored higher on the knowledge scores than did other races. Analysis of variance and post hoc tests also revealed a significant difference in obesity knowledge across grade levels. Freshman scored significantly less on the knowledge test compared to sophomores, juniors and seniors. School 4 students scored higher on the knowledge test than students from Schools 1, 2, and 3. Opinions on the subject varied widely. For example, 54.7% of subjects agreed that they would not date an obese person, while 72.6% of subjects would take the opinions of an obese person seriously. Furthermore, 44% of subjects do not feel sorry for obese individuals, and 45% said they would not judge an obese person. These results suggest that more education on the current obesity epidemic is needed. The media are raising awareness, but health care providers must take greater ownership of this problem. Based on knowledge and opinion results, there is a need for pharmacists and other providers to educate their patients about the obesity epidemic and to have conversations with patients as well as the community regarding how this epidemic can be ameliorated.

*This research was not supported by any intramural or extramural funding program.*
Pharmacists are one of the most accessible health care providers and often field a variety of questions about dietary supplements. With the knowledge that much of the information available to the public may not be accurate or easily interpreted, there is a growing need for pharmacists to have an up-to-date toolbox of information related to dietary supplements and to provide patient education in a manner that helps to promote the development of a quality healthcare provider-patient relationship. This study looks to measure the progression of student knowledge acquisition and self-efficacy as it specifically relates to Vitamins A, D, and K and the mineral calcium. The evaluation will be conducted within the elective course, Vitamins, Mineral and Nutritional Support. A pre/post survey methodology was used to assess the knowledge and self-efficacy levels of pharmacy students as they progress in the elective course. Knowledge and self-efficacy items were developed, as well as items to collect demographic information (age, sex, race). Both general knowledge questions, as well as questions that required more analysis, synthesis, and evaluation skills were utilized. The study population is comprised of thirty-nine at Midwestern University Chicago College of Pharmacy Class of 2014 students who were enrolled in this elective course in Fall 2012. Evaluation of the knowledge-based questions demonstrates a general improvement from the pre- to post-elective surveys. The greatest increase in knowledge occurred for Vitamin A. Currently statistical analysis is being performed on the self-efficacy portion of the instrument. The results of this study could be used as measure of course effectiveness and will serve as the pilot study for a longitudinal study that evaluates how well the current PharmD. curriculum prepares student pharmacists to counsel patients as it relates to vitamins A, D and K and the mineral calcium in their future practice of pharmacy.
The knowledge levels and attitudes of pharmacy students regarding immunizations

Alexis Bonnema, Courtney Linhart, and Thomas Reutzel

Department of Pharmacy Practice, Midwestern University Chicago College of Pharmacy, Downers Grove, Illinois

Currently, a clear understanding of pharmacy students’ attitudes and knowledge concerning immunizations does not exist. Pharmacists as immunizers is a newer concept that involves many unknowns, including where pharmacist involvement will advance to in the future. The objective of this research is to assess the knowledge levels and opinions of pharmacy students regarding immunizations, including views of the value of immunizations and willingness and confidence to administer immunizations. Questionnaires were administered to all students enrolled in the College of Pharmacy. They included demographic variables, a 17-item knowledge test, and ten opinion statements. P was set a priori at ≤ .05. The research was approved by the University’s Institutional Review Board. 608 of 837 students (73%) returned useable surveys. The mean score on the 17-item knowledge test was 52%. Over 95% of these students believe that the benefits of immunization outweigh the risks. Over 85% would be comfortable administering immunizations, and 72% think pharmacists should be able to give immunizations without a standing order or prescription. Upperclassmen scored higher on the knowledge test than underclassmen (65% and 45%, respectively). Those with pharmacy work experience were more knowledgeable than those without (53% versus 46%). Those that received immunization training from the College (31%) scored higher than those that did not (66% and 45%).

Upperclassmen are more comfortable administering immunizations. These future pharmacists have somewhat low levels of knowledge regarding immunizations. Positively, those that underwent training scored 20% higher than those that did not. These students felt positive about the value of immunizations and confident in their ability to administer them. College administrators should consider requiring a comprehensive immunization program for their students, including both classroom and hands-on components. Policy makers at the professional and organizational levels could seek to expand the role of pharmacists in providing immunizations.

This research was not supported by any intramural or extramural funding program.
Title: A Survey of Australian Pharmacists on Job Responsibilities and Satisfaction

Authors: Kristen Dabkey\textsuperscript{1}, Dr. Jennifer Phillips, PharmD\textsuperscript{2}, Dr. Sally Arif, PharmD\textsuperscript{2}

Objectives: The primary purpose of this survey was to categorize the types of responsibilities of pharmacists practicing in a large 600-bed teaching hospital in Perth, Australia and determine overall job satisfaction as well as identify factors that contribute most to overall job satisfaction. Opinions on transition to a doctor of pharmacy program were also assessed.

Methods: Survey questions were adapted from a previous survey of US pharmacists on employment satisfaction. An anonymous survey was constructed using SurveyMonkey, which was distributed electronically to 59 pharmacists employed at Sir Charles Gairdner Hospital (SCGH) in Perth, Australia in October 2012. Data collection lasted for 2 months and 2 reminders were sent. Pharmacists were asked to categorize their level of satisfaction with their current job. In addition, they were asked to identify how their time was divided among different tasks and how they would prefer to have their time divided among these tasks. Pharmacists were also asked to identify their level of satisfaction with a number of job-related factors.

Results: A total of 13 pharmacists responded to this survey, which represented a response rate of 22%. All respondents were full-time and had been at SCGH for a mean of 4 years. Most pharmacists (75\%, n=9) indicated a majority of their time was spent on the inpatient ward. Bachelor of Pharmacy degree was the most common type of education (87.5\%, n=7). The most significant difference between time desired and actual time spent was in reference to drug use management: pharmacists wanted more time spent than how much time they actually had (38.89\% vs. 48\%). Additionally, pharmacists wished to spend less time dispensing medications (24.6\% vs. 18.13\%) and doing activities that were classified as ‘other’ than consultation, drug use management, business management or medication dispensing (15\% vs. 8.75\%). Pharmacists were most satisfied with the following job-related factors: autonomy, benefits, level of clinical responsibilities, level of dispensing responsibilities, level of patient care responsibilities, and workload. Pharmacists were the least satisfied with the following job-related factors: opportunity for advancement/promotion, recognition of work, and utilization of skills.

Conclusions: Overall, pharmacists in Australia were satisfied with their current job responsibilities, but wished to spend more time with drug use management and less time dispensing medications. Promotion or advancement opportunities, increased recognition for work, and a change in job responsibilities that involves more utilization of skills may increase the level of job satisfaction even further.
Purpose: This study evaluated if a pharmacy student led pilot program would significantly improve the medication reconciliation process at Copley Memorial Hospital. This study aimed to increase continuity of care, interdisciplinary teamwork and the pharmacy’s role in direct patient care.

Methods: Fourth year pharmacy students performed a stepwise medication reconciliation pilot based in the emergency department (ED). Phase I compared medication lists generated by pharmacy students to those of ED nursing staff. Phase II added a discharge counseling program. Phase III combined phases I and II into one role. Surveys measured patient and staff satisfaction with the program. Outcome measures were: completeness of patients’ home medication lists, accuracy of medications upon discharge and satisfaction of staff and patients.

Results: Student pharmacists recorded 57.45% more medications per patient list when compared to nurses (7.4 vs. 4.7, p<0.0001). Medication lists completed by students included more over-the-counter (OTC) medication usage (average OTC medications per list 2.47 vs. 1.36, p=0.04). ED and inpatient nurses reported time savings of 35 and 42 minutes respectively when pharmacy students completed initial medication histories. Physicians and nurses surveyed agreed that pharmacists are the most qualified to complete home medication lists and to perform medication discharge counseling (77.5% and 82.5% respectively, n=40). Patient satisfaction scores for medication discharge counseling by pharmacy were 4.54 out of 5.0.

Conclusion: This pilot program improved patient transition through the hospital and at discharge. The program created a pharmacy driven role to provide optimal patient care through complete medication reconciliation.

This research was supported by Rush-Copley Memorial Hospital and Midwestern University Chicago College of Pharmacy.
The Impact of an Educational Program on Pharmacist Behaviors, Confidence and Knowledge of Probiotic Recommendations in a Grocery Store Chain Pharmacy

Akanksha Dudeja, PharmD1,2, Sonali Kshatriya, PharmD1, Klodiana Myftari, PharmD1, Susan R. Winkler, PharmD, BCPS2, Ana Quiñones-Boex, Ph.D.2, Thomas J. Reutzel, Ph.D.2

Dominick’s Pharmacy, Oak Brook, IL1, Department of Pharmacy Practice2, Midwestern University, Downers Grove, Illinois

Objectives: The primary aim of this study is to assess the impact of an educational program on pharmacist behaviors, confidence, and knowledge of probiotic recommendations. Secondary objectives include determining the factors pharmacists perceive as barriers to making probiotic recommendations and evaluating whether the measured outcomes vary by pharmacist demographic characteristics.

Methods: All pharmacists employed within a grocery store chain pharmacy (n=182) were invited to attend a live education session on the subject of probiotics. Those who attended were given an optional, anonymous, pre-survey to complete prior to the session. The pre-survey was designed to assess baseline knowledge, confidence, and behaviors as related to probiotic recommendations. The education session focused on the roles of normal gut flora in health maintenance, defining the term "probiotic", describing how probiotics can be used in therapy, and learning how to assist patients in selecting an appropriate probiotic product.

After the live education session, subjects received a written educational supplement to utilize at their respective pharmacies. The supplement served as a practical reference tool to reinforce knowledge gained at the live session. One month after the session, participating subjects received an electronic post-survey. The post-survey evaluated whether there was a difference in pharmacist knowledge and whether the program had an impact on their confidence and behaviors related to probiotic recommendations. Additionally, it allowed subjects to state their satisfaction with the program and provide feedback for future improvements. The data from the pre- and post-surveys was linked based on an unidentifiable code number and analyzed using SPSS version 19.0.

Results: Of the 189 pharmacists invited, 29 participants completed the pre-survey. Of the 29 study participants, 19 completed the post-survey. After the completion of the probiotic educational program, an increase was seen in the number of probiotic recommendations made per week, the range of patient populations probiotics were recommended to, and pharmacist familiarity with probiotic products currently on the market. A significant improvement was seen in pharmacists’ knowledge of probiotic recommendations (p=0.017) as well as in their confidence to provide evidence based probiotic recommendations and compare and contrast different products on the market (p<0.05).

This research was supported in part by American Lifeline Inc.
Differential effects of bortezomib on osteoblastic and osteosarcoma cell lines suggest resistance may be through anti-apoptotic Akt pathway.

Jay Fajiculay¹, B.S.; Zane Elfessi¹, B.S.; Gabriel Park¹, B.A., B.S.; Dr. Medha Joshi¹, Ph.D.; Dr. Annette Gilchrist¹, Ph.D.

Chicago College of Pharmacy¹, Midwestern University, Downers Grove, Illinois

Bortezomib (Velcade) is a proteasome inhibitor that has been clinically approved for the treatment of multiple myeloma (MM). Osteosarcomas are primary bone tumors of osteoblastic origin. These tumors, which primarily affect adolescent patients, are highly aggressive and metastatic. A recent report by Shapovalov et al. (Int J Cancer. 2010; 127:67-76) demonstrated that bortezomib selectively suppressed growth in two human osteosarcoma cell lines, namely 143B and OS187, while having no inhibitory effect on the growth of human fetal osteoblasts transformed with SV40 T antigen (hFOB 1.19). With this information in hand, we tested the effects of bortezomib using three cell lines; MC3T3, an osteoblast precursor cell line derived from mouse calvaria; ROS 17/2.8, a rat osteosarcoma cell line; and U2OS, a human osteosarcoma cell line. We differentiated the cell lines using 50 mg/ml ascorbic acid and 10 mM beta-glycerol phosphate. Initial studies measured cellular metabolism using AlamarBlue. Then, we examined cellular signaling components and determined if changes correlated with bortezomib sensitivity. For these experiments we have focused our attention on AKT, JNK, and EGR-1.

This work was supported through an internal CCP research grant (MJ), KAS student research award (GP), a Student Council Travel Award (ZE), and a Student Leadership & Research Award (ZE).
Indications and outcomes of epinephrine auto-injector use at a major urban hospital

Weronika M. Flis, PharmD Candidate\textsuperscript{1}, Rachel G. Ralph, PharmD Candidate\textsuperscript{2}, Michael A. Fotis, BSPharm\textsuperscript{3}, William Budris, BSPharm\textsuperscript{4}, Paul A. Greenberger, MD\textsuperscript{5}

\textsuperscript{1}Midwestern University; Chicago College of Pharmacy, \textsuperscript{2}University of Illinois at Chicago; College of Pharmacy, \textsuperscript{3}Northwestern University; Feinberg School of Medicine, \textsuperscript{4}Drug Information Department; Northwestern Memorial Hospital, \textsuperscript{5}Division of Allergy-Immunology, Northwestern University Feinberg School of Medicine

Epinephrine is a sympathomimetic drug that stimulates alpha and beta-adrenergic receptors and inhibits inflammatory mediator release in mast cells. Epinephrine is used intramuscularly in the treatment of allergic reactions - including anaphylaxis. EpiPen and EpiPen Jr. are auto-injection epinephrine pens designed to be safely used by patients experiencing an allergic reaction. They have been adopted by Northwestern Memorial Hospital (NMH) for staff and patient use in an effort to minimize needle stick injuries. The purpose of this retrospective review was to determine the indications, asthma, allergy history and outcomes in patients treated with EpiPen or EpiPen Jr.

This investigation was approved by the Northwestern University Institutional Review Board. Data was collected from patient electronic medical records, decision support records and billing records for a 3-month period. Patients were included in the “intent-to-treat” group if they either received EpiPen or EpiPen Jr. or were considered appropriate candidates for such treatment by the clinician, as evidenced by provision of EpiPen to bedside or to take home.

Of the 62 “intent-to-treat” patients, 44 actually received epinephrine either in the hospital or shortly prior to arriving in the emergency department (ED). The remaining 18 received EpiPen to bedside or to take home. Forty-seven (76\%) of the “intent-to-treat” patients had an allergic reaction or anaphylaxis, 41 (66\%) had a history of at least one allergy and 13 patients (21\%) had a history of asthma. Overall, 56 patients of the 62 (90\%) clinically improved, either with or without epinephrine. The subset of 44 patients who received an injection of the drug was used to determine admission rates (15 patients – 33\%), intubation rates (3 patients – 7\%) and adverse events (1 patient – 2\%). No mortalities were observed.

Overall, EpiPen and EpiPen Jr. use at the hospital was found to be clinically successful, in agreement with FDA indications and accepted clinical practice, with few adverse events and moderate admission and intubation rates. The findings of this Drug Utilization Evaluation (DUE) were reported at a NMH Pharmacy and Therapeutics Committee meeting.
Adherence to empiric guidelines for the treatment of community acquired pneumonia in a hospital setting

Mallory A. Fowler, PharmD Candidate¹, Jae Chang, PharmD Candidate¹, Jean A. Patel PharmD²,³, Michael Postelnick RPh²,³

¹Midwestern University, Downers Grove, IL, ²Department of Pharmacy, Northwestern Memorial Hospital, Chicago, Illinois, ³Department of Medical Education, Northwestern University Feinberg School of Medicine, Chicago, Illinois.

Despite advancements in antimicrobial agents, community acquired pneumonia (CAP) remains one of the top ten causes of death. In 2007, the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) issued guidelines on the management of CAP in attempt to decrease mortality. In accordance with these guidelines, Northwestern Memorial Hospital’s (NMH) empiric treatment of CAP includes ceftriaxone plus azithromycin or moxifloxacin for non-intensive care unit (ICU) patients and ceftriaxone plus moxifloxacin for ICU patients. The purpose of this study was to determine whether the treatment of patients with CAP at NMH was in compliance with empiric guidelines. This investigation was approved by the Northwestern University Institutional Review Board. All hospital admissions with an indication of CAP during the month of October of 2011 were studied. Information regarding antibiotic administration, microbial cultures, location of stay, and length of stay were collected retrospectively from electronic medical records. Patients were stratified based on the growth of microbial cultures and admission to the ICU. Treatment was considered to be outside guidelines if any of the recommended antibiotics were not given or if any additional antibiotics were administered. Of the 229 patients with a CAP indication, 51 had positive respiratory tract microbial cultures and were subsequently given pathogen directed therapy. As for those with negative cultures, 31 patients were admitted to the ICU during their stay while 147 had non-ICU stays. It was found that the treatment regimen for 55 of the non-ICU patients with negative cultures did not follow empiric guidelines. This reflects a 37.4 percent deviation from treatment guidelines. The IDSA/ATS guidelines state that deviation from recommended treatment should be expected in approximately 5 to 20 percent of cases and should be noted accordingly in patient medical records. At 37.4 percent, adherence to the guidelines at NMH is not in-line with IDSA/ATS expectations.
Development of a Health and Wellness Promoters Program for Secondary Schools
Facilitated by PharmD Students

Authors: Amina Ghalyoun‡, Ray WangΩ, Annette GilchristΦ

‡Student at Chicago College of Pharmacy, Midwestern University
ΦAssistant Professor, Department of Pharmaceutical Sciences, Midwestern University
ΩProgram Director, Chicago Area Schweitzer Fellows Program, Health and Medicine Policy Research Group

Objectives/Intent:
Through the Schweitzer Fellows program, a Health and Wellness program (HWP) was initiated in 2012 at the Young Women’s Leadership Charter School in Chicago. The objectives were to increase awareness and knowledge of chronic disease states; improve health literacy, and encourage students to become health prevention advocates within their communities.

Methods/Process:
Students met bi-weekly to attend lectures, watch pertinent movies, discuss health topics, and partake in activities that reinforced new skills. Concise lectures were provided by a pharmacy student facilitator. Information was then “relayed” by the students to their peers through “mini talks” during lunch or class time thus empowering them to serve as educators. Additionally, HWP hosted community events such as a “Pink Potluck” dinner and encouraged flu vaccination through education and incentives (a raffle). Finally, HWP students created a health blog to serve as an ongoing method of communication within the school community and help in expanding the program to neighboring schools.

Results
Several students became actively engaged and dedicated members of HWP, including adoption of healthier habits. The approach fostered leadership in both the pharmacy students and secondary students that participated. Several major public health issues (long term implications of obesity & smoking cessation, advantages to preventative care such as breast cancer screenings and vaccinations, misuse of OTC medications, etc) were addressed. In addition to pharmacy students developing their communication and health promotion skills, HWP students report they have shared their health knowledge with family and friends, and evaluations demonstrate they retained the subject matter.
HPV and HPV vaccines: The knowledge levels, opinions, and behavior of parents

Marlee Grabiel, B.S.¹, Thomas Reutzel, Ph.D.¹, Sheila Wang, Pharm.D.¹, Rochelle Rubin, Pharm.D.², Vinvia Leung, B.S.¹, Adrienne Ordonez¹, Maggie Wong¹, and Emily Jordan, M.A.³

Midwestern University Chicago College of Pharmacy¹, The Brooklyn Hospital Center², The University of Illinois at Chicago³

An estimated 20 million men and women are infected with the human papillomavirus (HPV). The numerous strains of HPV are capable of causing detrimental diseases such as cervical cancer, genital warts, and anal cancer. Currently, there are two vaccines (Gardasil® and Cervarix®) available as tools to decrease the incidence of HPV infection. However, controversy surrounds these vaccinations due to perceptions regarding side effects and concerns about implications for early sexual activity in children. The objectives of this research were to measure parent knowledge levels and opinions related to the human papillomavirus (HPV) and the two vaccines used to prevent it as well as to measure parent behavior in terms of whether or not to have their children vaccinated. Between June 19, 2012, and August 24, 2012, questionnaires were distributed to parents while waiting for their child to see their pediatrician at a local group practice. The survey was reviewed for face validity by College of Pharmacy social science and clinical faculty members, and an earlier version of it had been used successfully in a published study of biomedical students’ knowledge of and attitudes toward the HPV vaccine. 129 usable surveys were obtained. 48.1% of subjects said they learned about the HPV vaccines from the media, while 47.3% identified health care practitioner(s) as a source of knowledge. The mean score on a 20-item knowledge test regarding the infection and vaccines was 36% (range = 0%-80%). Opinions on the subject varied widely. For example, 22.4% of subjects agreed that schools should require that students be vaccinated before enrolling, while 3.2% agreed that vaccination causes patients to become sexually active. Subjects reported vaccination status for 253 children (mean age=13) as follows: 33% vaccinated; 28% not vaccinated but will be; 11% will never be vaccinated; and 28% not decided. These results are somewhat encouraging, because many parents are hearing about the vaccines from their providers. Although not an equally valid source, the media are also raising awareness. Based on the knowledge and opinion results of this study, though, there is a need for pharmacists and other providers to educate their patients about the vaccines and the virus and to converse with them regarding the moral and psychological implications of vaccination. Still, over half (61%) of these subjects had or plan to have their children vaccinated.

This research was supported by a Pilot Grant from the Midwestern University Chicago College of Pharmacy Research Grant Program funded by the Office of Research and Sponsored Programs (ORSP). Ms. Grabiel’s work was supported by a Chicago College of Pharmacy Student Research Award.
S Sam, J Clark, A Greenberg, C Sincak (Department of Pharmacy Practice), Zakir Shaikh, Ed Dominguez. Relationship between varying daptomycin MICs and outcomes in enterococcal bacteremia.

Abstract text:
**Background:** In vitro studies have demonstrated that *Enterococcus sp.* generally exhibit higher daptomycin (DAP) minimum inhibitory concentrations (MIC) than *Staphylococcus sp.* and *Streptococcus sp.* The purpose of this study is to evaluate the relationship between varying susceptible DAP MICs and treatment outcomes with standard dosing regimens. **Methods:** A retrospective review was conducted on patients treated ≥ 48 hours with DAP for enterococcal bacteremia from 2008-2011. Data was obtained and analyzed to evaluate clinical and microbiological outcomes between varying susceptible DAP MICs, time to microbiological cure, length of hospital stay, and incidence of elevated creatinine kinase. **Results:** Seventeen patients were evaluated for DAP outcome. Fifty-three percent of the patients were male with a median age of 62 years (range 36-92). Risk factors included indwelling catheters (82%), immunosuppression (65%), diabetes (53%), and renal failure (29%). Mean DAP dose was 5.9 mg/kg (4.4-7.7) and was given for a mean duration of 11.7 days (2-10). *Enterococcus sp.* isolated include *E. faecium* (47%), *E. faecalis* (41%), and *E. durans/hirae* (12%) and 65% of the isolates were vancomycin-resistant enterococcus (VRE). Overall, patients treated with DAP were found to have a microbiologic success rate of 88% (15/17) and a clinical cure rate of 41% (7/17). When stratified by DAP MIC, patients with MIC ≤2 (n=13) compared to patients with MIC >2 and ≤4 (n=4) had higher clinical (86% vs 14%) and microbiological (87% vs 13%) cure rates. Mean DAP dose and time to microbiologic cure were similar between the MIC groups, but length of hospital stay was slightly longer in the MIC ≤2 group (27 vs 13 days). CKP elevation occurred in only 2 patients (12%) both in the MIC ≤2 group with only 1 patient requiring discontinuation of DAP. The all-cause mortality rate was 18% (n=3). **Conclusions:** Enterococcal bacteremias with MIC >2 and ≤4 treated with an average DAP dose of 6 mg/kg appeared to be associated with worse clinical and microbiological outcomes compared to bacteremias with MIC ≤2. However, larger prospective studies are warranted to further characterize this relationship.

Authors
Sharon Sam, PharmD1*
Jessica Clark, PharmD3
Allyson Greenberg (PharmD Candidate 2013)2
Carrie A Sincak, PharmD, BCPS1,2
Zakir Shaikh, MD, MPH, FIDSA, FSHEA3
Ed Dominguez, MD3
* Presenting author

Affiliation:
1. Loyola University Medical Center, Maywood, Illinois
2. Midwestern University Chicago College of Pharmacy, Downers Grove, Illinois
3. Methodist Dallas Medical Center, Dallas, Texas
Title: Analysis of the completeness and accuracy of dietary supplement information in Wikipedia

Authors:
Connie Lam, PharmD Candidate
Jen Phillips, PharmD, BCPS
Lisa Mackowski, PharmD

Purpose: There is an increase in the number of people using dietary supplements. Since these products are not regulated and are available without a prescription, it is important for consumers to understand where and how to obtain reliable and accurate information about them. Many consumers look to online sources for information on medications and dietary supplements. Wikipedia is a popular Internet website that often shows up as one of the top search engine results when searching for dietary supplements. Thus, it is important to determine the completeness and accuracy of dietary supplement information found in Wikipedia.

Methods: The Institutional Review Board at Midwestern University approved this study and classified it as exempt since no human subject data was collected or analyzed. The Wikipedia articles for the top 20 herbal supplements, as identified by the National Center for Health Statistics (NCHM) will be analyzed for completeness and accuracy regarding therapeutic use(s), adverse effects, safety in pregnancy and lactation, and dosing. Accuracy of information will be determined by comparing the articles in Wikipedia to information contained in two leading dietary supplement references (National Medicines Comprehensive Database and Natural Standard). The revision history, page view statistics, Flesch-Kincaid reading level, and organization of the Wikipedia page will also be assessed. Descriptive statistics will be used to summarize the data.
Evaluation of transmucosal immediate release fentanyl (TIRF) use and implications under risk evaluation mitigation strategy (REMS)

Benjamin Lee¹, Rachel Ralph², William A. Budris³

Midwestern University¹, Downers Grove, Illinois; University of Illinois at Chicago College of Pharmacy²; Northwestern Memorial Hospital³

Transmucosal immediate release fentanyl (TIRF) is an important drug option for the management of breakthrough pain in cancer patients. However, serious complications and issues may arise if administered improperly or off-label. Thus, it is crucial to adhere to the TIRF REMS (Risk Evaluation and Mitigation Strategy) Access Program to mitigate risks of misuse, abuse, addiction, overdose, and other complications such as respiratory depression. The purpose of this review was to evaluate the usage and treatment pattern of TIRF at Northwestern Memorial Hospital (NMH). This retrospective chart review was approved by the Northwestern Memorial Hospital Institutional Review Board. The NMH electronic medical records (PowerChart, by Cerner) were investigated for fentanyl lozenge inpatient orders from the 17 month period of January 2011 to May 2012 to determine documented indications, frequency of TIRF ordering and dosing, and evidence for patient opioid tolerance. During this designated study period, a total of 22 patients were identified with 26 unique inpatient admissions. Of the 26 unique admissions, it was determined that 38 percent of TIRF orders were for indications other than those approved by the FDA and 23 percent had patients that were not opioid tolerant or could not be classified as opioid tolerant prior to the TIRF order. Of the 20 admissions that had patients documented with TIRF dose administration, it was found that 35 percent had patients that were improperly dosed: receiving doses more frequently and higher than recommended. Overall, 50 percent of TIRF medication orders placed between January 2011 and May 2012 and 65 percent of admissions in which a patient received TIRF medication during their inpatient stay were off-label. The results from this study indicate the need for active involvement by pharmacists, who can play a critical role in reducing adverse drug event (ADE) risks when TIRF orders are placed in the hospital setting. TIRF REMS education and certification requirements do not apply to prescribers of inpatient orders, which might explain the high percentage of TIRF orders that were off-label and consequently off-REMS. Thus, pharmacists can help reduce ADE risks by assessing the inpatient practitioner’s knowledge of the REMS Program requirements and educate on the risks and proper administration of TIRF prior to dispensing.

This research was supported in part by Federal Work Studies grants.
Formulations of Centhaquin Loaded Nanocarriers for Targeted Delivery to the Brain

Hyaera Lee, Shridhar V. Andurkar, Anil Gulati, Medha Joshi.

Department of Pharmaceutical Sciences, Chicago College of Pharmacy, Midwestern University, Downers Grove, Illinois, 60515.

Centhaquin [1-(3-methylphenyl)-4-(2-beta-quinolylethyl) piperazine] is a 4-arylpiperazine derivative that was originally discovered to produce antihypertensive effect. However, it has been recently established that centhaquin produces antinociceptive effect in the mouse tail flick and hot plate assay, and this effect is mediated by imidazoline/$\alpha_2$-adrenergic and opioid receptors but not by endothelin beta receptors (ETB). The transport of centhaquin directly to the brain is essential to enhance its analgesic activity and to promote its use as an adjuvant to opioid analgesics. To further enhance the antinociceptive effects of centhaquin by improving its delivery to the CNS, a nanocarrier based delivery of centhaquin was thought of. Nanotechnology has been successfully utilized to improve the delivery of various drugs to the CNS and has enhanced the ability to manage CNS diseases. Nanocarriers loaded with centhaquin were prepared using Purasorb PDLG-5004® 50/50 DL-lactide/glycolide copolymer. Either centhaquin base or its citrate salt was used. The two different surfactants that were used in the formulation of nanocarriers were Vitamin E TPGS (d-alpha tocopheryl polyethylene glycol 1000 succinate) and Pluronic F 127® (Block Copolymer of Ethylene Oxide and Propylene Oxide). The formulated nanocarriers were controlled for quality based on their particle size and zeta potential using Zetasizer Nano ZS (Malvern Instruments, Westborough, MA) at 25°C. Hydrodynamic diameter was measured using dynamic light scattering based on backscatter detention optics. The encapsulation efficiency of the nanocarriers towards centhaquin was determined using high pressure liquid chromatography (HPLC). The release kinetics was studied using dialysis bag method. Aliquots were withdrawn at the intervals of 0, 0.5, 1,2,3,4,6,12 and 24 h. The aliquots were analyzed by HPLC for centhaquin content. Nanocarriers formulated using Vitamin E TPGS as a surfactant resulted in the least particle size, and also showed the most negative zeta potential. The encapsulation was significantly higher when Vitamin E TPGS was used with centhaquin citrate. These findings suggest that nanocarriers of centhaquin citrate designed using Vitamin E TPGS as the surfactant, were found to have the desired characteristics for nanocarriers, which can have the potential to cross the BBB.

This research was supported by CCP start up funds for MJ

Title: Asian Community Health Education Initiative: students and faculty bridging gaps in healthcare disparities

Authors: Vinvia Leung\textsuperscript{1,3}, Brandon Chiu\textsuperscript{1,3}, Dr. Sheila Wang\textsuperscript{1}, Dr. Hong Liu\textsuperscript{2}

Midwestern University Chicago College of Pharmacy\textsuperscript{1}, Midwest Asian Health Association\textsuperscript{2}, PharmD Candidate\textsuperscript{3},

Purpose: The Asian American population is the fastest growing minority group in the United States, where a quarter of its population is living in poverty with poor access to medical care. However, Asian Americans continue to be stereotyped as the “model minority”. The Asian Community Health Education Initiative (ACHEI) is a student-run, self-sustained health awareness program dedicated to addressing the health disparities of the medically underserved Chinese community of Chicago, Illinois. Through this initiative, pharmacy students and faculty pharmacists collaborate with local community advocates to provide medical access and education in the patients’ native language.

Methods: Once a month, students and faculty pharmacists of the Asian Healthcare Association (AHA) at Midwestern University Chicago College of Pharmacy work with community leaders from the Midwest Asian Health Association (MAHA) to provide laboratory consultation and education. One-on-one review of patients’ laboratory results with general health educational points are provided and translated (in Mandarin and/or Cantonese) by students under the supervision of faculty pharmacists. AHA student leaders work to develop, translate and present educational material related to disease states disproportionately affecting this patient population such as hypertension, dyslipidemia, and chronic hepatitis B infection. The sustainability of monthly consultation visits is largely relied upon the students, who solicit and schedule qualified volunteer faculty pharmacists and student translators. Finally, to ensure accountability and reliability, interested students must undergo a training session covering common disease states and Chinese terminology, and shadow a senior student prior to being a translator. Student leaders, with faculty support, develop and implement the training and shadowing opportunities.

Results: ACHEI provides the only source of preventative care (screenings, health education, early medical management) for this local Asian community. Ninety-one percent lack health insurance, only 10% speak or understand English and up to 80% of this population is working-class with educational underachievement. Since April 2012, an average of 25 patients each month (41% of those screened) visits the clinic for laboratory consultation and education. The average patient age is 50 (range: 19-65) with females making up more than half the population (61%). Through ACHEI, patients with significant findings related to dyslipidemia, hypertension, hepatitis B, anemia, and hyperthyroidism have been identified.

Conclusion: ACHEI is a student-run, collaborative program dedicated to delivering care and improving patient awareness of preventative health conditions. This initiative allows for early detection of high-risk conditions, access to appropriate health care and ongoing education in the native language to improve and/or maintain a healthy lifestyle.
Monitoring medication waste and developing strategies to reduce medication expenditures at a tertiary academic medical center.

Beth Lubecke¹, Milena McLaughlin¹,², Chastity Franklin², Raymond Black II²

Midwestern University¹, Downers Grove, IL, Northwestern Memorial Hospital², Chicago, IL

The research was proposed to identify the quantities of expired medications in a tertiary care hospital and determine which departments have the greatest opportunities for cost savings due to expired medications. A plan could then be devised to decrease the number of expired medications and medication expenditures in the pharmacy department. This study utilized data retrospectively gathered from electronic reports at Northwestern Memorial Hospital, Chicago, Illinois from September 2011 through February 2012. The pharmacy satellite that services the ED and General Medicine floors had the highest quantity and cost of medications expire during the study interval with a total of 10,700 expired units and a potential savings of $48,345. The pharmacy satellite with the highest quantity of an individual medication that expired, lorazepam 2mg/mL injection, included the ED and General Medicine floors with a total of 377 vials. The pharmacy satellite with the most expensive expiration of a single drug, antihemophilic factor (AHF) VIII (recombinant), included the NICU, L&D, and Postpartum with a potential savings of $10,465. AHF VIII (recombinant) was also the most expensive individual medication that expired hospital-wide with the same potential savings. The medication that expired in the highest quantity hospital-wide was ephedrine 50mg injectable syringes with a total of 511 syringes. Medications that expired most frequently were rescue medications, short-dated compounded medication, and medications not stable at room temperature. Techniques that can be used to continue minimizing expenditures that result from outdated medication include: maintaining appropriate par levels in Automated Dispensing Cabinets (ADC), pharmacist oversight of ADC stock management, stock rotation, reallocation of short-dated medication, continual cost-benefit analyses, and adding secure areas within refrigerators for controlled substances. Further research could investigate individual drugs that had the greatest potential for cost savings before and after the previously mentioned strategies were employed to determine if they are effective.

This research was supported in part by Federal Work Study funds, the Student Leadership and Research Award, and the Student Council Travel Award.
Development of an enteric coating composition resistant to alcohol

Stephen C. Ly¹, Ayesha E. Abrar¹, Natarajan Venkatesan¹ and Guru V. Betageri²

Chicago College of Pharmacy¹, Midwestern University, Downers Grove, IL, USA. Graduate College of Biomedical Sciences², Western University of Health Sciences, Pomona, CA, USA.

The purpose of this study was to develop a coating material that is not only resistant to the gastric pH (1.2) but also is resistant to alcohol. Ibuprofen was chosen as the model drug. Commercially available uncoated tablets of store brand ibuprofen were used in this study. The tablets were coated using alginate and ethyl cellulose in varying composition. Coating was carried out using a Caleva Mini Coater/Drier-2. The coated tablets were then subjected to in-vitro dissolution using USP-Type 1 apparatus in 0.1N HCl with and without ethanol ranging from 5-40% v/v concentration at 100 rpm/37°C/1000 mL. The dissolution study was carried out for 2 h. Coated tablets which could withstand 40% v/v alcohol containing dissolution medium were subsequently subjected to dissolution studies in phosphate buffer pH 7.2 as dissolution medium. Dissolution samples collected at pre-determined time points were analyzed using UV spectrophotometer at 226 nm and 221 nm for alcohol containing and phosphate buffer containing dissolution medium respectively. Ibuprofen tablets coated with varying coating thickness (2-10% w/w) when exposed to 0.1N HCl containing 40% v/v alcohol showed resistance and could withstand the exposure to alcohol. Tablets with 2 and 4% w/w coating thickness showed resistance up to 45 and 60 minutes respectively. While tablets coated at 6% w/w were resistant up to 90 minutes. Tablets coated at 8% w/w level showed complete resistance to alcohol containing dissolution medium up to 2 hours and was found to release the drug completely upon exposure to phosphate buffer pH 7.2 containing dissolution medium. As the coating thickness increased, resistance to alcohol seemed to increase. Based on this study, it was evident that alginate when used in appropriate composition with other coating materials, not only protects the drug from gastric environment but also from unexpected alcohol exposure. This is an Encore Presentation. This abstract was presented at the APhA annual meeting March 1-3, 2013 at Los Angeles, CA.

This research was supported in part by CCP intramural research grant from Midwestern University, Downers Grove, IL.
OBJECTIVE: To assess if the Career Explorers Program (CEP) helps high school students prepare for college.

BACKGROUND: The CEP has been in existence since 2000. This program offers high school students the opportunity to experience the pharmacy profession firsthand through both classroom experiences hands-on practice in retail or hospital pharmacy settings. Past surveys have shown that the CEP increases an interest in the pharmacy profession, and changes the perception of the pharmacist role. This program is often the participants’ first encounter with a college environment. We decided to see if this program prepared students to be successful in college.

METHODS: A pre/post-survey was distributed to the 2012 CEP students (N=66) to assess their thoughts/actions regarding time management, study habits, problem solving/decision making, and professionalism. These characteristics have shown to be key to success in a collegiate environment. Responses of the pre-survey were compared to the post-survey using a standard McNemar test to determine significance.

RESULTS: 100% (N=66) of participants completed the pre-survey while 97% (N=64) completed the post-survey. Changes in the study habit characteristic showed the most significance. Student perceptions regarding cramming for exams changed from agree to disagree 43.9% (N=29) to 54.7% (N=36). Participants also felt that reviewing material shortly after it is taught is beneficial 28.8% (N=19) to 65.6% (N=42). 74.2% of participants thought that creating a schedule of homework assignments and activities is important for success.

CONCLUSION: The CEP changed student perceptions regarding study habits for college. Certain aspects of each category: time management, study habits, problem solving/decision-making, and professionalism showed significant changes between the start and end of the program. Since this class finished in July 2012, it is not known whether these changes will equate to actions.
Pharmacy involvement to improve admission medication histories.

Nabila Mirza¹,² Luke Jackson¹, Huzefa Master¹,², Sean Mirk¹,²

Midwestern University¹, Downers Grove, Illinois, Swedish Covenant Hospital², Chicago, Illinois

Medication reconciliation is vital to patient safety throughout all transitions of care. An accurate home medication list (HML) is an essential part of medication reconciliation; it can help diagnose, detect adverse drug events, identify non-adherence, avert medical errors and prevent interruption in drug therapy. Most methods to complete a HML involve a coordinated effort between a physician, nurse, or pharmacist to help complete a comprehensive medication history (CMH). Research shows the pharmacist involved in CMH taking produce a more complete HML. The primary objective of this study is to gauge the ability of pharmacy staff members to detect and document medication discrepancies. This study took place on two cardiac floors within an urban-based hospital. Two third-professional year student pharmacists were trained as pharmacy technicians. One of the roles as a technician was to perform CMH within 48 hours of admission. After each CMH, the patient’s current HML was updated in the electronic medical record (EMR). Medication discrepancies between the HML entered by the nurse and/or physician and the pharmacy technician were recorded. The types of discrepancies included: omissions; commissions; incorrect frequency; incorrect dose; both incorrect dose and frequency; incorrect formulation; and same drug class, different medication. The total number of discrepancies in each category was collected, as well as discrepancies amongst medications commonly associated with hospital admissions. There were a total of 47 patients used in the study, and 159 discrepancies that were recorded. The most prevalent discrepancy found was the number of medications that were omitted from the home medication list (39%), and the least was the wrong formulation being recorded in the EMR (1.4%). Patient demographic data was also collected. Increasing the role of pharmacy technician in the medication history component of medication reconciliation appears to help reduce medication discrepancies.
Identification of clinical predictors of elevated creatinine phosphokinase during daptomycin use: a matched case-control study

Daniel Barone¹; Archana Nath¹; Sonia Nevrekar¹,², Pharm.D.; Stephanie Kliethermes³; Amy Pavell², Pharm.D.; Sheron Mui¹; Carrie Sincak¹, Pharm.D.; Sheila Wang¹,², Pharm.D.

¹Midwestern University Chicago College of Pharmacy, ²RUSH University Medical Center, ³The University of Iowa Department of Biostatistics, *Pharm.D. Candidate

Daptomycin is a bactericidal antibiotic used to cover aerobic gram-positive pathogens, including methicillin-resistant Staphylococcus aureus (MRSA), with indications for complicated skin and skin structure infections and bacteremia with or without right-sided endocarditis. Recommended daily doses allow for concentration-dependent killing with a reduced frequency of creatinine phosphokinase (CPK) elevations and symptoms. However, reports of significant CPK elevations continue to be documented. The accumulation of daptomycin resulting in higher concentrations has been reported as a probable cause of CPK elevations. This retrospective matched case-control study is designed to determine clinical predictors of significant CPK elevations with or without symptoms in patients receiving daptomycin. Inclusion criteria consisted of patients 18 years of age or older who received daptomycin from July 2008 to August 2010 for at least 72 hours, were hospitalized for 7 or more days, and developed significant CPK elevations (greater than or equal to 3 times the upper limit of normal). Daptomycin cases with significant CPK elevations were matched 1:1 to controls according to age (plus or minus 10 years), gender and date of peak CPK elevation (plus or minus 30 days). The following variables were used in univariate analyses to determine association with significant CPK elevations: race, weight (including body mass index [BMI]), daptomycin dose and duration, kidney function, length of hospital stay, co-morbidities, mortality risk, source of infection, culture and susceptibility (including minimum inhibitory concentration [MIC]), and concurrent medications known to be associated with CPK elevations or related symptoms. Conditional logistic regression analyses were used to determine predictors associated with significant CPK elevations. Concurrent use of statins, weight, including BMI was found to be significant clinical predictors of CPK elevation. Additionally, female gender and daptomycin use for more than five days were significantly associated with severe CPK elevations. Careful monitoring of CPK levels may be warranted while receiving daptomycin, particularly in the setting of obesity and concurrent statin therapy. This study is ongoing and further analysis utilizing a larger sample size will be assessed.
Encapsulation in ceramide lipid nanoparticles enhances bortezomib-induced effects on metabolic activity

Gabriel Park, Annette Gilchrist and Medha Joshi

Midwestern University, Chicago College of Pharmacy, 555 31st Street Downers Grove, IL 60515

Bortezomib (Velcade) is a first-in-class proteasome inhibitor approved for multiple myeloma that induces apoptosis in several cancer cell lines. Using an osteoblast precursor cell line derived from mouse calvaria (MC3T3), a mouse pre-osteoclast cell line (RAW 264.7), and a human osteosarcoma cell line (U2OS), we established bortezomib treatment resulted in a time- and dose-dependent decrease in metabolic activity, indicative of enhanced apoptosis. To improve its delivery we examined two types of liposomal formulations namely cationic and ceramide. Liposomes were prepared by dry film evaporation technique, characterized in terms of particle size, zeta potential, and encapsulation efficiency, and then examined for their effects on metabolic activity using AlamarBlue. Decreased metabolic activity was seen with both bortezomib encapsulated liposome formulations, but there was a greater reduction seen with the ceramide liposomes. Thus, encapsulation of bortezomib into ceramide lipid nanoparticles may enhance its effects on osteoclast cells, which are up-regulated in multiple myeloma as well as osteosarcomas. This may lead to possible targeted therapy to increase efficacy of treatment and reduce side effects known to occur during chemotherapy, such as peripheral neuropathy.

Funding to GP is provided by Chicago College of Pharmacy Student Summer Research Grant and funding for this research provided by a Chicago College of Pharmacy’s Startup Research Grant
Navigating antimicrobial drug shortages: where are we one year later?

Zachary Pentoney, Erik Skoglund, Milena M. McLaughlin, and Marc H. Scheetz

Department of Pharmacy Practice, Midwestern University, Downers Grove, Illinois
Department of Pharmacy, Northwestern Memorial Hospital, Chicago, Illinois

Antimicrobial drug shortages have increased in recent years and continue to cause major concern for clinicians. Prospective data are lacking regarding projected resolution dates from manufacturers and actual resolution dates. Although national reports have offered information on the reasons and regulatory issues behind shortages, commonalities among the shortage drugs have not been well defined.

This study involved the collection of publicly available drug shortage information on a biweekly basis from the online ASHP Drug Resources and FDA Drug Shortages Centers. Pertinent variables such as shortage duration and reasons for shortage were collected. The following descriptive statistics were compiled using Microsoft Excel, Version 12.3.4 (Microsoft, Redmond, WA): number of products on shortage according to ASHP and FDA, number of products on shortage at Northwestern Memorial Hospital, reasons provided for shortages, brand and generic drugs on shortage, alternative formulations that went on shortage, durations of shortages, and estimated durations of shortages.

During the study period (6/29/11 to 6/28/12), forty-seven unique presentations of antimicrobial drugs, comprised of 418 products, were tracked as shortages between FDA and ASHP. Per ASHP data, 41% of presentations tracked were newly on shortage during the study period. However, at the end of the study period, only 27% of shortages of presentations (including ongoing and new) had resolved, per ASHP. Of the 12 presentations for which shortage resolution occurred (ASHP), the median time to resolution was 192 days (min: 56, max: 932).

For all drug shortages during the study period, at least one alternative formulation was available 64% of the time. Generic products were more frequently on shortage than brand-name products, and generic-only products accounted for 51% of all shortage products tracked. Three reasons for shortages accounted for more than 50% of all reasons provided by manufacturers: no reason provided (21%), discontinuations (19%), and manufacturer delays (17%). Manufacturers were able to provide an initial date-based estimate for shortage resolution 39% of the time. The differences between actual and projected resolution durations for oral and parenteral drugs were 51 and 16 days, respectively (expressed as median values).

Of all anti-infective drugs on shortage nationally, over 20% were realized at NMH during the study period (acyclovir, amikacin, clindamycin, foscarnet, ganciclovir, pentamidine, primaquine, streptomycin, SMX-TMP, and tobramycin).

ASHP appears to be more sensitive than FDA in capturing and reporting drug shortages. Results suggest that certain drugs (generics and ongoing shortages) are more likely to be on the shortage list for a prolonged period of time. Shortage causes appear to be multi-factorial. However, manufacturers frequently cannot provide reasons for shortages. It appears that for both oral and parenteral anti-infective drugs, the actual duration of the shortage is longer than the projected duration.

Zachary Pentoney was supported in part by a Midwestern University research grant.
Establishment of a quality evaluation program for a pharmacist led medication therapy management (MTM) clinic in a physician office

Marianne Pop¹, Amisha Mehta¹, Mary Ann Kliethermes², Pharm.D., Kathleen Vest², Pharm. D., CDE, Nicole Rockey², Pharm. D., BCACP

Pharm.D. Candidate 2013¹, Department of Pharmacy Practice², Midwestern University, Downers Grove, Illinois

Purpose: A core element of MTM services is to optimize medication use for improved patient outcomes. A growing number of Patient Centered Medical Home (PCMH) models include MTM services provided by pharmacists; where pharmacists implement therapeutic plans in collaborative practice with other healthcare providers. The purpose of this quality assessment project was to understand the needs of the patient population, referral patterns of physicians in a primary care clinic, and overall services and utilization of the MTM clinic.

Methods: A pharmacy student developed, with pharmacy practitioners in the PCMH, the items for quality measurement and collected data from three pharmacy maintained MTM clinics within the medical group. The health system's electronic medical record system was used to identify providers who, over a year and a half period of time, referred patients to the MTM clinics. The investigation involved reviewing patient electronic medical records to identify referral provider, reason for MTM referral, number of patients referred for MTM, date of referral, number of patient encounters with a pharmacist for MTM, and the number of patients that refused MTM.

Results: Fifty-seven providers referred patients to receive MTM; two of which provided 38% of referrals. Five major reasons were identified for patient referrals; medication review, disease state management, adherence, medication cost issues, and transition from warfarin to dabigatran. A total of 467 patients were referred from 1/11/2011-5/12/12 to the three MTM clinic locations. Of the 467 patients referred, 274 were general MTM encounters, 91 were referred for medication cost issues and 102 for warfarin to dabigatran transition. General MTM encounters included disease state management (Diabetes, Hyperlipidemia, Hypertension, COPD), medication adherence counseling, and medication review. Overall, there was a 77% show rate for MTM visits with 360 patients being seen. Of the patients seen, one hundred ninety six patients were counseled by pharmacists for medication review, disease state management, or medication adherence. Seventy one patients were seen for medication cost issues and 93 patients for warfarin transition to dabigatran. Patients had 620 encounters with a pharmacist; 273 of them over the phone. Seventy six patients refused MTM.

Conclusion: There was a trend towards increased MTM referrals to pharmacists by other healthcare providers as time progressed. Overall, patients were considered to be receptive to pharmacists’ involvement in a PCMH based on their 77% show rate. Pharmacists can provide medication reviews; recognize, resolve, and monitor medication issues, reduce polypharmacy, manage chronic disease medication regimens, plan adherence schedules, and recommend cost saving strategies. Identifying the vital benefits of a pharmacy led MTM clinic could lead to more need for pharmacists in a physician clinic setting. Further studies are needed to explore the effects of pharmacy interventions on patient outcome measures.
Impact of an International Experience in Guatemala on the Attitudes of Healthcare Professional Students

Marianne Pop, PharmD Candidate 2013, Hilary Sheridan, PharmD Candidate 2013, Jessica Johnson, PharmD Candidate 2013, Sally A. Arif, PharmD, BCPS, Thomas Reutzel, Ph.D

ILCCP Midwestern University, Downers Grove, Illinois

Abstract:
It is thought that participation in international experiences may affect the learning and teaching abilities of students in various ways. Medical missions afford healthcare students a chance to have clinical interactions with medical professionals and patients in a foreign country. The objective of this study was to quantify the impact that a medical mission in Guatemala could have on the outlook of healthcare professional students, compare and contrast attitudes of students from different educational backgrounds, and to collect subjective evidence about students’ perceived values and opinions about international experiential learning. The study participants included students from Midwestern University’s pharmacy, physician assistant, podiatry, and osteopathic programs. The study included the administration of an electronic socio-demographic questionnaire, a pre-survey (completed prior to the mission) and a post-survey (completed after the mission) to participating students to better understand their attitudes toward the two-week mission. The survey included both likert scale and open-ended qualitative questions. Of the 21 respondents who completed both pre and post surveys, there was a trend that conveyed improved attitudes after the mission in comparison to before the mission. The three aspects of the mission that students found most valuable were providing health care to patients from a different country, being able to apply clinical skills learned in school, and being able to work closely with other providers as part of an interdisciplinary team. Out of all the students who completed the post-mission survey (n=26), 100% agreed that they would recommend this program to other classmates. Overall, there was a positive impact on the healthcare values, clinical skills, and opinions of the students who attended this medical mission. The results of this study demonstrate that healthcare professional program curriculums should offer international experiences to improve public health understanding and the role of healthcare professionals in international settings.
Evaluation of Pyrrolidine Derivatives as CCR1 Antagonist for in vitro Inhibition of Multiple Myeloma

Daniel PyenΩ and Annette GilchristΩ
Chicago College of Pharmacy, Downers Grove, IL

Multiple Myeloma (MM) is characterized by an accumulation of cancerous plasma cells (B cells) within the bone marrow. The presence of myeloma cells in the bone marrow results in heightened osteoclast activity, ultimately leading to the formation of bone lesions. The chemokine CCL3 is up-regulated in MM patients and levels have been shown to inversely correlate with patient survival. At least two receptors are activated by CCL3, namely CCR1 and CCR5. In collaboration with Dr. J. Robert Merritt at the New Jersey Center for Science, Technology & Mathematics, we tested a collection of novel pyrrolidines based on a previously disclosed series of CCR1 antagonists. The compounds were tested using competitive binding assays with membranes isolated from human embryonic kidney cells over-expressing human CCR1 (HEK_hCCR1), or the human multiple myeloma cell line RPMI 8226 that endogenously expresses CCR1.

Our results indicate we have achieved potent inhibition of 125I-CCL3 binding, although there are clear differences in the affinities of the drugs tested. Furthermore, we find several of the compounds appear better suited for use with MM, having higher affinity with the RPMI 8226 membranes than the EHK_hCCR1 membranes. Future efforts will focus on examining these compounds using functional assays such as chemotaxis. In addition, we would eventually like to examine the ability of the compounds to competitively inhibit additional ligands for CCR1 such as CCL-5.
The number of drug shortages in the United States has been increasing in recent years, prompting a rise in interest from researchers and policymakers alike. While some literature exists on the causes and factors that lead to antimicrobial shortages, the need remains for more studies designed to accurately gauge the level of patient harm incurred as a result of realized antimicrobial shortages. In order to help address this need, our group piloted a novel method for gathering evidence of patient harm due to antimicrobial shortages, which was distributed as a public Survey Monkey® link in a recent issue of Pharmacotherapy as well as to Infectious Diseases email listservs. Clinicians who bore witness to adverse effects of antimicrobial shortages were asked to report information on the respondent’s institution (for de-duplicating purposes only), the patient’s age, sex, the antimicrobial product that was on shortage, the type of infection requiring treatment or prophylaxis, the adverse event, and the patient’s outcome. Causality was attributed to the adverse events due to a drug shortage using the National Cancer Institute’s Common Terminology Criteria for Adverse Events (CTCAE), and the severity of the adverse event was classified using modified Adverse Event Reporting System (AERS) criteria. Survey responses are presented as descriptive data in a case series where the harmful effects of antimicrobial shortages are detailed. Four unique institutions responded to our survey, all of which are in urban settings ranging from 100-740 beds. Reported adverse events ranged from an hour delay of treatment to death. Our pilot study demonstrates a novel approach for collecting data on patient harm due to antimicrobial shortages and has revealed patient harm due to antimicrobial shortages not reported elsewhere in the literature. This information may help guide policies aimed at allocating appropriate resources to control and prevent future patient harm due to antimicrobial shortages. Future assessments will aim to better capture the realized harms once dissemination of the electronic data clearinghouse becomes more publically available.
Changes in Lecture Handout Role and Value as the Professional Curriculum Evolves

Sandra K. Tooley, PharmD Candidate 2013 and Robin M. Zavod, PhD

Department of Pharmaceutical Sciences, Midwestern University, Downers Grove, IL

Objectives: The study objective was to assess the changes in perceived value and role of the lecture handout as an increase in active learning and use of technology was implemented.

Methods: Survey items that measure lecture handout role and value were piloted and clarifying modifications made. Data was collected at three points across the curriculum, including entry into pharmacy school, as well as completion of the PS-1 and PS-2 years. Six student cohorts were surveyed, three educated in the “old curriculum”, and three in the “new curriculum”. Descriptive and inferential statistics were performed.

Results: Regardless of curriculum type students prefer fully completed handouts. Statistically significant increases in preference occurred over time. The most valuable roles of fully completed handouts were identified as “It allowed me to pay complete attention to the lecturer.” followed by “It was easier to study from because I had all the notes needed to study for the exam.” Evaluation of all handout types (regardless of curriculum type) indicates the most valuable roles are “Study guide for outside of lecture learning.” followed by “Supplement to lecture material presented.” Statistically significant decreases in these roles occurred over time and are coupled with statistically significant increases in the role “Resource for use on rotations/practice of pharmacy.”

Implications: Irrespective of learning modalities used in the classroom, as the difficulty of the professional curriculum increases students increasingly value a fully completed handout. Surprisingly only limited changes in role were observed.
TITLE: Labeling Accuracy of Weight Loss Dietary Supplements

AUTHORS:

Jennifer Phillips, PharmD, BCPS – Midwestern University Faculty
Meghana Aruru, MBA – Roosevelt University Faculty
Cortney Valela, Midwestern University PharmD Candidate, Class of 2014

PURPOSE: A large number of consumers use dietary supplements for weight loss. Although dietary supplements are not approved by the Food and Drug Administration (FDA), this agency has specific requirements for labeling of these products. There is a lack of literature available specifically regarding weight loss supplements; however, research on other dietary supplements suggests there are issues with accuracy of labeling. In this study, the investigators will analyze the content and accuracy of 78 weight loss dietary supplement labels sold by a leading dietary supplement retailer.

METHODS: Labels were analyzed to determine if they conform to key requirements of the FDA’s guidance documents on appropriate labeling. Specifically, the percentage of products appropriately labeled as a dietary supplement and the percentage of products with a disclaimer that the product should not be used without consulting a healthcare provider, during pregnancy, or in pediatric patients was analyzed. In addition, all claims of effectiveness and adverse effects listed on the label were compared to a leading, well-referenced herbal/dietary supplement resource (National Medicines Comprehensive Database) to determine how well the information listed on the label correlates with the information listed in resource.

RESULTS/CONCLUSION: 94% of products analyzed had at least one ingredient considered “unsafe” or “possibly unsafe” by NMCD. 97% of products had at least one ingredient with an adverse reaction not listed on the label. 72% of products contained at least one ingredient considered “effective” or “possibly effective” by NMCD. For the products analyzed, 22% recommended that the patient consult a healthcare professional prior to use, 21% did not address whether a pregnant patient should consult a healthcare provider before use, and 10% did not address use in children. Although most products contained at least one ingredient deemed to be effective or possibly effective by NMCD, consumers need to be educated on the safety risks of using herbal weight loss supplements since almost all of the products analyzed in this study contained at least one unsafe or possibly unsafe ingredient.
Pharmacist Provided Medication Therapy Management in Ambulatory Care and the Impact on Adverse Drug Events

Sara Vander Ploeg, Mary Ann Kliethermes

Department of Pharmacy Practice, Chicago College of Pharmacy, Midwestern University, Downers Grove, Illinois

BACKGROUND: Medication Therapy Management Programs (MTM) established by the Medicare Prescription Drug, Improvement and Modernization Act of 2003 are aimed at Medicare patients with multiple diseases and taking multiple medications. Goals of MTM services are to optimize treatment outcomes by improving medication use and decreasing adverse drug events (ADEs) experienced by patients. ADEs are common in healthcare and cause patient suffering, result in hospitalizations and emergency room visits; and lead to substantial costs. The purpose of this study is to evaluate the effect of a pharmacist run MTM program on ADEs.

METHODS: Analysis of ADE data collected from a retrospective, non-randomized, cohort study conducted at the MTM clinic at University of Illinois at Chicago (UIC) medical center was completed. The intervention group patients seen in the MTM clinic that had at least 4 clinic visits over 6 months. The control cohort were 2:1 matched patients based on age, number of medications and who received standard pharmacy services from the UIC outpatient pharmacy for at least 6 months during the 3 year study period. Pre and post analysis was performed on intervention patients that had pre MTM clinic data.

RESULTS: ADEs from 333 patients (106 intervention and 227 controls) were analyzed. Approximately 1800 ADEs occurred during the 3 year study period. At least one ADE occurred in 52% of control and 67% of intervention patients. The overall incidence of ADEs were 2.6/1000 patient days for controls and 2.63/1000 patient days for intervention patients. However, for 44 intervention patients the pre MTM clinic versus post MTM clinic incidence of ADEs decreased from 6.02/1000 to 3.16/1000 patient days. Intervention patients had a higher incidence of serious ADEs (defined as hospitalization or ER visits) 26.54% vs 19.88%. The medications responsible for the highest number of ADEs were prednisone, tacrolimus, furosemide, insulin and warfarin in the control group and warfarin, furosemide, metoprolol, prednisone and insulin in the intervention group.

CONCLUSION: Pharmacist provided MTM services produced similar incidence of ADEs compared to patients receiving traditional pharmacy services as well as a slightly higher incidence of severe ADEs. Further research is needed to understand this surprising result. Improved detection of ADEs or greater medication exposure due to improved medication adherence may have contributed to the result.

The original study was supported by the UIC Institute for Health Research and Policy Pilot Grant.
Evaluation of Early-Stage Biomarkers of Cadmium Nephrotoxicity

Christopher D. Ackerman\(^2\), Walter C. Prozialeck\(^1\), Peter C. Lamar\(^1\), Joshua R. Edwards\(^1\)
Department of Pharmacology\(^1\), Department of Biomedical Sciences\(^2\); Midwestern University; Downers Grove, IL

Cadmium is an important industrial and environmental pollutant that is a major cause of kidney disease in many regions of the world. As a result of the widespread dissemination of cadmium in the environment, there has been considerable interest in the identification of early urinary markers of cadmium-induced kidney injury. Traditional biomarkers that have been used are metallothionein, cadmium, \(\beta_2\)-microglobulin and \(N\)-acetyl-\(\beta\)-D-glucosaminidase (NAG); however, they only identify late stages of cadmium-induced kidney injury. Unfortunately, by the time the markers are detected, kidney injury is often advanced and irreversible. Recent advances in understanding ischemic kidney injury have identified new and more sensitive biomarkers such as kidney injury molecule-1 (Kim-1), cystatin-C, clusterin and neutrophil gelatinase-associated lipocalin (NGAL). However, with the exception of Kim-1, these emerging biomarkers have yet to be evaluated in the context of cadmium toxicity. The objectives of the present study were to: 1) identify more sensitive biomarkers for the identification of cadmium-induced kidney injury and 2) to determine whether emerging multiplex analytical techniques can be used to efficiently measure levels of these biomarkers.

Male Sprague-Dawley rats weighing 250-300 grams were given daily subcutaneous injections of 0.6-mg (5.36 μmoles)/kg Cd 5-days per week, for up to 12 weeks as described previously (Prozialeck et al., 2007). At 3, 6, 9 and 12 weeks 24-hour urine samples were collected, aliquoted and later assayed for protein, pH, creatinine and the panel of biomarkers. The levels of the various biomarkers were determined using standard ELISA kits (\(\beta_2\)-microglobulin, Kim-1, cystatin-C, \(\alpha\)-GST and \(\pi\)-GST) and/or by state of the art Luminex xMAP Technology using the Millipore MagPix xPONENT 4.1 system with proprietary reagents (\(\beta_2\)-microglobulin, Kim-1, cystatin-C, clusterin, NGAL and albumin).

Albumin, \(\alpha\)-GST and \(\pi\)-GST can provide insight for the location of nephron damage. The glomerulus was not damaged from cadmium exposure. There was no change in urinary albumin excretion, and no statistical changes in serum levels of creatinine or cystatin-C. \(\alpha\)-GST (a marker of proximal tubule damage) increased at 9 and 12 weeks. \(\pi\)-GST (a marker of distal tubule damage) was not affected by cadmium. Histopathological analysis revealed that after 9 weeks, the Cd-treated animals exhibited more proximal tubular necrosis and apoptosis than the control animals. Conclusively, cadmium damage is focused within the proximal tubule.

Preliminary analysis showed that cadmium caused an increase in urinary volume and a decrease in urinary specific gravity that were evident at 9 and 12 weeks. Total urine protein excretion was significantly elevated by 9 weeks, and drastically increased at 12 weeks. Traditional ELISA analyses showed that \(\beta_2\)-microglobulin and Kim-1 were elevated (but not statistically significant) at week 6 and were significantly increased at 9 and 12 weeks. Cystatin-C was only slightly (but not significantly) elevated at 6 and 9 weeks, and was then markedly increased at week 12. MagPix technology yielded results that were similar to traditional ELISA data. With MagPix analyses \(\beta_2\)-microglobulin, cystatin-C and NGAL appeared in the urine with statistical significance at week 6. Kim-1 and clusterin showed a slight elevation (not statically significant) at week 6, but later had a major increased at weeks 9 and 12. Finally, correlative statistical analysis showed that MagPix and ELISA methodology yield similar results.

In summary, an increase in urine volume and protein excretion, with no change in urinary creatinine excretion is characteristic of proximal tubule damage. The two methodologies (MagPix and ELISA) used to quantify urinary biomarkers yielded similar results. However, MagPix yields a more robust result while also providing earlier detection of the urinary biomarkers with statistical significance.

The research was approved by the Animal Care and Use Committee at Midwestern University (Downers Grove, Illinois). Midwestern University’s Biomedical Science Program and Department of Pharmacology provided funding for this research.
Folate is an essential vitamin in eukaryotes, prokaryotes, and plants. The reduced derivatives of folate can be used to make DNA, RNA, and amino acids. Eukaryotes are not able to synthesize folate, forcing them to obtain the vitamin from the diet. *Escherichia coli* (*E. coli*), along with other various prokaryotes are able to synthesize folate. The mechanism of bacterial folate biosynthesis is well understood, however bacterial folate catabolism is not. Studying a pathway that differs between eukaryotes and prokaryotes provides new possible drug targets. In *E. coli*, the proteins encoded by the *abg* operon are involved in folate catabolism; two genes in this operon encode for subunits of the enzyme *p*-aminobenzoylglutamate hydrolase (PGH). This enzyme cleaves the folate breakdown product *p*-aminobenzoyl glutamate (PABA-GLU). This study focused on the role of metal on structure and activity of *E. coli* PGH. To study the metal binding characteristics of PGH, activity assays, size exclusion chromatography, equilibrium dialysis, and metal analysis experiments were performed. Genetic analysis, of PGH, predicted that each monomer contained one metal binding site. ApoPGH lacked enzymatic activity, but with addition of manganese PGH activity could be reconstituted. Equilibrium dialysis experiments demonstrated binding of one manganese ion per subunit. Interestingly, zinc was also present in PGH, with one zinc per AbgAB dimer; we hypothesize that it may play a structural role. Data from size exclusion chromatography experiments showed that apoPGH exists as a mixture of oligomeric species (tetramer, dimer, or monomer). In the presence of manganese PGH is primarily a tetramer. A better understanding of unique enzymes in bacterial metabolism, such as PGH, may lead to development of better antibacterial drugs.

Acknowledgements: This research was funded by Midwestern University and grant R15 GM085760 from the National Institutes of Health. Special thanks to Lenore Pitstick and Cassandra Larimer for technical assistance.
Epstein-Barr virus LMP2A enhances MIP-1α expression in a B cell lymphoma by utilizing Syk tyrosine kinase and p38 MAPK pathway

Jonathan Bardahl*, Ryan Incrocci#, Michelle Swanson-Mungerson#

*Biomedical Sciences Program, College of Health Sciences, #Department of Microbiology and Immunology, Chicago College of Osteopathic Medicine, Midwestern University, 555 31st Street, Downers Grove, Illinois 60515

Epstein-Barr virus (EBV) infects millions of people worldwide and is associated with the development of multiple diseases of the immune system, such as Hodgkin’s Lymphoma. Hodgkin’s lymphoma is a cancer of the immune system characterized by the presence of Hodgkin-Reed Sternberg (HRS) cells, which are malignant cells of the B cell lineage. Pro-inflammatory chemokines, such as MIP-1α and RANTES, are elevated in lesions of EBV-associated Hodgkin lymphoma patients and may play a role in tumor development and progression. One important EBV protein identified in HRS cells is Latent Membrane Protein 2 A (LMP2A). LMP2A is a membrane protein that is a functional homolog of the B cell receptor (BCR). Previous studies show that engagement of the BCR leads to an increase in MIP-1α. Therefore, we hypothesized that cells expressing LMP2A will have an increase in MIP-1α expression. To test this hypothesis, EBV- BJAB cell lines that do or do not express LMP2A were used to identify if LMP2A changes MIP-1α expression. We found that, through ELISA and qRT-PCR, LMP2A-expressing cells produced more MIP-1α at the protein and mRNA levels, respectively. In addition, this increased expression of MIP-1α at the protein level was also maintained when lower amounts of fetal calf serum were used. Furthermore, we wanted to identify the signaling pathway LMP2A utilizes to modulate MIP-1α production. We found protein levels of MIP-1α return to basal levels in cells expressing LMP2A with a mutation in the ITAM motif that interacts with Syk tyrosine kinase. To look further downstream, we used an inhibitor specific to the p38 MAPK pathway and found that MIP-1α expression decreased in LMP2A-expressing cells. These results indicate that LMP2A signaling through Syk and p38 kinase may enhance MIP-1α expression in Hodgkin’s lymphoma tumors and gives light to possible future pharmacological intervention in EBV-associated diseases.

This work is supported by NIH grant 1R15CA149690-01, Biomedical Science Program in the College of Health Sciences, and Midwestern University Intramural Funds.
Epstein-Barr virus (EBV) infects many individuals worldwide and causes a life-long, latent infection of B lymphocytes. EBV infection causes infectious mononucleosis in adolescents and is associated with multiple cancers of the immune system, including Burkitt’s lymphoma and Hodgkin’s lymphoma. The precursors of these EBV-associated cancers are latently-infected B cells that express the EBV viral protein Latent Membrane Protein 2 A (LMP2A). The influence of LMP2A on the transition from a latently-infected B cell to a tumor cell is unknown. Studies from our laboratory implicate that LMP2A activates the Ras/phosphatidylinositol 3-kinase (PI3K) pathway to increase interleukin-10 (IL-10) production. IL-10 production by EBV positive-cells may aid in the transition of a latently-infected cell to a tumor cell since IL-10 promotes B cell survival and suppresses tumor-specific T lymphocytes. The goal of this project was to confirm the requirement of the Ras/PI3K pathway and to identify targets that contribute to the increase of IL-10 production in LMP2A-positive cells. Experiments using a Ras inhibitor demonstrate that LMP2A requires Ras to enhance IL-10 production. In B lymphocytes, Ras has the ability to activate both the PI3K and the MAPK/p38k pathways. Therefore, we tested if Ras activates either or both of these pathways to mediate the LMP2A-dependent increase in IL-10 production. We first confirmed that the addition of a PI3K inhibitor abrogates the LMP2A-mediated increase in IL-10 production. Additional experiments that tested a downstream target of PI3K, mTor, indicate that this protein is involved in the LMP2A-dependent enhancement in IL-10 production. Since Ras can also lead to the activation of p38k, we tested if LMP2A required p38k activation to enhance IL-10 production. The use of a p38k inhibitor also decreases IL-10 production, suggesting that Ras potentially uses both the PI3K and MAPK/p38k pathways to enhance IL-10 levels. These findings indicate that these specific pathway inhibitors may be of further interest for the treatment of EBV positive cancers or other EBV-associated diseases.

This work is supported in part by the Biomedical Sciences Program in the College of Health Sciences and the National Institutes of Health Grant: 1R15CA14969-01.
Bilateral sectioning of the anterior ethmoidal nerves does not eliminate the diving response in voluntarily diving rats

Jill S. Chotiyanonta², Karyn M. DiNovo¹, and Paul F. McCulloch¹

Department of Physiology¹, Department of Biomedical Sciences², Midwestern University, Downers Grove, Illinois

The diving response is characterized by an immediate, intense bradycardia, apnea, and increased total peripheral resistance. This reflex response is initiated by stimulating the nose or nasal passages with water. Because the anterior ethmoidal nerve (AEN) innervates the nasal passages and is thought to play a major role in triggering the diving response, the present study examined the cardiovascular responses of voluntary diving Sprague Dawley rats before and after bilateral sectioning of the AEN. Heart rate (HR) and blood pressure (BP) were monitored using implanted biotelemetric transmitters (DSI). Rats were trained to voluntarily dive through a 5m long underwater maze, and their cardiovascular responses to diving were recorded. During diving, HR decreased from 503 ± 6 to 98 ± 2 bpm and BP increased from 137 ± 3 to a maximum 187 ± 4 mmHg. Rats were then randomly assigned to either an Experimental group that received bilateral AEN sectioning (N=6), or a Control group that received sham AEN sectioning (N=5). One week after AEN surgery, the cardiovascular responses to voluntary diving were again recorded. In the Experimental group, HR decreased from 498 ± 7 to 105 ± 2 bpm and BP increased from 138 ± 3 to a maximum 190 ± 5 mmHg during diving. Responses were similar in Control rats. Thus unexpectedly the diving response is still present even in the absence of both AENs. To eliminate the possibility that after AEN sectioning the rats were consciously initiating their diving response, all rats were anesthetized with urethane, and their nasal passages were stimulated with ammonia vapors. All rats showed an intense nasopharyngeal response (decrease in HR from 375 ± 10 to 205 ± 37 bpm, increase in BP from 133 ± 6 to a maximum 178 ± 3 mmHg). Responses were not significantly different between Experimental and Control rats. Since other studies have previously shown an altered nasopharyngeal response immediately after cutting the AENs, we conclude that another mechanism, possibly another nerve that innervates the nasal passages, can produce both the diving and nasopharyngeal response. In conclusion we find that the AEN is not essential for initiating the diving response in voluntarily diving rats, at least one week after being cut bilaterally.

This research was supported by the CHS Biomedical Sciences Program.
Graviola Fruit Extract Reduces TLR2 and TLR4 Induced TNF-alpha Production in J774 Mouse Macrophages

Aseel Dabbagh\textsuperscript{1,2,*}, Srikanth Manam\textsuperscript{1,*}, Natarajan Venkatesan\textsuperscript{3}, Mark A. Sanders\textsuperscript{4}, Ashlesh K. Murthy\textsuperscript{1}

\textsuperscript{1}Department of Pathology, \textsuperscript{2}Department of Biomedical Sciences, \textsuperscript{3}Department of Pharmaceutical Sciences, and \textsuperscript{4}Department of Family Medicine, Midwestern University, Downers Grove, Illinois 60515

The graviola fruit is the fruit from the tropical tree \textit{Annona muricata}. Recently, it has been shown that graviola fruit extract (GFE) exhibits anti-cancer properties. A role for microbe-induced chronic inflammation in the development of some cancers has been suggested by several studies; thus, we decided to do further research on GFE by studying its anti-inflammatory properties. To do this, we used the mouse macrophage J774A.1 cells. These cells express toll-like receptors (TLR) 2 and 4 which are pattern recognition receptors for microbial pathogens. When these receptors are stimulated by their cognate ligand, they signal the cell to produce a variety of pro-inflammatory cytokines. GFE was prepared from graviola fruit powder following a well-established ethanolic extraction procedure. To study the effects of GFE on cytokine expression, we designed our experiment to treat the cells with gradually increasing concentrations of the extract. After treatment for 8 hours, we induced cytokine expression by treating the cells with heat-killed \textit{Listeria monocytogenes} (HKLM), a TLR-2 ligand, and Lipopolysaccharide (LPS), a TLR-4 ligand. Since both TLR-2 and TLR-4 induce TNF-\alpha production, TNF-\alpha expression was measured by ELISA. We found significantly reduced TNF-\alpha production with even the lowest evaluated concentration (0.5 mg/ml) of graviola fruit extract. These results suggest a robust effect of GFE in reducing pro-inflammatory responses following stimulation by microbial pathogens. Based on these results, we plan to deduce the mechanism by which GFE is reducing cytokine expression. We also plan to study its anti-microbial properties on cells infected with bacterial pathogens.

\textit{This work was supported by Midwestern University Faculty Start-up Fund and NIH Grant 1R03AI088342 to AKM, and MWU Department of Biomedical Sciences Research Fund to AD.}

*AD and SM contributed equally
Role of the Retinoblastoma gene in the regulation of osteoblast differentiation.

Sehar Dadani, Oliver Couture and Nalini Chandar, Department of Biochemistry, College of Health Sciences, Midwestern University

Osteosarcoma (OS) or bone cancer is thought to occur from gene mutations in cell cycle regulators, like retinoblastoma (Rb) gene. Rb is a tumor suppressor that controls cell proliferation by regulating the G1/S progression, in the cell cycle. It allows DNA synthesis to occur only after being phosphorylated by CDK4 complexed with cyclin D1. This suppression of Rb then allows the E2F family to transcribe genes for the cell cycle to continue. Additionally Rb plays a role in regulating osteoblast specific gene expression during differentiation. This multistep process to forming determined bone cells from mesenchymal stem cells involves different signals or transcription factors to progress differentiation, like Runx2. Runx2 is required for mineralization of bone and is a master regulator of many genes involved in osteogenesis. Studies suggest Rb as a transcriptional co-activator of Runx2, involved in late osteoblast differentiation. Thus far, we have established a stable knockdown of Rb in MC3T3 osteoblast cell line using Rb shRNA. We have characterized these cells as having stable reduction in RB levels through RT-PCR, Real Time PCR, and Western Blot methods. We have investigated the effect of Rb loss both stably and transiently on the regulation of Runx2 gene promoter. There was an increase in Runx2 activity with transient loss of Rb function. These results will be discussed in terms of stage dependent role of Rb during osteoblast differentiation.
Immune Effects of DDE in a Mouse Model of Weight Loss

Terry Fokakis and Susan Viselli

Department of Biochemistry and Department of Biomedical Sciences, Midwestern University, Downers Grove, Illinois

The purpose of our research was to determine whether mice previously exposed to the anti-androgen, dichlorodiphenyltrichloroethylene (DDE), are at increased risk for immunological changes during weight loss. DDE accumulates in adipose tissue and we hypothesized that following weight loss DDE will be mobilized and have greater ability to influence immune cells. These experiments were carried out in mice from the Diet-Induced Obesity (DIO) C57BL/6J mouse strain (n=18). Nine of these mice were treated with DDE (200 mg/kg body weight in cottonseed oil) and fed a high-fat diet (60% kcal fat) for 2 months and then five of these mice were switched to standard rodent chow (10% kcal fat) for one month to allow weight loss and mobilization of DDE from adipose tissue. The other nine mice were the Controls and were treated with cottonseed oil vehicle alone and fed a high-fat diet (60% kcal fat) for 2 months. Five of these mice were then switched to standard rodent chow (10% kcal fat) for one month so that weight loss would occur. Four different groups of mice resulted: DDE-High Fat, DDE-Diet Change, Control-High Fat, and Control-Diet Change. The first goal of our study was to determine if the mobilization of DDE during weight loss would cause shifts to splenocyte and thymocyte subpopulations. Flow cytometry was used to assess percentages of cells expressing various surface markers. In the spleen we monitored percentages of cells expressing CD3+ (total T cells), CD4+ (T helper cells), CD8+ (T cytotoxic cells), and B220 (B cells). We found that DDE significantly increased the total CD3+ cells (14.07% vs 41.58%, p < 0.05) and CD8+ cells (38.44% vs 9.74%, p ≤ 0.05), while significantly decreasing the total number of B-cells (37.72% vs 3.99%, p ≤ 0.005). We also found that high-fat diet diet alone significantly increased the number of CD3+ cells (41.58% vs 14.07%, p ≤ 0.005) and CD4+ cells (35.97 vs 13.23, p < 0.01) in the DIO mice that underwent weight loss. In the thymus we monitored percentages of CD3+ positive cells (more mature thymocytes) and of CD4⁺CD8⁺ double-positive cells (immature thymocytes). We found that, independent of diet, DDE significantly increased the total number of the most mature thymocytes (CD3+) (30.06% vs 3.42%, p ≤ 0.05) but that neither DDE nor diet had any effect on the immature double positive CD4⁺CD8⁺ cells. The second goal of our study was to perform a comparative analysis between the DDE-treated groups and control groups for plasma concentrations of cytokines INF-γ, IL-17 and immunoglobulins IgM and IgG. We saw a trend of higher IgG and lower levels of IFN-γ in the mice treated with DDE that underwent weight loss, but results did not reach statistical significance. We also found significantly higher levels of IL-17 (p < 0.001) in the mice treated with DDE that underwent weight loss when compared to those treated with DDE and stayed on a high fat diet. Our findings indicate that DDE has the ability to alter splenocyte and thymocyte subpopulations. In addition, when DIO mice that are previously exposed to DDE undergo weight loss there are shifts in plasma cytokines and immunoglobulins that resemble the onset of autoimmune disease. More studies are needed to fully understand the relationship between DDE’s effects on immune cell subpopulations and how this influences cytokine and immunoglobulin levels.
Molecular and phenotypic consequences of loss of Prdm16 during embryonic mandible development using a novel conditional gene trap null allele of Prdm16 (Prdm16cGT).

Lauren N. Furlan, Brock T. Nelson, Lenore Pitstick, and Bryan Bjork

Department of Biochemistry, Midwestern University, Downers Grove, Illinois

Cleft palate, with or without cleft lip, is one of the most common birth defects seen in the human population. Scientists have identified numerous genes involved in normal craniofacial development. Many of these cause clefting or contribute to its etiology when mutated. One such transcription factor gene, Prdm16, is mutated to cause cleft palate in the ENU-induced cleft secondary palate 1 (csp1) mutant mouse strain. The csp1 mutant phenotype includes a small mandible, displaced tongue, and a cleft of the secondary palate. We proposed to investigate the molecular consequences of Prdm16 loss-of-function in the developing mouse mandible. Using whole-mount in situ hybridization, we compared the expression patterns of a subset of genes involved in normal mandible development between wild type embryos and Prdm16 null mutant littermates that carry a novel conditional gene trap allele of Prdm16 (Prdm16cGT). These comparative studies detected expression differences in several genes. Therefore, these data will allow us to begin to infer potential functions for Prdm16 in the regulation of genes and pathways at play during normal embryonic mandible development. Specifically, two of nine genes tested, Gsc and Msx2, exhibited reduced expression levels as a consequence of Prdm16 loss-of-function. Finally, we used the Prdm16cGT conditional null mutant mouse model to investigate the mechanism by which Prdm16 loss results in clefting. We have employed the Hand2::cre mouse strain for temporal and spatial ablation of Prdm16 expression specifically in the mandible. We aim to determine if loss of Prdm16 in the mandible but not in the palate is sufficient to disrupt proper elevation and fusion of the palate shelves.

This research was supported by CHS Biomedical Sciences Program funds.
Efficacy of centhaquin and selective serotonin reuptake inhibitors on behavior and oxidative stress in a rodent model of autism

Karolina Kata1, Seema Briyal2 and Anil Gulati2
Biomedical Sciences Program, Chicago College of Health Sciences1 and Department of Pharmaceutical Sciences, Chicago College of Pharmacy2, Midwestern University, Downers Grove, IL 60515, USA

Background: Autism is a complex neurodevelopmental disorder characterized by a spectrum of abnormalities in social interactions, hyperactivity, and repetitive behavior. Its neurobiology is proposed to be a result of genetic predisposition, environmental toxins, and oxidative stress. Impairment in the serotonin transport system has been found to be involved in autism, therefore, selective serotonin reuptake inhibitors, such as fluoxetine and paroxetine, are used to treat autistic behavior. Centhaquin has been reported to compete with paroxetine binding sites indicating that it may be inhibiting serotonin reuptake and may have therapeutic value.

Objective: To evaluate the effect of centhaquin, fluoxetine, and paroxetine on behavior and oxidative stress markers in a propionic acid (PPA) induced animal model of autism.

Method: Sprague-Dawley rats weighing ~300 g were given intracerebroventricular injections of either PPA (0.26 M; 5 µl) or saline (vehicle; 5 µl) twice a day for 7 consecutive days. PPA or vehicle treated rats were further divided into four groups. Each group received either saline, centhaquin (0.45 mg/kg), fluoxetine (10 mg/kg), or paroxetine (3 mg/kg) once daily for 7 days. Social behavior was examined by measuring olfactory response to a food stimulus, self-grooming behavior, sociability test, and locomotor activity. Subsequently the animals were sacrificed and brain tissue was evaluated for oxidative stress markers such as glutathione (GSH) and malondialdehyde (MDA).

Results: Body weight decreased in rats treated with fluoxetine, did not change with paroxetine, and increased with saline or centhaquin (P<0.0142) treatment in vehicle and PPA groups. Olfactory, sociability, and locomotor activity were similar in PPA and vehicle animals and were not affected by treatment with saline, fluoxetine, paroxetine or centhaquin. Self-grooming behavior was similar in vehicle and PPA groups treated with saline, fluoxetine or paroxetine. However, self-grooming behavior significantly (P<0.0025) decreased in rats treated with centhaquin in PPA group (8.43 sec) compared to vehicle group (43.56 sec). GSH levels were significantly decreased in PPA group compared to vehicle group (P<0.0001); this decrease was not altered following treatment with saline, fluoxetine, paroxetine, or centhaquin. MDA levels were significantly higher in PPA group compared to vehicle (P<0.0001) in saline and centhaquin treated rats (P<0.0001). MDA levels were similar in PPA and vehicle groups treated with fluoxetine or paroxetine.

Conclusion: Our findings support that PPA produced changes in oxidative stress parameters, which is an important mechanism in autism. However, fluoxetine, paroxetine, or centhaquin were not effective in reducing PPA induced increase in oxidative stress. Fluoxetine and to some extent paroxetine decreased body weight while centhaquin increased body weight. Centhaquin significantly decreased the self-grooming behavior suggesting that it may worth further investigating its role in treatment of autism.
Exercise Improves Glucose Sensitivity in a Mouse Model of Diet-induced Obesity: Role of Glucose Transporters

Komal B. Kenkare², Thomas P. Walsh², Jeff W. Kwak², Christian Evans²³, Kathy LePard¹², Mae J. Ciancio¹²

Department of Physiology¹, Department of Biomedical Sciences², Department of Physical Therapy³, Midwestern University, Downers Grove, Illinois

Background: High fat (HF) dietary intake and sedentary lifestyle are the primary causes of obesity and type 2 diabetes. Glucose transporters are important in sensing and transporting plasma glucose into most mammalian cells, and current literature suggests that the localization of glucose transporters 2 (GLUT2) and 4 (GLUT4) are impaired by a HF diet. Recent findings in our laboratory demonstrated the beneficial effect of voluntary exercise (Ex) in preventing HF-induced obesity. Objective: Determine the effects of a HF diet and Ex on glucose sensitivity and GLUT2 and GLUT4 levels in a model of HF diet-induced obesity. Methods: Male C57BL/6 mice were divided equally into 4 groups (n=4/group): low fat (LF; 10kcal% fat) sedentary (Sed; LF/Sed), LF/Ex, HF/Sed (60kcal%), HF/Ex. Exercise and body weights were monitored weekly for 12 weeks. Twenty-four hour food intake and oral glucose tolerance were determined at week 12. Upon completion of the diet and Ex protocol, excised pancreatic tissue and soleus muscles were homogenized in lysis buffer and analyzed using Western blot for total GLUT2 and GLUT4 levels, respectively. Immunohistochemistry of formalin-fixed pancreatic tissue was conducted to determine the cellular localization of GLUT2 in pancreatic islets. Results: Ex significantly prevented HF weight gain (LF/Sed = 27.1±0.05g; LF/Ex = 25.3 ±0.22g; HF/Sed = 33.1±1.2g; HF/Ex = 27.9±1.3g. p < 0.05). Oral glucose tolerance (OGTT), expressed as the area under the curve (mg/dL x min), was significantly improved by Ex in the HF group: HF/Sed = 32500±1440; HF/Ex = 24100±2500 (p = .001). Preliminary Western blot analysis demonstrated elevated pancreatic GLUT2 expression in HF/Sed mice compared to LF/Sed mice. However, preliminary confocal analysis of GLUT2 localization within pancreatic beta cells demonstrated reduced staining of GLUT2 in the apical membrane of HF/Sed compared to LF/Sed mice. Total GLUT4 levels showed no obvious influence of diet or Ex in preliminary Western blot. Conclusion: The current findings suggest that cellular localization of GLUT2 may be influenced by diet and Ex. Whether Ex can improve HF diet-induced insulin resistance by influencing GLUT2 and GLUT4 cellular localization requires further data acquisition and analysis. These results could have important implications for the development of a treatment for diet-induced hyperglycemia.

This research was supported by CHS Biomedical Sciences Program fund and CHS Research Facilitation Grant.
Characterization of SPATA22, a novel mammalian protein required for meiotic progression in mouse germ cells

J. Landaiche, E. Hays, and S. La Salle. Midwestern University, Department of Biochemistry, Downers Grove, IL, USA.

Identifying the cues that govern progression of germ cells through meiosis is critical to our understanding of the mechanisms that lead to the formation of healthy gametes. We have previously characterized the ENU-induced mouse mutation repro42, which causes both male and female infertility due to meiotic arrest. Recombination-based genetic fine mapping in combination with sequencing of candidate genes identified a nonsense mutation in Spata22 (spermatogenesis associated 22), a gene not previously known to play a role in gametogenesis. Analysis of mutant repro42 surface-spread chromatin determined that arrest takes place at the transition between zygonema and pachynema during meiosis I, and that synaptonemal complex (SC) formation, synapsis, and repair of DNA double strand break are all impaired in the absence of SPATA22. Since the precise requirement for Spata22 during meiotic prophase remains elusive, we further characterized SPATA22 regulation and localization during male germ cell development in the mouse. A bioinformatics analysis predicted a number of phosphorylation sites along the SPATA22 sequence, but immunoblotting analysis of testis protein extracts prepared in the presence or absence of phosphatase inhibitors uncovered no shift in molecular weight, suggesting SPATA22 is not phosphorylated. Previous immunohistochemical localization of SPATA22 in adult testis sections indicated SPATA22 is restricted to a specific population of meiotic germ cells. Analysis of surface-spread chromatin confirmed this and showed that SPATA22 is faintly detectable in foci across the nucleus of leptotene spermatocytes, while it becomes more readily detectable in zygotene spermatocytes. By late zygonema, numerous foci of SPATA22 are observed across the nucleus and these are mostly restricted to the SC. SPATA22 foci are observed along the length of all SCs (5-8 foci per SC on average) in a manner similar to RPA1 (replication protein A1), a component loaded onto transitional nodules (TNs) following RAD51 and DMC1, two components of early nodules (ENs). SPATA22 foci are still detected at early pachynema but localization is no longer restricted to the SC, and all foci have disappeared by late pachynema. Since we previously determined that both RAD51 and DMC1 are both present in repro42 mutant spermatocytes, we assessed if the same held true for RPA1. RPA1 was detectable in surface spread chromatin prepared from mutant repro42 spermatocytes. Taken together, these data further support the role of SPATA22 in meiotic prophase and suggest it is involved following formation of ENs.

This work was supported in part by startup funds provided by Midwestern University and by funds from the Biomedical Sciences Program/College of Health Sciences.
Comparison of HDL Antioxidant and Paraoxonase Enzyme Activities

Joseph Lorenz¹, Steven Klotz¹, and Sean M. Lynch²

¹Biomedical Sciences Program, College of Health Sciences, Midwestern University
²Dept Biochemistry, Chicago College of Osteopathic Medicine, Midwestern University

High density lipoprotein (HDL) is instrumental in the biochemical prevention of low density lipoprotein (LDL) oxidation. Paraoxonase-1 (PON1) is a calcium dependent enzyme in part responsible for this protective effect of HDL. The goal of this study was to explore the changes in PON1 antioxidant activity both over time and in different physiological conditions. Taking into account the calcium dependency of PON1, the purpose of our first experiment was to determine whether or not a significant difference in enzymatic activity occurred over the course of an eight day period in HDL isolated with and without calcium available. This was done through the use of a spectrophotometric assay measuring PON1’s phosphotriesterase activity with paraoxon as substrate. The results showed maintenance of approximately 90% PON1 activity for both conditions and therefore did not show any statistically significant difference. For our second experiment, we looked into the effect of calcium on HDL’s antioxidant activity over time. From the data collected over the same eight day period as before, the HDL augmented with calcium sustained 84% inhibition of LDL oxidation compared to HDL lacking calcium which sustained 60% inhibition. After performing a comparative analysis, we found no significant correlation between HDL antioxidant and PON1 activities. To conclude, our study demonstrates that although the presence of calcium may not change inherent phosphotriesterase activity, it can be stated that LDL is significantly more protected from oxidation when HDL is supplemented with calcium during isolation. These findings ultimately further knowledge of lipoprotein activities, and have future implications in the study of cardiovascular disease.

Funding for this project provided by Midwestern University’s Biomedical Sciences Program (JL and SK, and Office of Research and Sponsored Programs (SML).
Cyanobacterium *Anabaena* sp. Lipopolysaccharide (LPS) elicits Release of Matrix Metalloproteinase-9 from Rat Brain Microglia

David Macadam², Mary L. Hall¹, Domonkos Feher³, Philip Williams³, and Alejandro M.S. Mayer¹

¹Department of Pharmacology, ²Department of Biomedical Sciences, Midwestern University, Downers Grove, Illinois
³Department of Chemistry and Biochemistry, University of Hawaii at Manoa, Honolulu, HI

We recently reported that cyanobacterial lipopolysaccharide (LPS) elicited release of superoxide anion \( \text{O}_2^- \), thromboxane B₂ (TXB₂), and tumor necrosis alpha (TNF-α) by rat microglia (BMΦ) *in vitro* (The Toxicologist CD 126 (S-1), 2012). We hypothesized that freshwater cyanobacterium *Anabaena* sp. LPS (AnaLPS) would “classically” activate BMΦ *in vitro* and the concomitant release of matrix metalloproteinase-9 (MMP-9).

**Methods:** AnaLPS was prepared by hot phenol/water extraction. BMΦ were isolated from neonatal rats, and treated *in vitro* with 0.1-10⁵ ng/mL AnaLPS at 35.9 °C for 17 hours. TXB₂ and TNF-α were determined by ELISA, \( \text{O}_2^- \) by cytochrome C reduction, and MMP-9 by zymography. Results: \( \text{O}_2^- \) and TNF-α generation were observed at AnaLPS \( \geq 0.1 \) ng/mL and \( > 1,000 \) ng/mL, respectively, while TXB₂ production was observed at AnaLPS \( \geq 10 \) ng/mL. MMP-9 release was significant at AnaLPS 10,000 ng/mL. **Conclusions:** In our *in vitro* experimental conditions, AnaLPS classically activated BMΦ and triggered \( \text{O}_2^- \), TNF-α and TXB₂, thus confirming our previous observations (2012), and now demonstrating for the first time that microglia release the proinflammatory MMP-9. Taken together our results suggest that proinflammatory mediator release by cyanobacterial LPS -treated BMΦ *in vitro* includes lipids (TXB₂), free radicals \( \text{O}_2^- \), cytokines (TNF-α), as well as enzymes (MMP-9), which may play a role in the putative neurotoxicity of AnaLPS *in vivo*. Continued investigation of AnaLPS chemistry and immunotoxicology are currently ongoing in our laboratories. This research was funded in part by the University of Hawaii at Manoa.

*David Macadam was supported by the Biomedical Science Program.*
TNFR2 Expressing CD8⁺ T Cells Mediate to Upper Genital Tract Pathology in *Chlamydia muridarum* Infected Mice

Allison Maladore¹²*, Joshua D. Thomas¹²*, Srikanth Manam¹, Ashlesh K Murthy¹

¹Department of Pathology & ²Department of Biomedical Sciences, Midwestern University, Downers Grove, IL 60515;

Our group has demonstrated that tumor necrosis factor (TNF)-alpha production from CD8⁺ T cells mediates upper genital tract (UGT) pathology following vaginal chlamydial infection. We recently have also found that tumor necrosis factor (TNF-α) receptors 1 and 2 contribute to *Chlamydia*-induced UGT pathology. TNFR1 is expressed on most cells of the body, whereas TNFR2 is expressed on limited number of cell types including CD8⁺ T cells. In this study, we evaluated the contribution of TNF receptor 2 (TNFR2) expressed in CD8⁺ T cells to UGT pathogenesis following primary intravaginal *C. muridarum* infection. CD8⁺ T cells were purified from spleens of wild type C57BL/6J or TNFR2 KO mice using negative selection magnetic beads, and the purified cells (1 X 10⁷ cells/mouse) were adoptively transferred to TNFR2 deficient mice. One groups of C57BL/6J mice and another group of TNFR2 KO mice not receiving cellular transfers served as positive and negative controls for pathology. The groups (n=8) of mice were pre-treated on days -10 and -3 with depo-provera® and infected intravaginally on day 0 with *C. muridarum* (5X10⁴ IFU/mouse). Vaginal chlamydial shedding was monitored every third day after inoculation and was found to be comparable in all groups of mice. Serum anti-*C. muridarum* total antibody levels were measured on day 45 and were found to be comparable in all groups of animals. On day 80 after primary inoculation, we measured the incidence of hydrosalpinx and the degree of oviduct dilatation in the different groups of mice. As expected, C57BL/6J mice displayed high levels and TNFR2 KO mice displayed significantly reduced and low levels of oviduct pathology. TNFR2KO mice receiving C57BL/6J CD8⁺ T cells, but not TNFR2 KO CD8⁺ T cells displayed oviduct pathology comparable to C57BL/6J mice. These results suggest that TNFR2 expressing CD8⁺ T cells mediate oviduct pathology following genital *C. muridarum* infections in mice.

*This work was supported by Midwestern University Faculty Start-up Fund and NIH Grant 1R03AI088342 to AKM.*

*AM, JDT, and SM contributed equally*
Resuscitative efficacy of centhaquin in a rabbit model of uncontrolled hemorrhagic shock with tissue injury

Nora Mulloy1, Gwendolyn Pais2, Zhong Zhang2 and Anil Gulati2

Biomedical Sciences Program, College of Health Sciences1 and Department of Pharmaceutical Sciences2, Chicago College of Pharmacy Midwestern University, Downers Grove, IL 60515

Background: A significant cause of mortality and morbidity across economic and age groups is hemorrhagic shock resulting from traumatic injury. Centhaquin, a cardiovascular active agent, has shown efficacy as a resuscitative agent in studies of controlled hemorrhagic shock without tissue injury. To better simulate a true clinical scenario, these effects should be explored in a rabbit model of uncontrolled hemorrhage with tissue injury.

Objective: To develop a rabbit model of uncontrolled hemorrhagic shock with tissue injury, and to determine the resuscitative efficacy of centhaquin in this model.

Methods: Male New Zealand rabbits were placed under anesthesia with ketamine and xylazine and a laparotomy was performed with running sutures placed for later closure. Hemorrhage was induced via a single puncture injury to the infrarenal aorta with a 20G needle and the abdomen was immediately closed. After a 15-minute period to simulate arrival of emergency medical services, resuscitation was initiated and continued for 60 minutes. Animals were randomly assigned to one of three groups: Group 1: No resuscitation (control) (n=9), Group 2: normal saline resuscitation to MAP = 45 mmHg (n=13), Group 3: Centhaquin 0.05 mg/kg in normal saline resuscitation to MAP = 45 mmHg (n=11). Maximum infusion rate was set to 5 ml/min and infusion fluid volume was recorded. Animals were observed for an additional hour. The abdomen was re-opened to measure blood loss and animals were sacrificed by exsanguination. Cardiovascular parameters and arterial blood gas analysis was obtained before, following hemorrhage and various times after resuscitation.

Results: Blood lactate increased significantly from baseline value of 1.52 ± 0.27 to 13.53 ± 0.75 mmol/L following hemorrhage; this increase was similar in all groups. Animals that were not resuscitated did not survive to more than 5 min, while saline and centhaquin resuscitated animals survived for 2 hours after which they were sacrificed. Resuscitation significantly decreased lactate levels to 6.65 ± 1.34 and 6.14 ± 0.86 mmol/L in saline and centhaquin treated rats, respectively. The volume of fluid required for resuscitation in centhaquin (133.60 ± 11.91 ml) treated rats was significantly less (p=0.0011) compared to that required in saline (207.82 ± 9.08 ml) treated rats. The blood loss was 44.37 ± 6.55, 40.60 ± 3.12 and 38.34 ± 2.21 ml in no resuscitation, saline and centhaquin resuscitation, respectively. Centhaquin treated rats had less loss of blood compared to no resuscitation group. MAP and body temperature were similar in saline and centhaquin treated groups.

Conclusion: We have successfully developed a rabbit model of uncontrolled hemorrhagic shock with tissue injury in our laboratory and this model can be used to study effect and mechanism of action of various resuscitation procedures and agents. In the present study, centhaquin citrate demonstrated significant efficacy as a resuscitative agent.

Acknowledgements: Centhaquin citrate was synthesized and provided by Pharmazz India Private Limited, Greater Noida, India; courtesy Dr. Manish Lavhale.
Molecular and phenotypic consequences of loss of Prdm16 in a conditional gene trap null allele of Prdm16 during palate development

Brock T. Nelson, Lauren N. Furlan, Lenore Pitstick, and Bryan Bjork.

Department of Biochemistry, Midwestern University, Downers Grove, Illinois

Non-syndromic cleft lip with or without cleft palate (CL/P) is among the most common birth defects, affecting approximately 1 in 700 live births. While no single gene is responsible for CL/P, numerous genes have been discovered that effect pathways involved during craniofacial development. FOXE1, SATB2, MSX1, PAX9 and TBX22 are only a subset of the many genes identified as contributing to the etiology of CL/P. Prdm16 has been shown to be expressed during palate and tongue development during embryonic palatogenesis. We previously demonstrated that loss-of-function ENU-induced and gene trap null alleles of Prdm16 cause craniofacial abnormalities in mouse embryos, specifically cleft secondary palate. We have utilized whole-mount in situ hybridization to initiate the characterization of the molecular consequences of loss of Prdm16 using a conditional gene trap null allele of Prdm16 (Prdm16\textsuperscript{GT}) during embryonic craniofacial development. We also present data from preliminary studies designed to assess the mechanism of clefting in these mutants. We are using palate mesenchyme-specific (Osr2::cre) to ablate Prdm16 specifically in the palate mesenchyme and not the mandible. Our results suggest that Prdm16 may directly or indirectly regulate the expression of several genes of known importance during palatogenesis and craniofacial development. These studies may help to identify additional candidate genes and pathways possibly contributing to the etiology of human clefting.
Effect of Overexpression of miR-34b and miR-140 on p53 Dependent Osteoblast Differentiation.

Shivang M. Shah, Oliver Couture, and Nalini Chandar,

Department of Biochemistry, Midwestern University, 555, 31st Street, Downers Grove, IL 60515. Email: sshah59@midwestern.edu, nchand@midwestern.edu

MicroRNAs, small non-coding RNA sequences, are a relatively novel area of research that has been shown to play a multifaceted role in number of cellular processes by regulating a number of genes. Our laboratory has been investigating the role of p53 tumor suppressor gene in osteoblast differentiation and have found several miRNAs to be modulated in a p53 dependent way. In this study we chose to further analyze two such miRNAs, miR-34b-3p and miR-140-3p. These two miRNAs were chosen because miR-34b has been shown to regulate p53 expression and there is some evidence to show that miR-140 might regulate expression of BMP-2 a bone anabolic agent. Expression vectors containing these miRNAs were stably transfected into MC3T3 osteoblasts and genticin resistant single cell colonies were isolated and expanded. MiR-34b overexpressing cells showed a lower rate of growth when compared to control. MiR-140 overexpression however did not affect growth rate when compared to control. As expected p53 expression was increased in cells expressing miR-34b and not miR-140. Transient transfection of these miRNA constructs also produced similar results. Realtime PCR analyses of these cells showed that overexpression of miR-140 produced a 6 fold increase in BMP-2. In separate studies we were able to demonstrate that p53 acts as a transcription factor to directly affect the BMP-2 gene. These results indicate that miR 34b may play a role in influencing p53 expression and miR-140 may represent a p53 regulated miRNA important during osteoblast differentiation.
TNF-alpha Receptors 1 and 2 Contribute to the Development of Upper Genital Tract Pathology Following Primary Genital Chlamydia muridarum Infection in Mice

Joshua D. Thomas1,2,*, Srikanth Manam1,*, Justin H. Schripsema3, Kyle H. Ramsey3, Ashlesh K. Murthy1

1Department of Pathology, 2Department of Biomedical Sciences, 3Department of Microbiology and Immunology, Midwestern University, Downers Grove, IL 60515

We recently demonstrated that pathogenesis in the upper genital tract (UGT) following primary vaginal Chlamydia muridarum infection in mice is dependent upon TNF-α production. In this study, we evaluated the contribution of two cognate receptors, TNF receptor 1 (TNFR1) and TNFR2 to UGT pathogenesis following primary intravaginal C. muridarum infection (5x10⁴ IFU/mouse), using depo-provera ® treated mice deficient in TNFR1 (TNFR1 KO), TNFR2 (TNFR2 KO), or TNFR1 and 2 (TNFR1/2 DKO), and the corresponding C57BL/6J wild type mice. All groups (n=8) of mice displayed comparable chlamydial clearance following primary bacterial inoculation. The production of IFN-γ, IL-5, TNF-α, and IL-1β in the genital tracts, draining iliac lymph nodes, and spleens on day 9 following inoculation were comparable in all the groups. Serum anti-Chlamydia Total Ab, IgG2c, and IgG1 response on days 14 and 60 following primary inoculation were comparable in all the groups. On day 80 after primary inoculation, TNFR1 KO, TNFR2 KO, and TNFR1/2 DKO mice displayed significantly reduced hydrosalpinx (6%, 44%, and 0% oviducts, respectively), when compared to C57BL/6J mice (75% oviducts). Additionally, all KO mice displayed significantly reduced uterine horn dilatation in comparison to the C57BL/6J mice. Collectively, these results suggest that TNFR1 and TNFR2 do not contribute significantly to chlamydial clearance, but both TNFR1 and TNFR2, with a dominant role for TNFR1, contribute to the UGT pathology following primary genital chlamydial infection.

This work was supported by Midwestern University Faculty Start-up Fund and NIH Grant 1R03AI088342 to AKM, and MWU Department of Biomedical Sciences Thesis Research Fund to JDT. We thank Mr. Mark Zafiratos and Karan Varma for technical assistance.

*JDT and SM contributed equally
Gastric regional differences in nerve-stimulated contractions and relaxations contribute to delayed gastric emptying in type 2 diabetic mice.

Stacey Tinkoff2, K.J. LePard1,2, and Joseph Cellini1

Department of Physiology1, Department of Biomedical Sciences2, Midwestern University, Downers Grove, Illinois

Delayed gastric emptying is prominent in type 2 diabetes mellitus (T2DM). To investigate the relationship between solid gastric emptying rates and nerve-stimulated gastric motility in control and T2DM mice, we hypothesized that decreased emptying rates in T2DM results from decreased cholinergic, excitatory and nitrergic, inhibitory gastric smooth muscle contractions and relaxations. To assess gastric emptying, mice were fed pre-measured meals and allowed 0-3 hours to digest. Stomach contents were weighed to calculate emptying rates. Gastric emptying was slower in T2DM mice (35±4% vs. 52±4%). Fundus, corpus, antrum, and pylorus tissues underwent electric field stimulation (EFS) after treatment with vehicle, 4-DAMP (muscarinic antagonist), or L-NNA (NOS inhibitor). Corpus, antrum, and pylorus control tissues generated stronger contractions than diabetic tissues. 4-DAMP decreased EFS contractions more in diabetics (58±3%) than in controls (38±4%). L-NNA increased contractions more in control fundus (170±25%) than diabetic (77±10%). Contrastingly, L-NNA increased relaxation in diabetic corpus (42±10%) and antrum (40±5%). Smooth muscle relaxation was studied by adding SNP (NO donor) to pre-contracted tissues. Significant relaxations of the diabetic pylorus were evoked by SNP. This study determined that diabetics experienced increased contraction of the fundus and increased relaxation in the corpus and antrum all of which may stem from altered NO production and lead to retention of stomach contents.

This research was supported by the CHS Biomedical Sciences Program funds.
Mucin 3 (MUC3) Decreases Apoptosis in Rheumatoid Arthritic Synovial Fibroblasts

Matthew Wu1, Brian Zanotti2, Michael Volin2

1Biomedical Sciences Program, College of Health Sciences, 2Department of Microbiology and Immunology, Chicago College of Osteopathic Medicine, Midwestern University

BACKGROUND: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by the inflammation of synovial tissue. Pathogenesis of RA is characterized by lymphocyte and macrophage recruitment, angiogenesis, and hypertrophy/hyperplasia which eventually form a pannus resulting in inevitable joint damage. A feature of interest that enhances RA is decreased synovial fibroblast (SF) apoptosis that may promote hypertrophy and hyperplasia of the synovial lining. Decreased apoptosis has been implicated to increasing the survival of RA synovial fibroblasts and result in the thickening of the synovial lining present in RA synovial tissue. A key cell type involved in these processes is the SF that normally serves multiple functions throughout development. In a pathogenic state, SFs not only increase in number, but progress inflammation through production of proinflammatory mediators and anti-apoptotic factors. One family of molecules hypothesized to be involved in these processes is the SF that normally serves multiple functions. In particular, Mucin 3 (MUC3) has previously been identified to be overexpressed in cancer in addition to RA implicating its role as an anti-apoptotic factor in the pathogenesis of RA. OBJECTIVE: The purpose of this study was to further determine the role of mucins in particular Mucin 3 as an anti-apoptotic factor. METHODS: RA SF were treated with specific MUC3 siRNA in order to knockdown MUC3 expression. MUC3 knockdown was verified using Western Blotting with anti-MUC3 antibodies. Upon knockdown of MUC3, apoptosis was induced with BAY 11-7082, a NF-κB inhibitor. TUNEL assays and flow cytometry were used to determine the altered status of SF apoptosis. RESULTS: MUC3 was successfully knocked down using specific MUC3 siRNA. Next, apoptosis was induced in RA synovial fibroblasts by treating the cells with BAY 11-7082. Finally, knockdown of MUC3 in RA synovial fibroblasts resulted in an increase of BAY 11-7082 induced apoptosis. CONCLUSION: These results show that knockdown of MUC3 leads to increased apoptosis of RA synovial fibroblasts. Thus, the increased MUC3 expression by RA synovial fibroblasts may lead to a decrease in apoptosis of these cells promoting hypertrophy and hyperplasia of the synovial lining in RA.

This research was supported in part by the College of Health Sciences Biomedical Sciences Program (MW) and NIH grant R15AR056463 (MV)
CD8\(^+\) T cells and TNF-alpha Contribute to the Development of Atherosclerotic Pathology Following Primary Pulmonary \textit{Chlamydia pneumoniae} Infection in Mice

Mark T. Zafiratos\(^{1,2,*}\), Srikanth Manam\(^{1,*}\), Kyle K. Henderson\(^{3}\), Ashlesh K. Murthy\(^{1}\)

\(^{1}\)Department of Pathology, \(^{2}\)Department of Biomedical Sciences, \(^{3}\)Department of Physiology, Midwestern University, Downers Grove, IL 60515

Atherosclerosis leads to cardiovascular disease which is the leading cause of death in developed countries and is on the rise in developing countries. \textit{Chlamydia pneumoniae} is an obligate intracellular pathogen that infects the respiratory tract and is an important cause of community-acquired pneumonia. In addition to the effects of the acute infection in the respiratory tract, \textit{C. pneumoniae} infections have been identified as a strong risk factor for acceleration of atherosclerotic disease in the chronic phase. CD8\(^+\) T cells and TNF-\(\alpha\) have independently been implicated in the progression of atherosclerosis and are also induced during \textit{C. pneumoniae} infections. In this study, we evaluated the contribution of CD8\(^+\) T cells and TNF-\(\alpha\) production to the pathogenesis of \textit{C. pneumoniae}-induced atherosclerosis. To this end, C57BL/6J wild type mice, CD8 KO, and TNF-\(\alpha\) KO mice were intranasally infected on days 0, 14, and 28 with \textit{C. pneumoniae} and placed on a high-fat, high cholesterol diet. Weight change was monitored every two or three days between days 0-60 following primary infection as a measure of clinical illness. Infected CD8 KO, and TNF-\(\alpha\) KO displayed reduced bodyweight compared to infected wild type mice, suggesting a role for these components in protection against acute respiratory infection. CD8 KO, and TNF-\(\alpha\) KO mice displayed comparable serum anti-chlamydial antibody response at days 14, 60, and 90 after initial infection, suggesting the induction of robust and comparable adaptive immune responses in the different groups of mice following infection. Morphometric analysis in thoracic aortic segments was conducted at day 100 to measure atherosclerotic progression. Infected CD8 KO, and TNF-\(\alpha\) KO displayed significantly reduced pathology compared to infected wild type animals, suggesting these immune components contribute to \textit{Chlamydia}-induced atherosclerotic disease. Serum cholesterol levels on days 60 and 90 following initial infection were comparable in all groups of infected animals. This suggests that the observed differences in atherosclerotic disease were not due to differences in cholesterol profiles. Additionally, atherosclerotic pathology was greater in each infected mouse group compared to the mock-infected high-fat, high cholesterol diet fed C57BL/6J mice suggesting that the observed differences pertain to atherosclerotic effects of \textit{C. pneumoniae} infection and not that of the diet. These results suggest that CD8\(^+\) T cells and TNF-\(\alpha\) may mediate protective effects during acute respiratory \textit{C. pneumoniae} infection, but may contribute to atherosclerotic disease in the chronic phase.

This work was supported by Midwestern University Faculty Start-up Fund and NIH Grant 1R03AI088342 to AKM, and MWU Department of Biomedical Sciences Thesis Research Fund to MTZ. We thank Mr. Joshua Thomas and Karan Varma for technical assistance.

*MTZ and SM contributed equally
Occupational Therapy
The Effects of Scuba Diving on Occupational Performance in Individuals with Autism Spectrum Disorders

Shane Allen, Kelly Hayn, Megan Rowland and Kimberly Bryze

Occupational Therapy Program, College of Health Sciences, Midwestern University, Downers Grove, Illinois

**Purpose:** The purpose of the study was to determine how scuba diving affects individuals with Autism Spectrum Disorders (ASD), specifically their occupational performance and social participation. The perceived benefits from the perspectives of the individuals with ASD, their parents, and leaders of scuba diving groups were also included.

**Method:** A phenomenological study was conducted with 10 individuals with ASD and their parents, and 6 scuba diver leaders. The participants were recruited via electronic flyers, phone calls and emails through the Diveheart Foundation, an organization that offers scuba diving opportunities for individuals with disabilities. Individual, semi-structured interviews were conducted with each participant and parent, and a focus group was conducted with the leaders from Diveheart. The *Short Child Occupational Profile (Scope) Parent Report Form* to obtain descriptive data about each participant’s occupational performance. The constant comparative method of analysis was utilized to identify prominent themes. The student researchers reviewed the transcripts, independently identified common words, phrases and themes, then collectively ascertained salient themes. The themes were then compared within each group (participants, parents, and leaders), and across groups to identify overarching constructs.

**Results:** Four major themes were identified: *Feeling better about myself and what I can, Finding sensory freedom in the water, Social participation, and Not being defined by disability (or, everybody’s equal underwater)*. These themes were identified across all groups (participants, parents, and leaders). The findings suggest that scuba diving can promote performance and participation for individuals with ASD. Overall, scuba diving seems to be a beneficial or even therapeutic activity for individuals with ASD on multiple levels. The benefits identified indicate that scuba diving has the potential to be used as an occupation-based intervention and that occupational therapists who are involved in these scuba diving programs could facilitate their therapeutic value.
Children with Developmental Disabilities and Their Motivation to Play

Authors: Lindsey Askins, OTS-II, Dagmara Szewerniak, OTS-II & Brittany Diasio, OTS_II
Faculty Advisor: Susan M. Cahill, PhD, OTR/L

CHS- Occupational Therapy, Midwestern University, Downers Grove, Illinois

Abstract

Aim: The purpose of this phenomenological qualitative study was to examine how and when children with developmental disabilities, between nine and twelve years old, spontaneously demonstrated play behaviors indicative of intrinsic motivation.

Methods: Data was collected from the six child participants and five parent participants through the use of a formal evaluation tool and semi-structured photo-elicitation interviews. The Pediatric Volitional Questionnaire was used to obtain objective observation data of children engaging in play within the context of their natural environment. The PVQ consists of 14 items and the tool was administered twice to each child. In addition to the PVQ administration, a semi-structured interview was conducted with each of the child participants’ parents. Prior to the interview, parents were asked to take photographs to capture the child's demonstration of various volitional behaviors in natural environments based on specific descriptors derived from the PVQ. The interviews were then conducted using a photo-elicitation technique, with the parents’ photographs serving as the basis of the interview.

Results: Based on the PVQ administration and the interviews, two primary themes emerged from the data. Overall, the children who participated in this study sought out play experiences in their natural environments with which they were familiar. Specifically, they sought out experiences that afforded them the opportunity to exercise control over their environment and create a sense of predictability. Each of the children assumed the role of “orchestrator” and conducted his or her engagement in play occupations. The children demonstrated some spontaneous play within their social environment, however many developmentally age-appropriate behaviors were not observed.

Conclusions: The results suggest that children with developmental disabilities spontaneously demonstrate some behaviors associated with the intrinsic motivation to play in social environments when they: 1) have the opportunity to control specific environmental parameters and 2) orchestrate events. Even when many resources are made available to them within a rich social environment (e.g., toys, pets, siblings), children with developmental disabilities often required additional support to try new things, seek challenges, remain task directed and pursue activities to completion. In order to increase participation and develop competency in play, occupational therapists should create opportunities that complement the child’s natural desire for control, yet challenge him to expand his play repertoire in order to further develop skills.

Key Words: Occupational Therapy, Pediatrics, Developmental Disabilities, Volition
The contribution of occupational therapy for unmet life skill needs of children in the foster care system

Authors: Prerna Basnet, OTS-II, Cheryl Bathan, OTS-II, & Ashley Mcgaughy, OTS-II
Faculty Advisor: Mark Kovic, OTD, OTR/L
CHS – Occupational Therapy, Midwestern University, Downers Grove, Illinois

Abstract
The purpose of this study was to determine how occupational therapists can address limitations and barriers faced by children in the foster care system with regards to learning adequate life skills. This study also attempted to gather information regarding experiences of foster parents concerning developmental milestones and services provided from foster care agencies. Qualitative data was gathered through conducting interviews via phone. Interview questions covered topics such as experiences with occupational therapists, necessary life skills, whether any services were provided and important factors one should be aware of before committing to adoption. Three adoptive parents and one foster parent participated in this study. The results indicated that there were three main themes that related to unmet life skills, which included lack of social skills, self-care, and education/job skills. These parents also highlighted the definite gap of services provided verses services needed. Based on the interviews conducted there appears to be a need for occupational therapy in the foster care system.

Keywords: Occupational therapy, foster care children, life skills, adoptive parents
**Experiences of Role and Responsibility Changes in Transitionally Housed Single Mothers**  
Authors: Cara Bredeson, OTS-II; Natalie Cramarosso, OTS-II; & Chelsey Straight, OTS-II  
Faculty Advisor: Emily K. Simpson, PhD, OTR/L  
*College of Health Sciences, Occupational Therapy  
Midwestern University, Downers Grove, Illinois*

**Aim:** The purpose of this study was to explore the life experiences of single mothers living in transitional housing facilities and the impact that residential displacement has had on both the role of mother and their participation in meaningful activities.

**Methods:**  
A phenomenological study was conducted on the role and responsibility changes of mothers living in transitional housing. Participants were referred by transitional housing staff and provided written informed consent as well as consent to be audiotaped. The Occupational Performance History Interview-Version 2.1 (OPHI-II) was used to conduct individual interviews with five participants and a 60-minute follow up focus group was also conducted with three additional participants. The constant comparative method of analysis was used to assist in identifying themes across the data. Efforts to enhance rigor included the following: 1) three researchers coded each transcript, 2) data analysis meetings were conducted to review findings, and 3) findings/interpretations were peer reviewed.

**Results/ Conclusions:**  
Three themes were identified as being consistent with the data: prior events, adaptation to supportive living, and role transition. Prior research has identified that the structure and environment within transitional housing for women can both support and inhibit many of their roles and responsibilities. Overall, the findings within this sample support previous literature and emphasize the importance of increasing employment opportunities for occupational therapists within transitional housing facilities. Occupational therapists can assist mothers by collaboratively working with them and their families to enhance role participation, routines and occupational engagement.
Young Adults’ Perspective on Parental Cancer: A Mixed Methods Study on Resilience, Coping, and Occupational Identity

Corinne Beskovich, Vanessa Niland, Marie Therese Smith and Kimberly Bryze

Occupational Therapy Program, College of Health Sciences, Midwestern University, Downers Grove, Illinois

Purpose: The purpose of this study is to examine resilience, coping, and occupational identity of young adults who have encountered, or are currently experiencing, parental cancer.

Method: This study was conducted using a mixed methods framework with twelve participants between the ages of 20 and 30 years. Quantitative data was collected using the Connor-Davidson Resilience Scale (CD-RISC). Qualitative data was collected through the use of the Occupational Performance History Interview (OPHI-II) and a cancer narrative interview developed by the researchers.

Results: Quantitative results found no significant differences in resilience within this sample and when compared to other samples of young adults. Qualitative data analysis revealed four themes which included Protecting the Parent from Painful Emotions (which emphasized the young adults’ need to guard their parent from any negative emotions); Resultant Actions given the Reality of Cancer (which stressed their need to take preventative steps against cancer); Time is Valuable: Family Time (which highlighted the importance of dedicating more time to their parent); and, Taking on Additional Responsibilities (which focused on ways in which the young adult assumed extra obligations for their parent during this experience). Overall, findings suggest a shift in occupational identity and occupational role enactment in young adults due to parental cancer. More research needs to be completed with a larger sample size in order to get a better understanding of how coping mechanisms and resilience impact occupational identity and roles in young adult children.
Key determinants to clinical reasoning for use of electrical stimulation with persons with stroke

Authors: Jacqueline Cummings, OTS-II, Lana Lobdell, OTS-II, & Sarah Shivley, OTS-II
Research Advisor: Mark Kovic, OTD, OTR/L

College of Health Sciences, Occupational Therapy
Midwestern University, Downers Grove, Illinois

Purpose: The purpose of this study is to explore how electrical stimulation (ES) is used within the clinical setting by occupational therapy personnel, on patients with an upper motor neuron lesion (i.e. Cerebral Vascular Accident (CVA/Stroke)).

Significance: Occupational therapy personnel play a crucial role in caring for patients with upper extremity (UE) hemiparesis following a stroke. It is the therapist’s responsibility to identify appropriate and effective clinical interventions that may contribute to the restoration and functioning of an individual’s UE, and overall enhance their quality of life.

Methods: For the task of data collection, the investigators have developed a collaborative relationship with occupational personnel from SWAN Rehabilitation, and Mayo Clinic, who have agreed to assist with this study. Demographic and interview questionnaires were sent out to occupational therapy personnel at SWAN Rehabilitation in the Southwestern region of the U.S. and Mayo Clinic in the upper Midwestern region of the U.S. The demographic questionnaire obtained background information about the participating clinicians. The interview questionnaire gathered specific information related to how ES is used by individual occupational therapy personnel, during their treatment sessions.

Results: When comparing the results of our data, we came across multiple similarities among how electrical stimulation was utilized in the clinic by the participating research participants. Demographics among the therapist's differed; however, the way in which they utilized electrical stimulation was very similar. The most notable differences in demographics included age, year of graduation and level of degree, as well as, region of education. The clinical outcomes among the research participants included strengthening, muscle re-education, and sensory re-education. However, the type of electrical stimulation utilized by the therapists differed slightly. The participants reported that they both used NMES in similar ways, however, while comparing their responses from the interview questionnaire, one therapist listed the specific type of current used, while the other therapist indicated using a pre-programmed setting. This provided the researchers into insight about clinical reasoning.

Conclusion: In conclusion, occupational therapists’ clinical reasoning on ES still remains an area that needs to be explored and researched further. It is the opinion of these researchers that the location, severity, and time since the CVA occurred will be, key determinants in the type of electrical stimulation utilized on each individual patient, as well as, the time since the CVA occurred. From our research, there is no clear standard of care as to how clinicians should utilize ES on a patient with an UMN lesion.
Occupational Therapy Practitioners' Comfort Level Addressing Driving with Youth who Experience Difficulty Learning

Authors: Kathryn Dragich, OTS-II, Erin Mangin, OTS-II, & Shannon Yorke, OTS-II
Faculty Advisor: Brad Egan, OTD, OTR/L
CHS – Occupational Therapy, Midwestern University, Downers Grove, Illinois

**Aim:** The purpose of this quantitative research study was to examine occupational therapy (OT) practitioners' comfort level addressing driving with youth (ages 13-22) who experience difficulty learning due to limitations in motor control, visual perception, and/or executive functioning, all of which may negatively impact their ability to learn to drive and obtain a driver’s license.

**Methods:** A study-specific, online survey was developed to examine how occupational therapists and certified occupational therapy assistants who were currently serving clients between the ages of 13 and 22 in a variety of practice settings view this emerging practice area. Participants were recruited through snowball sampling. Data was analyzed using Microsoft Excel and SurveyMonkey®. Inferential and descriptive statistics were performed related to comfort level of addressing the occupation of driving, comfort level of addressing the components of driving, comfort level as it relates to level of formal education of driving, and barriers to providing driving related services.

**Conclusions:** Although driving is clearly presented in the OT Practice Framework and AOTA has identified driving for teens with disabilities as an emerging and high priority area of practice, very few practitioners in this study felt comfortable addressing driving. Interestingly, however, almost all clinicians reported feeling very and most comfortable assessing and addressing underlying components of driving (i.e. motor control, visual perception, and executive functioning). According to responses, clinicians who felt more comfortable addressing driving with youth reported that driving was formally included in their occupational therapy training, which further underscores the relationship between including driving-specific content in entry-level OT curricula and efforts to prepare future clinicians to meet the driving needs of the growing number of youth with disabilities. In addition to limited training, respondents also identified that the following barriers most significantly impact service provision: funding and reimbursement issues, appropriateness of driving as an IEP transition goal, uncertainty about what constitutes driving-related services, and a lack of resources at worksites to effectively implement driving-specific interventions.

**Key Words:** Occupational Therapy Practitioner, Comfort Level, Driving, Difficulty Learning
Education and Technology used to Improve the Quality of Life for People with Diabetes Mellitus Type 2

Authors: Brooke Dudley, OTS-II; Brianne Heiland, OTS-II; & Elizabeth Kohler-Rausch, OTS-II
Faculty Advisor: Mark Kovic, OTD, OTR/L

College of Health Sciences, Occupational Therapy
Midwestern University, Downers Grove, Illinois

Background: The incidence of diabetes mellitus type 2 (DMT2) is expected to continue to rise. Current research has analyzed various tools, strategies, programs, barriers, and supports in regards to the self-management of this condition. However, past researchers have yet to analyze the education process; including the adaptation of specific strategies in daily activities and roles as well as the influence of healthcare providers in the integration of these strategies.

Objectives: The purpose of this qualitative study was to identify the strengths and limitations of the current model of diabetes education in the United States, hypothesize how technology can impact occupational balance and quality of life, and explore occupational therapy’s role in diabetes education and self-management.

Methods: Key informants on diabetes education were recruited via snowball sampling from diabetes education centers through the American Association of Diabetes Educators. Semi-structured interviews were conducted with participants.

Results: Healthcare practitioners convey limited knowledge of DMT2. Individuals with DMT2 often have limited understanding of the implications of poor self-management. There appears to be no consistent standard of care for how to effectively incorporate self-care strategies. There is limited education for the use of technology for self-management. Diabetes educators describe that technology could be beneficial.

Conclusion: Findings suggest the key relevance of care providers in emphasizing the implications of poor self-management, how a trans-disciplinary approach may enhance the education process, and the impact of a lack of technologies, which incorporate a holistic approach to diabetes self-management.

Contribution to occupational therapy: Occupational therapists may address some of the limitations in the current model of diabetes education. Occupational therapists may address quality of life, activity limitations, barriers to routine management, and occupational balance for individuals with DMT2 in a variety of settings.

Keywords: health promotion, quality of life, diabetes mellitus type 2, technology, health education
Facilitating Leisure-Time Physical Activity for American Veterans with Traumatic Brain Injury and Posttraumatic Stress Disorder

Brenna Duffy, Nathan Hebda, and Kimberly Bryze, PhD, OTR/L

Occupational Therapy Program, College of Health Sciences, Midwestern University, Downers Grove, Illinois

Purpose: The purpose of this research is to examine the association between physical activity and occupational performance in veterans with TBI or PTSD. The research questions that guided the study were: What barriers and supports exist for participation in leisure time physical activity? and What meaning is attributed to participation in leisure time physical activity?

Methods: A qualitative, phenomenological approach to study the meaning of leisure time physical activity as well as the supports and barriers to participation was utilized. Seven participants were recruited through local organizations serving veterans with disabilities specifically TBI or PTSD. Semi-structured interviews were conducted in person with four participants and a semi-structured discussion group was conducted with three participants. These interviews were audiotaped and transcribed verbatim. The data were analyzed by three researchers throughout the process of data collection using constant comparison methods to identify major themes, concepts and typologies and detect variability and relationships among data. The literature review was triangulated with the data and supported the identified themes.

Results/Conclusions: Seven identified themes were associated with meaning and seven themes were associated with supports and barriers. Most of our themes corroborate findings from previous research studies, however, two themes were unique to this study: helping/guiding and the importance of activity. Veterans with TBI or PTSD may find greater significance in physical activities in which they can directly or indirectly help, guide, or share with other veterans. Further, the physical activities chosen by the veterans involved activities with a purpose or goal rather than mere exercise. Meaningful physical activities, such as fishing or hunting with others, was found to provide occupation and structure to the daily routines of veterans with TBI or PTSD.
Aim: The purpose of this study was to gain knowledge regarding the amount of education given to caregivers who are providing care to individuals who have sustained a traumatic brain injury (TBI). Using this knowledge, researchers sought to determine possible evidence for the creation of an education program in which the preparation and recovery process of individuals and their caregivers who are experiencing the effects of a TBI are addressed to facilitate more efficient patient outcomes.

Methods:
A mixed-methods study on caregiver education regarding traumatic brain injury was conducted with a sample size of 17 participants between the ages of 18 and 65. Eleven participants were individuals with a TBI, while six participants were caregivers of individuals with a TBI. The participants were located through key informants working with a Clubhouse in the Chicago metropolitan area and a Clubhouse in northeast Florida. Individual, semi-structured interviews were conducted with participants from the Chicago area Clubhouse. Interviews were audio-taped and transcribed verbatim. Participants from the Clubhouse in Florida completed surveys in which they were given questions with specified options to choose from; however, there was also an option to obtain more information from participants by asking “Why?” or providing a space for “Other”. The constant comparative method of analysis was utilized to identify prominent themes in the semi-structured interviews as well as to guide further data collection and analyses. Researchers coded each interview transcript and analyzed quantitative data collected through the surveys to determine study conclusions.

Results/ Conclusions:
From the semi-structured interviews and survey findings, there were seven themes that emerged for individuals with a TBI and seven themes that emerged for caregivers. Overall, these themes indicate that formal training, further education, and the ability to provide emotional support should be addressed during caregiver education. The implications of these themes indicate to the researchers that occupational therapists should use their scope of practice to create and promote an education program to provide adequate caregiver preparation.

Key Words: Traumatic Brain Injury, Caregiver, Caregiver Education, Occupational Therapy
Improving adaptation in adults with acquired disability: Using narratives to support identity reconstruction – A systematic review

Debbie Morey and Kimberly Bryze

_Occupational Therapy Program, College of Health Sciences, Midwestern University, Downers Grove, Illinois_

OBJECTIVE. To determine if the use of narratives as intervention can improve adaptation through identity reconstruction in adults with acquired disability.

METHOD. A systematic review of the literature was conducted, searching electronic databases specific to occupational therapy practice from the years 1993 to 2013. This search, guided by the application of specified inclusion and exclusion criteria, yielded 57 qualitative journal articles. The studies were analyzed and coded for consistent terms and themes.

RESULTS. All studies addressed the use of narratives in occupational therapy practice, but differed with respect to patient characteristics, types of narratives utilized and analysis of data. Results suggest that occupational therapists can improve adaptation in adults with acquired disability with the use of client narratives in therapeutic treatment.

CONCLUSION. Narratives enable deeper understanding of past events and provide a framework for the creation of future life stories. When used in treatment, narratives can improve adaptation in adults with acquired disability; enabling clients to reconstruct identity by linking past and present events with possible visions for the future.
Ex-offenders in Transitional Housing: Needs for Successful Community Reintegration

Author: Nikki Neumann, OTS-II
Faculty Advisor: Emily K. Simpson, PhD, OTR/L
College of Health Sciences, Occupational Therapy
Midwestern University, Downers Grove, Illinois

Purpose
The purpose of this study was to identify the life skills necessary for successful community reintegration and to describe the difficulties encountered upon release from prison among ex-offenders.

Methods
A phenomenological study was conducted with 31 ex-offenders between the ages of 20 and 66 currently residing at St. Leonard’s House, a transitional residential facility (TRF) in Chicago. Data was collected via a focus group and a qualitative survey. Both the student researcher and the faculty advisor analyzed data using content analysis to identify common themes.

Results/Conclusions
Themes identified include: Reintegration Process, Barriers to Reintegration, and Facilitators of Reintegration. Barriers include stigma, lack of services in prison, lack of support in and out of prison, and lack of structure upon release. Facilitators include individualized services in prison, access to work and education before release, and connection to family and community.
Participants of this study identified the need for supportive, rehabilitative services both within and outside of prison to break the cycle of recidivism and return ex-offenders to productive, successful lives. The absence of facilitators of successful reintegration in the participants’ lives underscores the impact of barriers to reintegration. Occupational therapists are uniquely qualified to assist offenders with the skills they need for successful reintegration before and after release from prison.
Impact of cancer diagnosis on adolescents and young adults: 
Systematic review

Author: Allison Porschakin, OTS-II
Faculty Advisor: Mark Kovic, OTD, OTR/L
College of Health Sciences, Occupational Therapy
Midwestern University, Downers Grove, Illinois

Purpose:
The impact of cancer has continued to gain attention. However, less focus has been on the impact
of cancer on younger populations. The purpose of this review was to explore the current research
related to the impact of a cancer diagnosis on adolescents and young adults.

Methods:
A thorough search was conducted, focusing only on literature from 2000 onward. The final
analyzed sample of fifty-three articles included qualitative data, quantitative data, systematic
reviews, and research review articles. The articles were analyzed to determine main conclusions,
common themes, and areas for future research.

Findings:
The major themes found throughout the research included unmet needs and the need for age
appropriate care, the psychosocial impact of the diagnosis, the long-term impact of cancer, and
the positive impact of the diagnosis. Common issues this population faced were feelings of
isolation, loss of identity, and re-adjustment to life after their diagnosis. Overall occupational
therapy (OT) services could benefit this population during the adjustment period after initial
diagnosis. OT is particularly skilled to assist with occupational engagement. The research
suggests that although this population experiences many of the same physical side-effects as
older populations, their experience is unique and requires special attention.
Occupational Therapists’ Perceptions of Best Practice for Parkinson’s disease

Authors: Alex Robinson, OTS-II, & Kiley Rich, OTS-II
Faculty Advisor: Emily K. Simpson, PhD, OTR/L
CHS – Occupational Therapy, Midwestern University, Downers Grove, Illinois

Purpose:
The purpose of this study was to identify occupational therapy practitioner perspectives on best practice for Parkinson’s disease (PD), including the identification of common intervention strategies and the clinical reasoning that supports their use in practice.

Methods:
A survey design was utilized in an attempt to replicate findings from a Delphi survey conducted in the UK. The Delphi survey was modified to reflect practice in the USA and was administered electronically to eligible occupational therapy practitioners in order to provide information regarding their experiences providing occupational therapy (OT) services to individuals with PD. Study participants were recruited by way of key informants, snowball sampling, electronic postings to OT Connections (an open forum for members of AOTA), LSVT certified clinician database, and USA state OT association Facebook pages. Of the 255 individuals who initiated survey completion, 209 responded to all questions totaling an 82% response rate. Data was initially reviewed by researchers in order to visually scan for patterns or apparent trends. Following this, data was analyzed using descriptive statistics in an attempt to create a comprehensive display of the variation within findings.

Conclusions:
Overall, the findings of this survey provide an increased understanding of current occupational therapy practice as it relates to Parkinson’s disease. This research may serve as a step towards identifying best practice, a concept that remains undefined for this population. Specific findings related to common intervention strategies and common intervention influences may further assist in understanding of the complexity of best practice.

Key words: occupational therapy, Parkinson’s disease, best practice, clinical reasoning, Delphi survey
Survivors of brain injury: The narrative experiences of undergraduate students
Authors: Jamie Rotter, BS/OTS, Kara Lyons, BS/OTS, Antonina Marrone, BS/OTS
Research Advisor: Susan M. Cahill, PhD, OTR/L
College of Health Sciences, Occupational Therapy
Midwestern University, Downers Grove, Illinois

Purpose: The purpose of this study was to better understand the lived experiences of individuals who self-identified with a traumatic brain injury (TBI) and attended a two-year or four-year college. The intent was to explore the social and academic demands faced by college students with a brain injury in order to determine if there are areas in which support services may be beneficial. Through this study the researchers explored: 1) the influence of a brain injury on the role of a student; 2) the areas of student life that were most impacted; and 3) the services that were offered, utilized, and/or beneficial in supporting academic and social participation.

Methods: The eight participants were recruited via flyer distribution and through the investigators’ professional networks. Researchers utilized a phenomenological approach in order to discover emerging patterns among the participants’ experiences of meeting the academic and social demands associated with being a college student. These experiences were captured through the use of semi-structured interviews conducted by three student researchers. The interviews were transcribed verbatim and the data were analyzed using the constant comparative method and filtered through the investigators’ conceptual framework (i.e., the Person-Environment-Occupation paradigm).

Results: Data analysis revealed that all of the participants experienced the phenomenon of being “a square peg in a round hole”. This sense of misfitting emerged from: 1) the interaction between the participants’ perception of their abilities and their actual abilities, 2) the demands and expectations associated with the student role, and 3) the interaction between themselves and the college environment. Participants identified coping strategies and implemented them with varying levels of success in an attempt to better “fit”.

Conclusions: The expectations and demands associated with attending a college or university influenced each participant’s perception of his or her own abilities and the coping strategies implemented to better manage life as a college student. The college environment played a major role in each participant’s perception of his or her academic abilities, as well as the ability to form relationships with professors and peers. Stigma was an overarching barrier within each participant's environment which impacted his or her decision to share or hide their brain injury with others, and a determining factor in whether or not additional services were sought. The interplay between the above factors greatly impacted the participants’ occupational performance as college students.
**Occupational Therapy Interventions with Cancer Patients:**
**A Systematic Review of Outcomes-Based Literature**

Authors: Rebecca Yelle, OTS-II  
Faculty Advisor: Emily Simpson, PhD, OTR/L  

*CHS-Occupational Therapy, Midwestern University, Downers Grove, Illinois*

**Purpose:** The purpose of this qualitative systematic review was to examine the evidence that exists to support specific occupational therapy interventions within cancer rehabilitation.

**Methods:** The systematic review was conducted through electronic search of the databases PubMed, CINAHL, EBSCO, & Medline. Additionally, an exhaustive search of three journals specific to occupational therapy (AJOT, CJOT, BJOT) was also conducted. Inclusion criteria for articles required articles to be: published 2000-to current, specific to outcomes of occupational therapy (OT) intervention, peer reviewed, experimental in design, and within the adult population who have had or currently have cancer. Interventions that required certified training in lymphedema were excluded due to the ability of other disciplines to obtain certification. 167 articles were examined through abstract review. 49 full articles were thoroughly reviewed and, of those, 4 articles were found to fit the inclusion criteria.

**Results:** Research studies included a randomized control trial (RCT) of a breast cancer recovery program, a single center factorial RCT of an educational intervention for cancer related fatigue, a retrospective audit of the use of relaxation as an intervention for patients with cancer, and a feasibility study of an RCT of a telephone-delivered-problem-solving-occupational therapy intervention for rural breast cancer survivors. Six major themes were identified from content analysis: 1) utility of OT in addressing barriers to participation, 2) need to individualize care, 3) lack of OT research, 4) application of interventions with other populations, 5) exercise and relaxation programs, and 6) support for program development.

**Findings:** The review found insufficient evidence to support the broad range of occupational therapy interventions done within the area of cancer rehabilitation, and revealed that research does not fully represent the role of occupational therapists in this area. There is a larger body of qualitative evidence that exists to describe the experiences of cancer patients and the role of occupational therapy in oncology. The results of the review underscore the need for more experimental research with outcomes measures for this population in order to better support AOTA’s vision of evidence based practice.
Implementation of an animal assisted therapy group for severely mentally ill clients residing in a long term care facility.

Krista Escamillo; Dr. Diana Semmelhack, PsyD, ABPP

Department of Psychology, Midwestern University, Downers Grove, Illinois

There are few treatment options for severely mentally ill adult clients residing in long term care facilities outside of medication management and behavioral/life skills management groups. According to the National Alliance on Mental Illness (NAMI) and other research, studies suggest that a biopsychosocial model of treatment most effectively facilitates positive therapeutic change in this population. People are social beings and require emotional contact with others. Individuals in institutions typically feel isolated and disconnected from society. Additionally, many cases of individuals in these institutions perceive themselves to be depersonalized, marginalized, and isolated. It is hypothesized that increasing opportunities for positive interpersonal interactions through animal assisted therapy results in a positive outcome. In response to this hypothesis, we propose a six week animal assisted therapy group. The group is designed to meet for 45 minutes weekly and will have a membership of eight participants. The social services department of the institution will refer participants for this research study/therapy group. A graduate student and the certified therapy animal will facilitate the group. Topics to be covered during the six week program include: week 1 – the purpose of animal assisted therapy; week 2 – pets and their value to individuals; week 3 – pets and the grieving process; week 4 – grieving the loss of a pet; week 5 – self-care and grooming; week 6 – social skills and interactions. After the completion of the program, researchers will assess the effectiveness of the program. Effectiveness of the program includes: the quality of positive interactions between group members, the members’ overall evaluation of the effectiveness of the group, and the group leaders’ countertransference to the group, members, and the certified therapy animal. Possible limitations of the study include members’ severe psychopathology, the restrictiveness of the setting, and organizational resistance to implementing such group with an animal in a state licensed institution. Solutions to these problems include the well-contained six-session structure, consistent feedback from an outside organization through professional animal therapy training, and the leader’s openness to accept feedback from the individuals involved in the group. Future quantitative measures will explore increases in group cohesion, decreases in levels of depression and anxiety, and an increase in members’ capacity for self-initiative.
Benefits of Sutureless Wound Healing in Third Molar Extractions.

Lama Alghanem, Hector Trevino, Bilal Alnahass, Katie Riesenber, Emily Carley, Raj Darji, Cory Grathwol, Ryan Kuebler, Matthew Manious

College of Dental Medicine – Illinois, Midwestern University
Downers Grove, Illinois

INTRODUCTION: Third molar extractions are a common yet complicated surgical procedure. Postoperative complaints often include pain, infection, and hemorrhage. Sutures are traditionally used post operatively for third molar extractions to aid in the wound healing process. The purpose of our study is to evaluate the surgical outcome advantages to when alternatives to sutures are used for wound closure.

MATERIALS AND METHODS: In our study we performed a literature search of PubMed articles supporting the use of sutureless alternative for intra-oral wound healing.

RESULTS: The sutureless flap design facilitates drainage, improves hygiene and reduces pain which are typical surgical complications following third molar extractions. Although there are times where the use of sutures proves more beneficial than alternative techniques, sutureless wound healing decreases postoperative complications and promotes a healthy environment for proper tissue healing.

Cloning, Purification and Partial Characterization of *Escherichia coli* Transcriptional Regulator AbgR

Cody Boals (DMD-I, MBS-II) and Jacalyn Green, Department of Biochemistry, Midwestern University, 555 31st Street, Downers Grove, IL 60515

Folic acid is essential in many cellular processes that are needed for the survival of humans, plants, and microorganisms. Folic acid can be synthesized in plants and bacteria in a pathway that is well known, although the genes and enzymes involved in the catabolism of folic acid are less understood. The *abg* region of *E. coli* encodes for proteins that enable the uptake and cleavage of *p*-aminobenzoic acid glutamate (PABA-GLU), a derivative of folic acid. The *abg*T gene is responsible for encoding a transporter for the uptake of PABA-GLU, while *abg*A and *abg*B encode for PABA-GLU hydrolase, an enzyme that cleaves PABA-GLU. These genes may be regulated by AbgR, which is encoded by a gene divergently transcribed from the operon. Sequence analysis suggests that AbgR is a Lys-R-type transcriptional regulator. The *abg* genes are found only in bacteria; also, there are different patterns in the *abg* sequence between pathogens and non-pathogens that suggest that absence of *abg*R may increase virulence. Our goal was to clone, purify, and characterize AbgR, in order to better understand the possible significance of the presence (or absence) of AbgR and its role in bacterial physiology. Two separate cloning systems were used in this study. The first system was used to create and over-express *abg*R using a high-copy plasmid vector (pUC19). Each clone was designed with a polyhistidine tag: one on the amino terminus of the protein, and one on the carboxy terminus. While cloning of *abg*R was successful, purification yields of the transcriptional regulator AbgR protein were poor, possibly due to cellular toxicity. The poor expression and unsuccessful purification of AbgR led us to use a system specifically designed for isolation of toxic proteins, the Expresso™ T7 Cloning and Expression System; this system allows for controlled induction of the target gene, and is used for improved control over gene expression. The Expresso™ T7 Cloning and Expression System was successfully utilized to clone and purify AbgR. AbgR was purified using metal affinity chromatography and the predicted protein molecular weight (34 kDa) was confirmed by gel electrophoresis. Better understanding of this protein and its role in the breakdown of folic acid can potentially lead to the development of new and better antibiotics, as well as provide clues regarding the differences between benign bacteria and their pathogenic cousins.

Acknowledgments: This research was funded by Midwestern University and by grant R15 GM085760 from the National Institutes of Health. A special thanks to Lenore Pitstick and Cassandra Larimer for their assistance in this project.
DEVELOPMENTAL SIMULATION OF FACIAL GROWTH RESTRICTION IN THE RHESUS MACAQUE (MACACA MULATTA)
Gregory B Brown1 and Michelle Singleton, Ph.D.1,2,3
1College of Dental Medicine-Illinois, 2Department of Anatomy, Chicago College of Osteopathic Medicine, 3The Field Museum
Midwestern University, Downers Grove, Illinois

Possession of an excavated suborbital surface is a key feature that distinguishes anatomically modern humans from Archaic Homo sapiens. A similar midfacial feature distinguishes Old World monkeys of the genera Lophocebus and Cercocebus from close relatives, such as the rhesus macaque (Macaca mulatta), which lack a suborbital fossa. The developmental basis of the primate suborbital fossa is yet to be determined. It has been shown that differences in bone remodeling rates are partially responsible for the disparity in suborbital morphology between Cercocebus and Macaca, but it has been hypothesized that different patterns of sutural growth also contribute to suborbital morphology diversity. Interestingly, recent experimental studies show that surgical restriction of growth at midfacial sutures in juvenile pigs results in a more excavated suborbital region in comparison with normal controls. While these results suggest that the suture-growth hypothesis could be correct, tests using a primate model would provide stronger support. Three-dimensional (3D) developmental simulation, which employs multivariate regression to estimate ontogenetic shape change, can be used to manipulate facial development in silico, eliminating the need for live specimens. The specific aim of this study is to apply 3D developmental simulation methods to investigate the effects of midfacial growth restriction in a nonhuman primate, the rhesus macaque.

Macaque developmental trajectories were represented by vectors of regression coefficients generated by multivariate regression of shape variables on dental stage. Variables were 3D coordinates of 177 landmarks collected from a mixed-sex, cross-sectional ontogenetic series of M. mulatta crania (N=20) as part of a previous study. Landmarks were aligned by generalized Procrustes analysis (GPA) to bring specimens into a common shape space. Trajectories were calculated for five developmental scenarios that represented varying degrees of growth restriction (GR) by removing midfacial landmarks from the original data set. Vectors for the full landmark set (as a control) and the five GR scenarios were applied to the coordinates of the average cranial landmark configuration to project its development to dental maturity. To visualize simulation results, a virtual model of a dp4-stage M. mulatta cranium was morphed to the simulated adult landmark configurations. Simulated adults were compared using landmark superimposition, principal components analysis, and semi-landmark grids.

The control adult falls slightly beyond the distribution of the original sample on principal components 1–2 but within the same ontogenetic trajectory, validating the simulation procedure. The five GR adults fall outside the distribution of the original sample and possess an excavated suborbital surface that progressively becomes more accentuated as simulated growth is further restricted. Additionally, the suborbital surface lateral to the excavation is more anteriorly located and the superior zygomaticial suture becomes more prominent, protruding anteriorly, as the level of GR is increased. Results support the hypothesis that growth regulation at midfacial sutures contributes to differences in suborbital morphology among primates. Additionally, results provide evidence that midfacial suture growth regulation may have played a role in the evolution of modern human suborbital morphology.
Phylogenic Alterations of Gastrointestinal Bacteria as a Result of High Fat Diet and Exercise.

Joseph Dougherty\textsuperscript{1,2} and Samantha Laskowski\textsuperscript{3}; Jeff Kwak, MS\textsuperscript{1}; Mae Ciancio, Ph.D.\textsuperscript{1}; Christian C. Evans, PT, PhD\textsuperscript{1,4}

\textit{Midwestern University, Downers Grove, Illinois. College of Health Sciences, Department of Biomedical Sciences\textsuperscript{1}; College of Dental Medicine Illinois\textsuperscript{2}; College of Osteopathic Medicine, Department of Physiology\textsuperscript{3}; College of Health Sciences, Department of Physical Therapy\textsuperscript{4}.}

\textbf{Background:} Diet induced obesity (DIO) is an epidemic with serious health, social and economic implications. Previous research has identified a shift in the enteric microbiome, specifically the relative ratio of \textit{Bacteroidetes:Firmicutes} \textit{(Bact:Firm)}, which may play a role in DIO. While exercise (Ex) has been shown to prevent DIO, whether Ex impacts the \textit{Bact:Firm} ratio has not been determined.

\textbf{Objective:} The purpose of this study was to determine the effect of Ex on the \textit{Bact:Firm} ratio using a mouse model of high fat (HF) DIO.

\textbf{Methods:} To test the effect of diet and Ex on the enteric microbiome, male C57BL/6 littermates (5 weeks) were distributed equally into 4 groups (n=6/group): low fat (LF; 10kcal\% fat) sedentary (Sed; LF/Sed), LF Ex (LF/Ex), HF Sed (HF/Sed; 60kcal\% fat) and HF Ex (HF/Ex). Bacterial DNA was isolated from fecal pellets collected at 0, 6, and 12 weeks and analyzed using both quantitative PCR and sequencing of 16S rDNA. In addition, body weights, distance run, epididymal fat pad weight, 24-hour food intake, and oral glucose tolerance were evaluated.

\textbf{Results:} A two-way ANOVA indicated that Ex significantly decreased weight gain, improved oral glucose tolerance, and decreased the \textit{Bact:Firm} ratio of delta Ct values, p<0.05. There was also a significant inverse correlation between total distance run and the \textit{Bact:Firm} ratio, p<0.05.

\textbf{Conclusion:} These results suggest that the altered \textit{Bact:Firm} ratio in response to Ex may play a role in prevention of weight gain on a high-fat diet. Further analysis of lower taxonomic level changes of enteric bacteria with Ex may provide important insights into the prevention of obesity.

\textit{Acknowledgements:} This research was supported by CHS Biomedical Science Program Funds, the KAS Summer Research Fellowship, and a CHS Research Facilitation Grant.
Understanding the functions of tumor suppressor gene Rb in maintaining normal osteoblast homeostasis.

Seunghyun Jae¹, Oliver Couture², Nalini Chandar³.

College of Dental Medicine – Illinois¹, Department of Biochemistry²,³, Midwestern University, Downers Grove, Illinois.

Osteosarcoma is a malignant mesenchymal tumor that has various presentations but osteosarcoma of jaw is one of the dental clinical presentations. Even though the etiology of the osteosarcoma remains unknown, loss of function of p53 and Rb tumor suppressor genes have been strongly implicated in its genesis. The actions of these genes are critical during late osteoblast differentiation to maintain normal bone remodeling. P53 loss in mesenchymal stem cells preferentially allows the formation of osteosarcomas, while the presence of at least one copy of the Rb gene appears to be essential for osteosarcoma formation. In this study we attempted to determine what mechanisms might explain the role of Rb in osteosarcoma genesis. Rb is also important for chromatin modification during differentiation. For this reason we compared osteosarcoma mouse cell lines, with complete loss of Rb with a line containing both copies of Rb using a PCR array containing chromatin modifying factors. Several genes show large differences in expression, including Hdac1 which was reduced 130 fold in the absence of Rb and Ncoa6 and Smyd1 was increased 26-30 fold in the absence of Rb. In separate studies we compared bone marker expression after siRNA mediated reduction of Rb in osteoblasts. Reduction in Rb dosage caused a large increase in a bone specific transcription factor osterix while it reduced another bone specific factor CBFA-1. Rb is known to interact with and activate CBFA-1. We followed Rb and CBFA-1 gene expression during osteoblast differentiation to determine kinetics of its interaction with CBFA-1. These results will be discussed to explain Rb’s potential role in osteoblast differentiation.
Expression of angiopoietin-2 in oral Kaposi’s sarcomas

Antonio I. Rossi¹, Bruno C. Jham¹

¹College of Dental Medicine, Midwestern University, Downers Grove, Illinois

Kaposi’s sarcoma (KS) persists today as a highly vascular and prevalent form of cancer that is often found in HIV patients. Studies have shown that angiopoietin-2 (ANG2), an angiogenic protein, is involved in the pathogenesis of this tumor. The aim of this study was to investigate the expression of ANG2 in samples of oral KS. Fourteen oral KS cases were acquired from Texas A&M University Baylor College of Dentistry and clinical information such as age, gender, race, location of tumor lesion, size, color, appearance, and HIV status, was obtained. Immunohistochemistry was utilized to evaluate the expression of ANG2 in KS and degrees of expression were analyzed in a semi-quantitative manner [negative, weak (<20% of cells positive, moderate (20-50%) and strong (>50%)]. The patients were all white males, mostly HIV+, with a mean age of 40 years. The lesions presented as dark red/blue/purple masses, ranging from 1-2.5 cm in size and were seen in various oral locations such as the tongue, palate, and gingiva. Thirteen of the 14 cases expressed ANG2, with 51% showing moderate or strong expression. Our results show that ANG2 is involved in the pathogenesis of oral KS and could potentially serve as a therapeutic marker for KS patients.

This research was supported by Midwestern’s University College of Dental Medicine start-up funds
CCP RESIDENTS
Assessment of Pharmacists' Knowledge Necessary to Provide Community-Based Pharmacogenomic Interventions

Courtney N. Ammons, PharmD1,2; Elizabeth Gozdziak, PharmD1; Susan R. Winkler, PharmD, BCPS1,2; Megan Wagner, PharmD1

New Albertsons Incorporated1, Franklin Park, Illinois, Department of Pharmacy Practice2, Midwestern University, Downers Grove, Illinois

Purpose: Pharmacogenomics, the study of how human genetic differences impact drug response, may help to individualize drug therapy, and potentially improve the safety of many drugs with high incidences of adverse drug reactions. It has been proposed that pharmacogenomic interventions could be incorporated into many existing medication therapy management (MTM) programs. Pharmacogenomics is an underutilized concept in the community pharmacy setting. In this setting, pharmacists have the unique ability to capitalize on the use of genetic testing to promote positive therapeutic outcomes; however, one of the barriers to implementation is pharmacists’ lack of knowledge. The primary objective of the study is to assess pharmacists’ knowledge necessary to provide community-based pharmacogenomic interventions. Secondary objectives include determining if a relationship exists between demographic data and pharmacogenomic knowledge as well as identifying educational needs of community pharmacists.

Methods: An invitation to complete a brief web-based survey was distributed electronically to community pharmacists employed by SUPERVALU Pharmacies. The survey was comprised of 11 demographic questions and 8 knowledge-based questions. The survey was available for six weeks, and one reminder communication was provided. All surveys completed by pharmacists currently practicing in the community setting were evaluated. No identifiers were collected as part of the electronic survey. The data is presently being analyzed by descriptive statistics and multivariate logistic regression analysis.

Results/Conclusions: To be presented.

Implications: This research may help to streamline the educational needs of pharmacists that would be required to identify, interpret and counsel on pharmacogenomic data if a service were implemented in the community setting. Regardless if a class was taken, preliminary data has revealed that having a pharmacogenomics class offered in pharmacy curricula may increase respondent pharmacogenomics knowledge.

The research was supported in part by the American Pharmacist Incentive Grant for Practitioner Innovation in Pharmaceutical Care.
The Impact of an Educational Program on Pharmacist Behaviors, Confidence and Knowledge of Probiotic Recommendations in a Grocery Store Chain Pharmacy

Akanksha Dudeja, PharmD1,2, Sonali Kshatriya, PharmD1, Klodiana Myftari, PharmD1, Susan R. Winkler, PharmD, BCPS2, Ana Quiñones-Boex, Ph.D.2, Thomas J. Reutzel, Ph.D.2

Dominick’s Pharmacy, Oak Brook, IL1, Department of Pharmacy Practice2, Midwestern University, Downers Grove, Illinois

Objectives: The primary aim of this study is to assess the impact of an educational program on pharmacist behaviors, confidence, and knowledge of probiotic recommendations. Secondary objectives include determining the factors pharmacists perceive as barriers to making probiotic recommendations and evaluating whether the measured outcomes vary by pharmacist demographic characteristics.

Methods: All pharmacists employed within a grocery store chain pharmacy (n=182) were invited to attend a live education session on the subject of probiotics. Those who attended were given an optional, anonymous, pre-survey to complete prior to the session. The pre-survey was designed to assess baseline knowledge, confidence, and behaviors as related to probiotic recommendations. The education session focused on the roles of normal gut flora in health maintenance, defining the term "probiotic", describing how probiotics can be used in therapy, and learning how to assist patients in selecting an appropriate probiotic product.

After the live education session, subjects received a written educational supplement to utilize at their respective pharmacies. The supplement served as a practical reference tool to reinforce knowledge gained at the live session. One month after the session, participating subjects received an electronic post-survey. The post-survey evaluated whether there was a difference in pharmacist knowledge and whether the program had an impact on their confidence and behaviors related to probiotic recommendations. Additionally, it allowed subjects to state their satisfaction with the program and provide feedback for future improvements. The data from the pre- and post-surveys was linked based on an unidentifiable code number and analyzed using SPSS version 19.0.

Results: Of the 189 pharmacists invited, 29 participants completed the pre-survey. Of the 29 study participants, 19 completed the post-survey. After the completion of the probiotic educational program, an increase was seen in the number of probiotic recommendations made per week, the range of patient populations probiotics were recommended to, and pharmacist familiarity with probiotic products currently on the market. A significant improvement was seen in pharmacists’ knowledge of probiotic recommendations (p=0.017) as well as in their confidence to provide evidence based probiotic recommendations and compare and contrast different products on the market (p<0.05).

This research was supported in part by American Lifeline Inc.
Efficacy and safety of tranexamic acid versus ε-aminocaproic acid in cardiovascular surgery

Olabisi Falana, PharmD, BCPS¹,², Gourang Patel, PharmD, BCPS, MSc¹

College of Pharmacy, Midwestern University, Downers Grove, Illinois¹, Department of Pharmacy, Rush University Medical Center, Chicago, Illinois²

Blood conservation is a major concern in the management of surgical patients due to limited supply, cost, and transfusion-related complications. Tranexamic acid (TXA) and ε-aminocaproic acid (EACA) are lysine analogues used in cardiac surgery to reduce total blood loss and decrease the number of blood transfusions. TXA and EACA both inhibit fibrinolysis by interacting with the lysine binding site of plasminogen. TXA is about 10 times more potent and 100 times more expensive than EACA. A 2011 analysis of the Blood Conservation using Antifibrinolytics in a Randomized Trial (BART) concluded that EACA has increased clinical value compared to TXA due to comparative efficacy and safety, and its greater cost-effectiveness. However, the 2011 Society of Thoracic Surgeons and Society of Cardiovascular Anesthesiologists Blood Conservation Guideline recommend lysine analogues (TXA or EACA) for intraoperative blood management. The objective of this study was to evaluate the efficacy and safety of tranexamic acid compared with ε-aminocaproic acid in the management cardiovascular surgical bleeding. Prior to commencement, Rush University Medical Center and Midwestern University Institutional Review Boards approved the study. This was a single-center, retrospective, and observational cohort study. Inclusion criteria were patients 18 years of age or older, undergoing cardiac surgery with or without cardiopulmonary bypass, who received at least one dose of intraoperative TXA or EACA during the study period. Patients undergoing cardiac transplant, left ventricular assist device, or congenital defect surgery were excluded from the study. A data collection tool for demographic data, baseline characteristics as well as primary and secondary outcomes was completed for each patient using EPIC® electronic medical record. The study included 120 patients with 60 patients in the TXA group and 60 patients in the EACA group. There was no statistically significant difference in baseline characteristics between the two groups, although more patients in the TXA group had renal insufficiency and more patients in the EACA has diabetes. The primary endpoint, massive perioperative bleeding occurred in 10 patients (16.7%) in the TXA group compared to 5 patients (8.3%) in the EACA group (p=0.17). There were no statistically significant difference in the secondary endpoints of 30 day mortality, thromboembolic events, renal impairment, and seizure. Based on the results of this study, the authors concluded that there were no statistically significant difference in the primary and secondary outcomes between TXA and EACA. Furthermore, the outcome trends of this study are similar to the BART trial, 8.3% vs. 16.7% for primary outcome (12.1% in BART), and 3.3% vs. 6.7% for 30-day mortality (3.9% and 4% in BART). Considering the substantial cost difference and comparable efficacy and safety, EACA may have better clinical value for use in cardiac surgery.
Impact of a Diabetes Intervention Tool on the Frequency of Recommendations Made by Pharmacists during a Comprehensive Medication Review

Brittany N Hoffmann, PharmD, MBA, Amir Masood, PharmD, Megan Wagner, PharmD, Susan R Winkler, PharmD, BCPS

Department of Pharmacy Practice, Midwestern University, Downers Grove, IL
Jewel-Osco Pharmacies, Franklin Park, IL

Pharmacist-led Medication Therapy Management (MTM) services within community pharmacies offer additional opportunities for patients with diabetes to manage their condition. Lack of standardized documentation forms and different payer billing requirements are two major barriers to providing MTM services in this setting. The primary objectives of this study are to assess the impact of a diabetes intervention tool on the frequency of diabetes recommendations made by pharmacists and to measure the change from baseline in documentation on the comprehensive medication review (CMR) form after implementation of the tool. A secondary objective is to assess pharmacists’ satisfaction with the intervention tool. Fourteen pharmacists within a large community pharmacy market, who have been in their current role since January 2012, were selected to participate. As part of the pre-implementation phase, each pharmacist received training on use of the intervention tool via a webmeeting. A standardized data collection tool was implemented to record CMR recommendations documented at baseline and during the 3-month study period. A follow-up survey was administered to pharmacists to assess their satisfaction with the tool. Descriptive statistics were used to compare baseline and post-implementation documentation frequency and number of recommendations, and to evaluate pharmacists’ satisfaction with the diabetes intervention tool. Seventeen pre and 6 post CMRs were reviewed with the standardized documentation form. No aspirin recommendations were made 41% of the time prior to implementation of the tool. After implementation of the tool, there were 0 cases where an aspirin recommendation could have occurred but did not. Nine out of 14 clinical specialists responded to the satisfaction survey. 63.7% of clinical specialists disagreed that the tool added a significant time burden during their visits. 90.9% stated they would use a similar tool for other disease states. Based upon a review of the CMRs, it appears that the diabetes intervention tool increased documentation rates and clinical specialists find the tool useful.

This study was supported in part by the Midwestern University College of Pharmacy Research Stimulation Grant.
Dexmedetomidine use and associated fever of unknown origin: impact of drug substitution during the propofol shortage

Sharlene Huang¹, Kasey Greathouse, Pharm.D.³, Sonia Nevrekar, Pharm.D.¹,²,³, Sheila Wang, Pharm.D., BCPS AQ-ID¹,²,³

Chicago College of Pharmacy¹, Department of Pharmacy Practice², Midwestern University, Downers Grove, IL, Rush University Medical Center, Chicago, IL³

During the 2009 to 2011 propofol drug shortage, the infectious diseases service was consulted for fever of unknown origin in several Intensive Care Unit (ICU) patients, and empiric broad spectrum antibiotics were often initiated. A correlation between use of dexmedetomidine, an alternative sedative agent used during the shortage, and fever was often questioned since fever has been documented as a dexmedetomidine adverse event. Knowledge of a significant association between dexmedetomidine use and fever could deter unnecessary broad spectrum antibiotics initiation in ICU patients. To identify an association between dexmedetomidine use and drug fever in ICU patients, the study was conducted as a single-centered, retrospective, observational analysis of ICU patients who received either propofol or dexmedetomidine and had documented fever with an infectious diseases consult between January 2008 and December 2011. A list of patients who received dexmedetomidine or propofol during this time period was obtained from the Rush University Medical Center, Department of Pharmacy database. Patients who received propofol or dexmedetomidine during admission were identified, and problem lists were assessed to identify ICD-9 codes for ‘fever’. A thorough assessment of the patient chart during the corresponding admission period was conducted to identify the fever source. If no source was identified and it was documented that the fever was indeed of ‘unknown origin’, further review of the patient chart was done to confirm the staffing of an infectious diseases consult service and the initiation of empiric broad spectrum antibiotics. When all possible sources contributing to a fever were excluded, the fever was then attributed to the use of dexmedetomidine or propofol. Careful analysis of patients who fit these parameters resulted in the observation of two cases of fever of unknown origin while these patients were on dexmedetomidine. Consequently, both patients were started on a course of broad spectrum antibiotics. Observation of fever of unknown origin cases in association with dexmedetomidine use provides insight for future studies to assess the true association of fever and dexmedetomidine in the setting of various confounding factors.

This research was not supported by any funding sources. All authors have nothing to disclose.
Incidence of adverse bleeding events in patients on dabigatran or rivaroxaban for stroke prevention in patients with atrial fibrillation
Mindy Joseph*, PharmD, BCPS; Kimberly Ackerbauer, PharmD, BCPS
Midwestern University/Rush University Medical Center, 1653 W Congress Parkway, Chicago, IL 60612

Purpose:
Dabigatran and rivaroxaban are new oral anticoagulants used for the prevention of stroke and systemic embolism in patients with atrial fibrillation. In terms of safety and efficacy, each agent has been compared separately to warfarin, however, little is known about the comparison between the two new agents. Identifying the incidence of bleeding in patients on dabigatran or rivaroxaban may be beneficial in guiding the selection of the newer anticoagulant in patients with non-valvular atrial fibrillation. The primary objective of this study is to identify the incidence of bleeding between groups.

Methods:
This is a retrospective cohort study of hospitalized patients at Rush University Medical Center who received either dabigatran or rivaroxaban between December 2011 and November 2012. Patients were enrolled in the study if they had a diagnosis of atrial fibrillation and were started on dabigatran or rivaroxaban for stroke or systemic embolism prevention and had at least one follow-up visit post-initiation of therapy. Patients were excluded if they had any other indication for anticoagulation, a contraindication to use of any of the agents or were started on therapy prior to the specified time period.

Results:
Of the 190 who were evaluated, 103 patients met inclusion criteria. The primary endpoint of any bleeding was reported in 14.5% of patients in the Dabigatran group and 12.2% of patients in the Rivaroxaban group (p=0.285). Secondary endpoint of stroke and systemic embolism was observed in 9.8% of patients in the dabigatran group versus no patients in the rivaroxaban group (p=1.00). Also, the secondary endpoint of death was not observed in the dabigatran group and in 2.4% of patients in the rivaroxaban group (p=1.00). The average time to event was approximately 50 days, with the mean time to event being 53 days in the dabigatran group versus 45 days in the rivaroxaban group.

Conclusion:
The results of this study reveal that bleeding rates between dabigatran and rivaroxaban are similar. Also, the event rates in this study mimic the real world setting, which may be higher than what has been previously reported in studies.
Comparing Patients’ and Fourth Year Professional Pharmacy Students’ Perceptions of Communication and Confidence in the Ambulatory Care Setting

Lisa M. Mackowski, PharmD1, Kathleen M. Vest, PharmD, CDE, BCACP1, and Jennifer J. D’Souza, PharmD, CDE, BC-ADM1

Department of Pharmacy Practice1, Midwestern University College of Pharmacy, Downers Grove, IL

Objective: Minimal research has been performed in the ambulatory care setting evaluating students’ self-assessment of communication and confidence following each patient interaction or comparing the student self-assessment to the patient’s perceived experience. The primary aim was to describe the differences between the overall patient and student perceptions of communication and confidence following a student-led patient interview in an ambulatory care setting during the first and last week of a rotation cycle.

Methods: Surveys were distributed to the students and patients for 4 consecutive days from the start of the first independent student-led interview (first week), and then during the last 4 consecutive days of interviews (last week). Both surveys contained two similar sections: 1) questionnaire on communication and confidence and 2) demographic information. Results of the overall patient and student perceptions of communication and confidence are analyzed descriptively. Fisher’s test (level of significance <0.05) was used to determine the difference in frequency of ‘strongly agree’ responses and matched agreement for responses over time.

Outcomes: There were 11 students and 76 patients during the first week and 9 students and 37 patients during the last week who completed surveys for analysis. Communication assessment responses that had ‘strongly agree’ selected, was reported by 64.8% of students’ responses and 86.2% of patients’ responses during the first week (n=522), and during the last week (n=257) by 85.2% and 84%, respectively. Confidence-based responses selected with ‘strongly agree’ was reported by 64.5% of students’ responses and 81.4% of patients’ responses during the first week (n=366) and during the last week (n=179) by 84.4% and 79.9%, respectively. The frequency of strongly agreeing significantly increased over time from the student perspective for both communication (p<0.001) and confidence (p<0.0001). There was no significant change in amount strongly agreed by patients over time for both areas assessed. Students’ and patients’ perceptions during the first week matched 61.7% for communication skills and confidence, and during the last week, the responses matched 73.2% for both. This change was statistically significant for communication (p=0.0017) and confidence (p=0.0095).

Conclusions: Overall, the patients tend to have a favorable perception on students’ communication and confidence skills. There is a statistical increase in percentage for the matched agreements of perceptions over time. The initial gap between the confidence and communication perceptions may be alleviated with additional clinical preparation in the classroom.
Quantifying the Magnitude of Clinical Virulence of KPC through Translational Study

Milena McLaughlin¹², Maria Renee Advincula¹, Michael Malczynski², Grace Barajas², Chao Qi²³, Marc Scheetz¹²

Midwestern University, Downers Grove, IL¹, Northwestern Memorial Hospital, Chicago, IL², Northwestern University, Chicago, IL³

*Klebsiella pneumoniae* (KP) producing carbapenemase (KPC) KP has widely disseminated and may cause poor patient outcomes. Clinical studies of KPC virulence have found discordant estimates of pathogenicity, but comorbidities have confounded the ability to discern attributable effects. To obtain a pure estimate of the impact of KPC virulence, we employed a validated *Galleria mellonella* (GM) host-pathogen interaction model and obtained virulence scores to predict clinical outcomes for KPC clinical blood stream infections (BSIs). Isolates were collected from blood cultures from March 2010-August 2011 and used to define groups for a retrospective cohort study. 15 KPC(+) and 15 randomly selected KPC(-) BSIs were tested in the GM model with appropriate controls. Virulence scores were calculated as the area under the Kaplan-Meier survival curve. 3 more KPC(-) isolates were matched with KPC(+) patients in addition to those from the patients above (total 15 KPC(+) and 60 KPC(-) patients). Baseline patient variables were collected (including KPC status) and were analyzed with a step-wise multivariate model to assess impact on patient morbidity and mortality. In the GM model, KPC(-) isolates had more extensive, rapid killing than KPC(+) isolates (p<0.001). The converse was observed in the clinical study bivariate analysis where KPC(+) status predicted patient mortality (OR 3.8, 95%CI 1.0-14.3). In the second multivariate step, Apache 2 score was associated with a 15% nonsignificant increase in mortality (OR 0.99-1.34), and KPC(+) status was a similar predictor (OR 3.3, 95%CI 0.8-13.2) relative to the first model. In a final stepwise multivariate analysis, virulence score negated the effect of KPC(+) status on mortality (95%CI 0.2-31.1). In this novel pilot study, KPC status predicted clinical mortality; however, this effect was severely reduced when measured virulence was imputed. Further studies with increased power are needed to fully elucidate the clinical virulence of KPC(+)KP.

*This research was supported in part by a grant from Midwestern University Chicago College of Pharmacy, Downers Grove, IL and the Society of Infectious Diseases Pharmacists.*
Pharmacy involvement to improve admission medication histories.

Nabila Mirza\textsuperscript{1,2}, Luke Jackson\textsuperscript{1}, Huzefa Master\textsuperscript{1,2}, Sean Mirk\textsuperscript{1,2}

\textit{Midwestern University\textsuperscript{1}, Downers Grove, Illinois, Swedish Covenant Hospital\textsuperscript{2}, Chicago, Illinois}

Medication reconciliation is vital to patient safety throughout all transitions of care. An accurate home medication list (HML) is an essential part of medication reconciliation; it can help diagnose, detect adverse drug events, identify non-adherence, avert medical errors and prevent interruption in drug therapy. Most methods to complete a HML involve a coordinated effort between a physician, nurse, or pharmacist to help complete a comprehensive medication history (CMH). Research shows the pharmacist involved in CMH taking produce a more complete HML. The primary objective of this study is to gauge the ability of pharmacy staff members to detect and document medication discrepancies. This study took place on two cardiac floors within an urban-based hospital. Two third-professional year student pharmacists were trained as pharmacy technicians. One of the roles as a technician was to perform CMH within 48 hours of admission. After each CMH, the patient’s current HML was updated in the electronic medical record (EMR). Medication discrepancies between the HML entered by the nurse and/or physician and the pharmacy technician were recorded. The types of discrepancies included: omissions; commissions; incorrect frequency; incorrect dose; both incorrect dose and frequency; incorrect formulation; and same drug class, different medication. The total number of discrepancies in each category was collected, as well as discrepancies amongst medications commonly associated with hospital admissions. There were a total of 47 patients used in the study, and 159 discrepancies that were recorded. The most prevalent discrepancy found was the number of medications that were omitted from the home medication list (39%), and the least was the wrong formulation being recorded in the EMR (1.4%). Patient demographic data was also collected. Increasing the role of pharmacy technician in the medication history component of medication reconciliation appears to help reduce medication discrepancies.
Recent literature supports the preferential use of antistaphylococcal penicillins (i.e. oxacillin) or first generation cephalosporins (i.e. cefazolin) for the treatment of methicillin-susceptible Staphylococcus aureus (MSSA) bloodstream infections (BSI). Due to case reports of cefazolin treatment failure, antistaphylococcal penicillins are often used in clinical practice for severe MSSA infections. Given the lack of data regarding the comparative efficacy and safety of these agents, this study aimed to assess clinical outcomes of patients with MSSA BSI that are treated with cefazolin or oxacillin. In this retrospective, observational study conducted at Rush University Medical Center (RUMC) and Northwestern Memorial Hospital (NMH), adult patients with a positive blood culture for MSSA, hospitalized from 1/2010-8/2012, and treated with at least one dose of study drug within 48 hours of finalized culture results were considered for analysis. Pertinent patient variables were collected and evaluated including: site of infection, baseline demographics, treatment regimen, time to first negative blood culture, and adverse drug events. The primary endpoint was differences in in-hospital mortality. Secondary endpoints included time to death, duration of bacteremia, adverse events, clinical cure versus treatment failure, and outcomes of high burden diseases (i.e. endocarditis and endovascular infections). Of the 209 patients with MSSA BSI at RUMC, 110 patients were included, and 95 and 15 received cefazolin and oxacillin, respectively. Baseline characteristics were well balanced between the groups in regards to age, co-morbidities and APACHE II score. The most common sources of infection were central line or bone/joint, and 33.7% of cefazolin and 40% of oxacillin-treated infections were considered high burden. There was only 1 case of in-hospital mortality in each arm; however, 6.3% of cefazolin versus 26.7% of oxacillin treated individuals were deemed to be treatment failures. The rates of adverse drug events were similar between the groups.

Conclusion: Cefazolin may be associated with similar rates of clinical cure as oxacillin with 84% vs. 67% cure of high burden infections, respectively. Length of stay may be shorter in the cefazolin treatment group; however, definite conclusions cannot be made until statistical analysis is completed. Additionally, 33% of cefazolin treatment failures were discharged home on cefazolin for convenience, and there were no dosing differences observed in the treatment failures of either group.
Evaluation of Clinical Outcomes In Patients With Gram-negative Bloodstream Infections According To Cefepime MIC

N. James Rhodes¹,², Sonia N. Nevrakar¹,³, Milena M. McLaughlin¹,², Sheila K. Wang¹,³, Christopher W. Crank³, Chao Qi⁴, Marc H. Scheetz¹,²

Department of Pharmacy Practice¹, Midwestern University, Downers Grove, Illinois; Department of Pharmacy², Northwestern Memorial Hospital, Chicago, Illinois; Department of Pharmacy³, Rush University Medical Center, Chicago, Illinois; Northwestern University, Chicago Illinois⁴

The CLSI has lowered the breakpoints for all cephalosporins except for cefepime. At present it is unclear if organisms that display higher cefepime minimum inhibitory concentrations (MICs) are amenable to treatment. We sought to assess the morbidity-adjusted effect of cefepime MIC on patient mortality in the setting of Gram negative bloodstream infections (GNBSI). Patients from author institutions with a GNBSI between 09/11 and 8/12 and treated with cefepime were reviewed for inclusion. Frequency matched groups, maximum of 4:1, were obtained to ensure representation from all MIC categories. Baseline demographics, APACHE 2 score on the day of infection, pathogen species, immunocompromised status, and antimicrobial dosing were collected. Multivariate regressions and Classification and Regression Tree (CART) were performed to predict risk-adjusted hospital death according to cefepime MIC. 463 patients were screened, and 83 patients met inclusion criteria. The median APACHE 2 score on the day of infection was 16 (IQR 13-20). GNBSI was most commonly E. coli (38%), Pseudomonas sp. (30%), and Klebsiella sp. (17%). Risk of hospital death increased incrementally with cefepime MICs between 1mg/L and 64 mg/L (p=0.03, Figure 1). CART found less death in patients with cefepime MIC < 32 mg/L and APACHE 2 < 12.5 (i.e. 0% vs. 21%). A secondary split was found for patients with MIC < 2 mg/L and APACHE 2 >12.5 (i.e. 17% vs. 33% death).

Conclusions: Increasing cefepime MIC appears to predict mortality among patients who received cefepime. We recommend considering the MIC=2 mg/L as the clinical breakpoint for critically ill patients.
Colchicine for Prevention of Post-Operative Atrial Fibrillation (POAF)

Elizabeth J. Short1,2, Nikki Cool1, Amy Wilson1, Travis Abicht1; Patrick M. McCarthy1

Northwestern Memorial Hospital, Chicago, Illinois1, Midwestern University, Downers Grove, Illinois2

Atrial fibrillation is one of the most frequent complications after cardiac surgery. Beta-blockers and amiodarone are effective therapies to reduce the incidence of post-operative atrial fibrillation (POAF). Colchicine as a single therapy in cardiothoracic surgery patients has also shown benefit. A newly developed protocol for the use of colchicine in addition to a beta-blocker to prevent POAF has recently been implemented at Northwestern Memorial Hospital for valve replacements and coronary bypass surgeries. Pharmacists and cardiac surgery nurse practitioners dose adjust colchicine in hepatic or renal impairment as well as for drug interactions with P-glycoprotein or CYP 3A4 inhibitors. The purpose of this study is to evaluate the newly developed colchicine protocol for the efficacy of colchicine in addition to a beta-blocker to prevent POAF.

Methods: This is a retrospective cohort study of cardiac surgery patients undergoing valve replacement or coronary bypass surgery at Northwestern Memorial Hospital who received a beta-blocker along with colchicine per the protocol from May 1, 2012 to December 31, 2012. The control group is cardiac surgery patients who received a beta-blocker without colchicine prior to the initiation of the protocol. The primary end point is the incidence of POAF at the first outpatient follow-up visit. Secondary endpoints include the incidence and reasons for discontinuation of therapy, such as side-effects or non-compliance. This study is IRB approved by Northwestern Memorial Hospital and Midwestern University.

Results/Conclusions: Data collection and analysis are currently in progress.
Evaluation of Sildenafil Use in Pulmonary Hypertension Patients with Left Ventricular Assist Devices Prior to Orthotopic Heart Transplant

**Ryan Van Engel, Pharm D¹,², Nikki Cool, Pharm D, BCPS², Amy Wilson, Pharm D², Andrew Sauer, MD², Karen Meehan, ACNS-BC, CVRN²**

*Midwestern University, Downers Grove, IL¹, Northwestern Memorial Hospital, Chicago, IL²*

**Purpose**

Sildenafil is an oral phosphodiesterase 5A inhibitor (PDE-5) that decreases peripheral vascular resistance (PVR) and increases cardiac index in patients with pulmonary hypertension secondary to chronic left sided heart failure. Sildenafil was recently studied in conjunction with left ventricular assist device (LVAD) therapy to lower PVR to optimal levels for heart transplantation. At Northwestern Memorial Hospital (NMH), sildenafil therapy is added and titrated to the maximal tolerated dose in patients with pulmonary hypertension and an LVAD. There are no current evidence based guidelines that describe optimal sildenafil dosing or documented statistical benefit in these patients. The purpose of this study is to evaluate the RV failure rates at one year in patients with pulmonary hypertension who received sildenafil therapy along with an LVAD for bridge to orthotopic heart transplant (OHT).

**Methods**

This was a retrospective cohort study evaluating the efficacy and tolerability of sildenafil therapy in end-stage heart failure patients with pulmonary hypertension that have undergone LVAD implantation prior to OHT at NMH. Patients hospitalized from December 2007 through September 2012 and identified from the NMH LVAD registry were considered for inclusion. Variables collected included: age, race, type of LVAD device implanted, etiology of cardiomyopathy, INR, serum creatinine, and liver function tests. Echocardiograms and right-heart catheterization reports were assessed for documentation of pulmonary hypertension resolution prior to LVAD implant, post LVAD implant, at the first biopsy post OHT, at the fourth biopsy post OHT, and at one year post OHT. Sildenafil dose was also collected at these time points. The primary end point was to evaluate the incidence of RV failure at one year. Secondary endpoints included sildenafil dose optimization and side effects after the addition of therapy and LVAD implementation. This study was approved by the institutional boards at Northwestern Memorial Hospital and Midwestern University.

**Results/Conclusions**

Initial results show that there is a relatively low incidence of RV failure in this patient population at one year regardless of sildenafil dose. Further analysis is needed to determine if sildenafil has a role in improving outcomes in these patients and if a specific dose is needed to acquire that outcome.
Evaluation of Patient Interest in Mobile Apps for Health-Related Education.

Nicole M. Wegrzyn, PharmD¹, Sean M. Mirk, PharmD¹

Department of Pharmacy Practice, Chicago College of Pharmacy¹, Midwestern University

Pharmacists regularly provide health-related education to patients. The type of education varies from patient to patient and can include information such as drug indication, mechanism of action and purpose of therapy, drug interactions, side effects, proper administration, and disease-specific information. Pharmacists face a number of challenges in providing adequate health-related education to their patients. Information should be tailored to each patient. Topics can be complex and often require continual reinforcement. Appropriate time to devote to health-related education and resources available may be lacking. Despite these challenges, health-related education provided by a pharmacist has been proven to improve health outcomes. Mobile apps may help alleviate some challenges and provide a new method for pharmacists to provide health-related education. There is limited published information evaluating the utilization of mobile apps as educational tools for patients. Furthermore, desirable features and patient needs for health-related education via mobile technology remain largely unknown. This IRB-approved study surveyed ambulatory patients regarding the use of a mobile app for patient education to (1) quantify patient interest, (2) determine desirable features and (3) determine if a relationship exists between patient variables and interest in an a mobile app for patient education. Patients were recruited to complete a written survey. The survey comprised of 19 multiple-choice questions and one open-ended question for general comments. It was administered to consenting patients receiving care at pre-determined pharmacy-run ambulatory care clinics. To ensure a standardized baseline level of knowledge and provide a reference point for patients as a platform identifier, a laminated information card titled “What is an iPad©?” was provided to the patient after the patient’s knowledge of an iPad© was assessed. A sample size of 120 completed surveys was calculated in order to investigate the relationship between certain patient demographics and an interest in a mobile app. There are nine variables of interest: chronic disease state(s), perceived level of health, knowledge of an iPad©, types of technology used, age, sex, race/ethnicity, level of education, type of health insurance. Inferential statistics will be conducted using Chi-square for dichotomous variables. Mann-Whitney U or Kruskal Wallis will be used for ordinal data. Descriptive statistics will be reported for all parameters. Data collection and data analysis are currently in progress. A total of 24 surveys have been completed to date. Preliminary results show that a majority of respondents are interested in using a mobile app to understand medication information (62.5%) and would use an app recommended by a healthcare provider (75%). Information about medications and about health conditions was rated as the top two types of information respondents would find beneficial. Interactive tutorials, articles with text, and images and diagrams were the most common ways respondents indicated they would like information presented. This research will aid pharmacists to develop and test mobile apps as educational interventions and investigate their impact on health outcomes.
Evaluating men’s health education in US pharmacy practice curriculum
Rebecca Zaworski, PharmD\textsuperscript{1}, Kelly A Lempicki, PharmD, BCPS\textsuperscript{1}

Department of Pharmacy Practice, Midwestern University, Downers Grove, Illinois\textsuperscript{1}

Purpose: With a lower life expectancy and longer hospital stays compared to women, men accounted for just under half of the United States population in 2010. In pharmacy training, there has been little attention to men’s health as compared to women’s health. The objective of this study was to evaluate men’s health education in the pharmacy practice curriculum of colleges/schools of pharmacy in the United States. The primary aim was to determine what men’s health topics were taught in the colleges’/schools’ pharmacy curriculum. The secondary aim was to evaluate where men’s health information was taught, length of time given to teach this information, and the departments’ views about incorporating men’s health in their curriculum.

Methods: The study was conducted via an online survey using Survey Monkey. A list of department heads from colleges/schools of pharmacy in the United States was obtained from American Association of Colleges of Pharmacy (AACP) and schools in the pre-candidate status were excluded. An email was sent to the department heads one week before the release of the survey informing them of the survey. The survey was open for four weeks with a reminder email sent half way through. The survey included demographic questions about the college/school of pharmacy, the men’s health topics covered, where the information was covered, if student organizations were teaching men’s health, and the colleges’/schools’ views about incorporating men’s health in their curriculum. Data was analyzed using descriptive statistics. The impact of demographic variables on the number of hours of men’s health taught was assessed using Mann-Whitney U or Kruskal Wallis. The project was given exempt status by the Midwestern University Institutional Review Board.

Results: A total of 143 surveys were sent to heads of the department of pharmacy practice. There were 22 started surveys and 19 completed surveys. All schools/colleges (n=20) were teaching benign prostatic hyperplasia and erectile dysfunction in a required didactic course. Most other men’s health topics were taught in required didactic courses. Most of the schools/colleges were teaching at least one hour of men’s health topics. The average number of hours of men’s health topics taught was 10 hours. There was no significant difference between the colleges' demographics and total hours of men’s health topics taught. Only 10.2% (n=2) of pharmacy student organizations were educating the public on men’s health topics. Most schools/colleges felt that men’s health topics should be included in the required curriculum only. Eighty-nine percent of schools/colleges felt the main barrier to incorporating men’s health topics in the curriculum was lack of time in the curriculum.

Conclusions: The majority of men’s health topics are being taught in required didactic courses for an average total of 10 hours. The schools/colleges would like to incorporate more men’s health into the curriculum; however, many barriers, especially lack of time prevent this from occurring.
CCOM RESIDENTS
ABSTRACT:

Intracranial aneurysms in children are rare and poorly understood. Children can present to the emergency department with variety of complaints caused by non-traumatic hemorrhagic stroke. A 7 y/o African American male was brought to St. James Chicago Heights Emergency Department by ambulance in full cardiac arrest. Patient was attending a family party and was under constant supervision. Prior to the arrest, the child noted a “bug” on him and whisked it away. Few minutes later, patient grabbed his head, said “my head hurts” and had syncope. Total downtime was 12 minutes by the time the patient was brought to the ED. Patient has history of mild asthma, never had any surgery, and used the albuterol inhaler as needed. Both mother and father denied any family history besides asthma. Patient had no medication allergies. Patient lives at home with mother and three other siblings but spends every other weekend with his father and step-mother. Patient attended 2nd grade at this time and did well in school. No exposure to second hand smoke. Pt does not drink or known to do any drugs. Immunizations were up to date.

Once he arrived to the ED, patient was placed on a monitor and found to be in asystole. Chest compressions were resumed. Copious amount of pink aspirate was suctioned prior to intubation. During pulse check, patient was intubated using a Mac 2 blade and endotracheal-cuffed tube (size 6) was placed on first attempt and secured 18 cm at the lip. ET tube placement was confirmed by equal bilateral breath sounds and a color change in carbon dioxide detector. Intravenous access was obtained and patient was given epinephrine intravenously. An orogastric tube was placed for stomach decompression. The heart rate increased to 150 beats per minute with strong pulses appreciated in all four extremities. Within 3 minutes after the epinephrine, patient’s heart rate dropped to 60 beats per minute. Patient was given IV atropine, but did not respond and CPR was resumed. Second epinephrine was injected and his heart rate again increased to 130 beats per minute. Patient was also given IV sodium bicarbonate and calcium gluconate for Asystole. Methylprednisone was given for possible anaphylaxis.

Patient was given epinephrine drip of 3.75 mcg/min, which enabled to maintain his heart rate above 100 beats per minute. Patient was placed on a ventilator. Patient’s vital signs improved to heart rate of 117, blood pressure 70/32, respirations of 28, SaO2 of 98% and accu-check of 116. CT head without contrast revealed an acute intraventricular and subarachnoid hemorrhage due to rupture of basilar artery aneurysm, with impending transtentorial herniation. Patient’s family was notified of the poor prognosis. Patient was transferred to Children’s Hospital for organ donation as requested by family.

Aneurysms in pediatric population are rare and poorly understood. Children may present with a variety of symptoms such as sudden headache, vomiting, focal deficits, seizures, hemorrhagic stroke and even cardiac arrest. Posterior cerebral artery aneurysm rupture may cause cardiac arrest due to autonomic disturbance at the brainstem. Although rare, aneurysm rupture may be found in previously healthy children with no family history of brain aneurysms. With an incidence of less than 3/100,000 children, brain aneurysms can occur in the pediatric population and should be considered as part of differential diagnoses in children who present to the emergency department in cardiac arrest.

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Emergent TPA administration for Acute PE
Thomas Brozek D.O. and Steven Vuckovic D.O.
Midwestern University/CCOM Emergency Medicine
St. Anthony’s Hospital, Crown Pointe, IN

ABSTRACT:
TPA administration for a pulmonary embolism is a topic many young clinicians may be familiar with in textbooks but may not have experienced in the Emergency Department. Awareness of current guidelines and protocols are of utmost importance to the practicing emergency room physician.

A 71-year-old female who arrives at the emergency department via EMS in extremis complaining of severe sudden onset of shortness of breath. Patient was noted to be extremely cyanotic with no palpable blood pressure per EMS with an oxygen saturation of 91% of room air. Upon arrival, the patient was very air hungry, unable to speak secondary to her profound shortness of breath and is showing signs of fatigue and early failure. Patient was emergently intubated. On speaking to the patient’s daughter it became known that the patient has been complaining of calf pain for the last two weeks and has been under the care of PMD who thought that she had some early superficial thrombophlebitis.

Vitals: BP difficult to obtain even by palpation, HR 140, R 36 and shallow,

Patient had IV access established, RSI rapid sequence intubation was performed, patient had a right femoral triple lumen catheter placed followed by a left femoral arterial line. Versed gtt for sedation, dopamine and dobutamine were started to maintain BP of 90 systolic.

The patient’s blood pressure continued to remain labile despite the dopamine and dobutamine. A STAT CT scan of the chest pulmonary embolism protocol was obtained which demonstrated evidence of massive bilateral PE, COPD and fibrotic changes in the lung bases posteriorly. The patient was heparinized prior to going to the CT.

Upon returning the patient’s blood pressure remained extremely labile despite the addition of pressors. The findings were discussed with cardiology and PMD and in lieu of the fact that the patient remained hypotensive with significantly massive PEs, it was felt that the patient was a candidate for thrombolytic therapy. The risks, benefits, alternatives and complications of the procedure were explained to patient’s family in lay terms.

The patient was front loaded with 100mg of tissue plasminogen activator per cardiac protocol. Of note was the fact that the patient’s BP after the first bolus of thrombolytics improved to high 90s to low 100s. The patient was transferred to ICU post-therapy with active hypotension being supported with dopamine and dobutamine.
Combined Osteopathic Physicians’ Careers After Residency (COPCAR)

Daniel S. De Feo, DO; Christopher Colbert, DO; Thomas Olmstead, DO; Saisho Mangla; OMS III

Department of Post Doctoral Education, Department of Emergency Medicine, Midwestern University/St. James Hospital

Abstract

Objectives: To evaluate the hypothesis that graduates of Osteopathic Emergency Medicine/Primary Care residencies currently practice primarily Emergency Medicine, as well as to investigate factors that may influence their decision, and set a foundation for further research investigating this topic.

Methods: An anonymous, electronic survey consisting of 16 questions was emailed to the director of medical education of each Emergency Medicine/Primary Care residency that is currently training residents in the United States, with the instructions that it was to be forwarded to alumni of that program. Attempting to contact non-responders, the survey was sent to individual program directors and coordinators of each of these programs, with the same instructions. The primary endpoint of this study was which individual specialty each physician spent the majority of their time practicing. Other data collected included demographics, as well as questions to help determine which factors currently influence the respondents’ practice habits.

Results: In total, 37 graduates from various Osteopathic dual-training programs responded. An overwhelming majority (33/37, 89%) practice primarily Emergency Medicine, while 3 physicians (8%) practice both equally, and 1 (3%) physician practices primarily their primary care specialty. Nine physicians (24%) practice both of their trained specialties, and 26 (70%) would repeat the residency.

Conclusions: Emergency Medicine combined with a primary care specialty appears to afford trainees a well-rounded post-graduate education, while also providing a greater knowledge base and career flexibility to graduates. While an overwhelming majority of respondents primarily practice Emergency Medicine when finished with residency, nearly a quarter of them find time to practice primary care as well, and seven out of ten would repeat the residency again, despite the extra year of training.
Obstetricians and Educating Women about Breastfeeding, Is there a Role?

Michele L Finkle DO and Ashlee Bergin MD
Midwestern University OPTI- Resurrection Medical Center
Obstetrics & Gynecology Residency Program
Little Company of Mary Hospital

ABSTRACT:

Introduction:
A number of demographic, socioeconomic, and psychosocial factors have been identified as influencing a woman’s decision to breastfeed. This has led to breastfeeding initiatives across the United States designed to educate women of all backgrounds in hopes of increasing knowledge about breastfeeding and thus increase the rate of breastfeeding. Studies have also looked at the roles both family and pediatric physicians and residents may play in influencing a patient to breastfeed. However, there is not much known about the role Obstetricians and Obstetric residents play in educating patient about breastfeeding. This study was created to identify whether disparities exist in breastfeeding education provided to patients by Obstetricians and obstetric residents, as well as expand awareness and promote the importance of breastfeeding education among the Obstetric community.

Objective: To administer a survey to postpartum women to identify the role Obstetricians and Obstetric residents have in educating and aiding women in their decision to breastfeed.

Methods:
A 15-item survey was distributed to post partum patients in a community-based hospital on the south side of Chicago. Patients included in the study received prenatal care from various providers, ranging from private and hospital-employed practices and nurse midwives, to a resident run public aid clinic. A consent form was placed as a face sheet for the survey to educate the participants. Surveys were handed out to women on the post partum floor by nursing staff and collected in a similar fashion. Out of 100 surveys dispersed, 72 were completed.

Results: A total of 72 surveys were completed from July 2012 to September of 2012. Statistical analysis showed that the majority of women received their care from an Obstetrician, and 86.6% of women report discussing breastfeeding with their Obstetricians during their pregnancy. However, 63.9% of patients under an Obstetricians care stated that their physician did not aid in their decision to breastfeed.

Conclusion: Although Obstetricians are discussing breastfeeding with women throughout pregnancy, the effectiveness of their discussions in influencing patients to breastfeed is uncertain. Studies identifying obstacles that may prevent Obstetricians from successfully educating women about breastfeeding are need to identify disparities to ascertain how Obstetricians can have more of an impact on their patient’s decision to breastfeed.
Changing How We Care: Bolivia

Katie Gualandri, DO, Steven Bujewski, MD

Resurrection Medical Center, Solidarity Bridge

OBJECTIVE: The objective of this project is to understand the patient’s perception of the care provided by American healthcare volunteers through a survey so that improvements can be made to serve this particular community in the future and be a model for similar organizations.

METHODS: A team of twenty medical volunteers from the United States with assistance from local medical personnel worked together to provide care in the fields of obstetrics/gynecology, general surgery, anesthesiology, cardiology, neurology, and dermatology in both the clinical and hospital settings from the days of September 29 to October 8, 2011 in Corioco, Bolivia and surrounding villages. An 8 question survey was read by one provider to 50 patients regarding demographics, prior healthcare resources, and satisfaction.

RESULTS: Patient satisfaction was unanimous with care provided, belief of making a difference in the community and desire for further care yet no specific suggestions for improvement was given at the time of the survey.

CONCLUSION: Patient’s of Coroico, Bolivia are happy with the care provided by the American healthcare volunteers, believe their community is effected in a positive way, and would desire to receive care if available in the future.
Does insurance status affect the rate of psychiatric bouncebacks to the Emergency Department?

April Brill, D.O., Ryan Misek, D.O., Ashley DeBarba, D.O., Katherine Nonweiler, Robert Long, Lauren Fontana, Alecia Clary, Erik Frost

Franciscan St. James Health Emergency Medicine Residency, Olympia Fields, Illinois

Emergency psychiatric care is extremely limited in the United States. Patients experiencing psychiatric emergencies often require resources not available at the hospital to which they present and require transfer to an appropriate psychiatric facility, often after being held in the Emergency Department (ED) until a psychiatric bed is available. Boarding of psychiatric patients, defined as a length of stay greater than 4 hours after medical clearance, is ubiquitous throughout emergency departments nationwide (ACEP 2008). The boarding of patients is recognized as a major cause of ambulance diversions and ED crowding (Falvo T 2007), and has a significant impact on health care providers, patient satisfaction, and hospital costs (Park 2009). Furthermore, there are numerous anecdotal accounts of a “revolving door” for ED psychiatric boarders whereby patients who board in the ED and are eventually transferred to an inpatient psychiatric facility, return to the ED in crisis when unable to obtain adequate outpatient psychiatric care (ACOEP 2008). To investigate whether insurance status has an effect on patients rebounding to the ED in psychiatric crisis, the authors conducted an electronic retrospective multicenter cohort study of all patients presenting to two community EDs from July 1, 2010 through June 30, 2012 assessed to require inpatient psychiatric hospitalization at St. James Hospital Olympia Fields and Chicago Heights campuses. All patients were admitted through the ED and deemed to require inpatient psychiatric treatment, based on appropriate ICD-9 codes. The main outcome measure was placement into a psychiatric facility. Patients were followed to see if they re-presented to one of the two participating EDs within a year of initial presentation for a complaint requiring psychiatric evaluation. Study participants were evaluated for: time from presentation to the ED to decision to admit; time from admission decision to transfer to a psychiatric facility; time of transfer to a psychiatric facility; and number of dates to first re-presentation to the ED within 12 months following initial ED presentation. Our research will help identify an “at risk” population of patients who are unable to obtain appropriate outpatient psychiatric follow up after discharge, and to determine whether there is accessible psychiatric care available to patients regardless of their insurance status. The identification of this underserved population will bring attention to the need for increased psychiatric services and could help alleviate a major cause of overcrowding in the emergency department.
Surgical management of elderly women with endometrial cancer in a community setting

Schriefer, JE¹ and Chapman-Davis, E²
¹ Midwestern University OPTI/Resurrection Health Care Consortium Obstetrics and Gynecology Residency Program ²Department of Gynecologic Oncology, Advocate Christ Medical Center, Oak Lawn, IL

Objective: To describe the treatment and outcomes of elderly women diagnosed with endometrial cancer at a community hospital.

Methods: Women 75 years of age and older who were diagnosed with endometrial cancer at Advocate Christ Medical Center between January 1, 2005-December 31, 2012 were identified retrospectively from the cancer registry. Demographic information, pathology findings, surgical outcomes, and survival outcomes were analyzed and findings compared.

Results: 68 women age 75 and older were diagnosed with endometrial cancer over the study period. 55 of those patients underwent surgery. The patients who underwent surgery were significantly younger (p=0.011) and had earlier stage cancer (p>0.001). 36 patients had open surgery and 19 had robotic surgery. Robotic surgery was associated with decreased blood loss (p=0.005), shorter hospital stay (p=0.006) and longer operative time (p=0.001). There was no difference in the number of cases that had intra-operative or post-operative complications. While there was no difference in survival based on age (75-79 year old vs >80; p =0.965), overall survival was longer in the group that underwent surgery versus those who did not (p=0.002, Mean survival 3.8 years (95%CI 2.7-4.2), vs. 1.9 years (95% CI 0.9-2.9)).

Conclusion: Elderly women may safely be offered surgical options for treatment of endometrial cancer. Women age 75-79 and those with earlier stage cancers are more likely to be offered surgical management. With the introduction of robotic surgery for the treatment of endometrial cancer, elderly women had similar survival outcomes and incidence of complications as compared to open surgery. There was also less estimated blood loss and shorter hospital stay in the robotic group despite longer duration of surgery.
Ectopic Pregnancy
Christy Short, DO, and Tom Green, DO
FOEM Case Poster Presentation Abstract

Introduction
Abdominal pain and nausea are complaints heard quite frequently in the emergency department when patients present with pregnancy. Although our approach to abdominal pain in pregnancy is similar to that in nonpregnant females, there are some noteworthy challenges. The clinician needs to take into account the physiologic changes of pregnancy that may affect the evaluation of abdominal pain. Ultimately however, ectopic pregnancy should always be part of the differential when evaluating a pregnant patient presenting with abdominal pain. Failure to diagnose ectopic pregnancy may lead to internal hemorrhage, which is the leading cause of pregnancy related maternal death in the first trimester. Symptoms of ectopic pregnancy tend to present early in the first trimester, usually between 6-8 weeks. The classic clinical picture of ectopic pregnancy is history of delayed menses, abdominal pain, followed by vaginal bleeding. Abdominal pain is usually severe, constant, and peritoneal in nature. Requisite diagnostic imaging should always be performed when ectopic pregnancy is a consideration. This unique case highlights the importance of pelvic ultrasound as imaging modality of choice in pregnant patients with abdominal pain, regardless of having mild or atypical symptoms of ectopic pregnancy.

Case
A 32 year old healthy pregnant female presents to the ED with complaints of lower pelvic pain, slightly worse on the right x 1 day. Patient notes pain was initially sharp, lasting a few minutes earlier that day, however, now minimal in the ED. Patient also notes some associated nausea, but, states nausea typical of prior pregnancies. Patient denies vaginal discharge, vaginal bleeding, dysuria, hematuria, emesis, weakness, dizziness. Patient EGA to be 10 weeks based on LMP. Patient G5P2, with a prior miscarriage 2 years prior and right ectopic pregnancy 8 months prior, terminated with methotrexate, no complications. Patient has had no prenatal care with her current pregnancy.

On exam, patient appears well, in no distress, vital signs stable, minimal right lower abdominal tenderness noted, no adnexal tenderness on bimanual exam, no vaginal bleeding/discharge noted. Given patient’s complaints of pelvic pain with pregnancy, labs, urine, pelvic OB US ordered. Patient mildly anemic with Hgb of 11.4, beta hCG 73,889. Pelvic ultrasound noted viable 10 week ectopic pregnancy in right adnexa, FHT 151, no free fluid.

Patient remained stable in ED, with very minimal abdominal discomfort, vital signs remained stable. Upon pelvic US results, patient was subsequently transferred to a tertiary care center, where she underwent diagnostic laparscopy and exploratory laparotomy for right cornual resection of a live pregnancy at 10 weeks gestation. Patient had post-operative complication of symptomatic anemia, improved with 2 units PRBCs. Patient was discharged in good condition 3 days post-operative.

Conclusion
Ectopic pregnancy, or abnormal pregnancy site implantation, is an increasing problem seen in the ED that poses a major risk for women of reproductive age. Many times the history and physical exam of the patient with ectopic pregnancy are nonspecific. Further studies are necessary in the pregnant patient who presents with abdominal pain with or without vaginal bleeding to locate the pregnancy and determine its viability. Transabdominal/transvaginal ultrasound is the diagnostic modality of choice to identify gestation location, gestational age, and assess fetal viability. The above case highlights the importance of pelvic ultrasound as imaging modality of choice in pregnant patients with abdominal pain, to assess for life threatening ectopic pregnancy, even if the patient is well-appearing with minimal or atypical symptoms of ectopic pregnancy.

References
When Back Pain is More Than Just Back Pain
FOEM Case Poster Presentation Abstract
Christy Short, DO, and Jennifer Ron, MD
Department of Emergency Medicine
Swedish Covenant Hospital, Chicago, IL

Abstract
Back pain is a complaint that is heard quite frequently in the emergency department, however, not all back pain is simply back pain. A 31 African male with pmh of chronic low back pain, presented with complaints of right lower back pain. Patient states he has had this back pain for ~2 years and had been seen and treated in the ER on numerous occasions for his ongoing back pain. The patient attributed his back pain to lifting heavy meat containers at a meat packing plant. Patient noted he had been laid off a few months ago and hadn’t been lifting anything heavy in quite awhile, however, his back pain persisted. The patient reported flexeril and naproxen seemed to help relieve his symptoms in the past. On this visit, the patient also relayed his pain radiated slightly anterior, just over the right iliac crest. The patient denied painful radiation into the groin, no problems with urination, no parathesias or radiation into his legs, no muscle weakness. He also reported an upcoming scheduled appointment with a pain specialist for his ongoing back pain. Additionally, the patient reported a 10lb weight loss over ~2mos without intention. Patient denies fevers/chills, night sweats, cough, hemoptysis, dyspnea, chest pain. On physical exam, the patient is in no apparent distess, his vital signs are within normal limits. There is an appreciable swollen area to the right lateral low back, approximately 8cm in diameter, with a spongy consistency. There is no associated erythema, increased warmth or cellutic or infectious appearing presentation. When the patient is questioned about the swollen area, he reports he has had a small area of swelling since 2011 in that area, but it had increased in the last several days, along with worse low back pain. Given the patient’s unintentional weight loss with back pain and the appreciable mass, our initial work-up included labs and a bedside ultrasound on the swollen area of the right low back, which revealed a large anechoic area, consistent with a possible fluid collection. Labs were only significant for a mild microcytic anemia, hgb of 11.7. We then proceeded with a CT abdomen/pelvis with contrast to further evaluate the fluid filled collection. CT revealed multiple abnormal lobulated fluid collections throughout the right abdomen and pelvis. Specifically, there was a 10x8.4x4.6cm right gluteal fluid collection, a 13.5x4x7.4cm fluid collection within the right iliopsoas, and a 4.2x4x3.8cm fluid collection in the presacral space. The patient was admitted to the hospital and underwent US guided drainage of the fluid collections, where 300cc of pus was aspirated and a drain was placed. The patient was found to have a positive PPD and positive quantiferon gold and ultimately was diagnosed with active tuberculosis with tuberculous abscesses. He was treated with the following TB medications: INH, Rifampin, Ethambutol, and Pyrazinamide. The patient was ultimately discharged home in stable condition with continuation of the above TB medications and close outpatient follow-up. Although most chronic low back pain is just that, this case provided a good example of how important taking a good history and doing a thorough physical exam can help broaden your differential and further guide your work-up to help arrive at your diagnosis.

References
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Objective: To evaluate women’s knowledge about risk factors and screening tests for heart disease, breast cancer, colon cancer, and cervical cancer.

Methods: A 15 question survey was developed based on information from the CDC, USPSTF, and ACOG to study women’s knowledge about heart disease, breast cancer, colon cancer, and cervical cancer. Participants also completed demographic questions including age, race, education, employment, insurance, income, marital status, and parity. The primary outcome was the number of questions that women answered correctly. Secondary outcomes were demographic characteristics of women who demonstrated lack of knowledge. Multiple logistic regression analysis and Pearson Chi-squared analysis was performed. P value < 0.05 was considered significant.

Results: 256 surveys were complete. Total correct scores ranged from 0-15. 48% of women correctly answered 10 questions or less. The largest group, 19%, correctly answered 11 questions. 49.8% correctly answered all questions about breast cancer. 59.8% correctly answered all questions about colon cancer. Only 7.4% correctly answered all questions about cardiovascular disease and 11.7% correctly answered all questions about cervical cancer. Multiple logistic regression analysis demonstrated statistically significant relationship between education and total number of questions answered correct (p=0.01). There was a significant association between lack of knowledge and race and income status based on Pearson Chi-Squared test (p<0.05).

Conclusion: Physicians should focus on educating women of minorities, lower income, and less formal education about risk factors and screening tests for heart disease and cervical cancer. Women most at risk, aged 44-60, can benefit from further counseling about heart disease prevention. Young women, aged 18-25, can benefit from further counseling about cervical cancer screening and prevention.

Acknowledgements
Ann Impens, PhD, MPH, Manager of Clinical Research, Research Assistant Professor, Internal Medicine Midwestern University and Jason M. Kamilar, PhD, Manager of Bio-Clinical Statistics, Midwestern University
Diabetic-associated neuropathy of the autonomic nervous system may cause a disruption in proper gastromotility, causing gastroparesis, a decrease in the rate of stomach emptying after an ingested meal. This study examined the effects of insulin resistance with accompanying euglycemia or hyperglycemia on the expression of cleaved caspase-3 (CC-3), an apoptotic marker, and Glut4, an insulin-dependent glucose transporter, in cell bodies of vagal neurons with intact projections to the stomach. We hypothesized that the number of gastric vagal neurons expressing CC-3 or Glut4 would be higher in type 2 diabetic (T2DM) mice compared to control mice and would increase with duration of T2DM (0-16 weeks). Four to 24 weeks old KK.CgA/J mice, which develop insulin resistance and hyperglycemia at 8 wks of age, and KK control mice, which develop insulin resistance at 8 wks of age but remain euglycemic, were used in this study. Under ketamine and xylazine anesthesia, fluorogold (FG), a fluorescent chemical endocytosed by nerve terminals and retrogradely transported to cell bodies, was superficially microinjected into the gastric fundus. Six days after FG injection, mice were perfused with 4% paraformaldehyde to fix the brain. Six brainstem sections throughout the vagal nucleus were stained for either CC-3 or Glut4. Fluorogold labeled neurons, CC-3 positive (+) cells, Glut4 + cells, double labeled FG/CC-3 neurons, and double-labeled FG/Glut4 neurons were counted. The % of total FG neurons expressing CC-3 or Glut4 was calculated and data were analyzed by 2-way ANOVA with the factors of age and control/diabetic. The numbers of FG-labeled neurons, CC-3 + cells, Glut4 + cells, and double-labeled FG/Glut4 neurons were similar in control and diabetic animals. In both groups of mice, the % FG neurons expressing Glut4 increased between 4 as compared to 16 and 24 weeks of age, and between 8 as compared to 16 weeks of age. Insulin resistance played a stronger role than hyperglycemia in altering GLUT4 expression. The number of FG/CC-3 double labeled neurons was greater in 4 week old KK.CgA/J mice as compared to KK mice and a trend (p=0.054) was observed at 8 weeks of age. In both groups of mice, the % total FG neurons expressing CC-3 increased with age (p=0.053) suggesting a role in maturation. The development of insulin resistance, rather than hyperglycemia, altered the expression of Glut4 and CC-3 in gastric vagal neurons.

Funding provided by ORSP at Midwestern University
Gene expression profiles resulting from stable and transient loss of p53 mirrors its role in tissue differentiation.

Oliver Couture, Eric Lombardi, Kendra Davis, Emily Hays and Nalini Chandar

Department of Biochemistry, Chicago College of Osteopathic Medicine, Midwestern University, Downers Grove, IL 60515

The tumor repressor gene, p53, is involved in a variety of cellular activities ranging from cellular stress responses to differentiation, and cell cycle regulation. In our previous studies we have shown p53’s transcription activating role to be important in osteoblast differentiation. There is still a debate in the literature as to whether p53 inhibits or promotes differentiation. We have found p53 heterozygous mice to show a p53 dependency on some bone marker gene expression while the same is absent in p53 null mice. This deficiency of p53 has also been shown to produce more osteosarcomas than a complete loss of p53. This suggests that the presence of p53 is able to modify the environment within pre osteoblasts based on its ability to regulate key bone specific genes. In the present study we compared changes in gene expression resulting after either a transient or stable reduction in p53. Accordingly we reduced p53 levels in C2C12 cells capable of both myoblast and osteoblast differentiation transiently, and compared the changes in gene expression of candidate genes to cells with stable p53 knockdown. Using a PCR array to assay p53 target genes, we have found differential expression profiles when comparing stable versus transient knockdown. As expected several of genes that were profoundly affected after transient p53 loss were related to apoptosis and cell cycle regulation. Stable p53 loss produced a greater change in MyoD and other transcription factors with tissue specific roles suggesting that long term effect of p53 loss affects tissue homeostasis to a greater degree than changes resulting from acute loss of p53. These differences in gene expression were also validated by measuring promoter activities of different pathway specific genes involved in differentiation. These studies suggest that an important role for p53 is context dependent, with a stable reduction in p53 expression profoundly affecting normal tissue physiology than its acute loss.
Gap Junction Protein Connexin 43 Contributes to Upper Genital Tract Pathology Following Chlamydial Infection

Srikanth Manam¹, Sophie La Salle², Yong Zhang³, Michael J Holtzman³, Bruce J Nicholson⁴, Ashlesh K Murthy¹

¹Department of Pathology & ²Department of Biochemistry, Midwestern University, Downers Grove, IL 60515; ³Department of Internal medicine, Washington University School of Medicine in St Louis, St Louis, MO, 63110; ⁴Department of Biochemistry, University of Texas at Health Science Center at San Antonio, San Antonio, TX, 78212.

We have shown previously that CD8⁺ T cells play a major role in Chlamydia induced upper genital tract pathology but has minimal role in bacterial clearance. To understand whether the pathology is caused by Chlamydia specific or bystander CD8⁺ T cells, we used OT-1 mice. CD8⁺ T cells from OT-1 mice mount response only against SIINFEKL peptide of Ovalbumin protein but not against any other, including chlamydial, antigens. OT-1 mice infected with Chlamydia muridarum displayed similar bacterial clearance but minimal oviduct pathology compared to C57BL/6J mice, suggesting that Chlamydia induced upper genital tract pathology occurs in an antigen specific fashion. Thus, Chlamydia specific CD8⁺ T cells may not target infected cells efficiently but uninfected cells to cause the damage. This begs the question “How do uninfected cells acquire chlamydial peptides”? We hypothesize that chlamydial peptides will be transferred from infected cells to uninfected cells by Gap Junction Mediated Antigen Transfer (GMAT). GMAT occurs via channels formed by connexin proteins. There are several connexin proteins and CX43 is the one predominantly expressed in oviduct epithelium, the main site of Chlamydia-induced pathology. We have found that HeLa cells engineered to express CX43, but not those without Cx43, efficaciously transfer peptides to co-cultured mouse antigen presenting cells (APC) and subsequently activate OT-1 specific CD8⁺ T cells. In this system, we are currently evaluating the transfer of chlamydial peptides. Furthermore using the elegant Cre-Lox technology, we generated mice with a conditional deletion of CX43 in ciliated columnar epithelial cells, including the oviduct epithelium (FoxJ1Cre-Cx43flox mice). Upon intravaginal infection with Chlamydia muridarum, FoxJ1Cre-Cx43flox mice displayed bacterial clearance similar to wild type C57BL/6J mice, but displayed significantly reduced oviduct dilation suggesting that CX43 in the oviducts may play a major role in Chlamydia induced upper genital tract pathology. The contribution of CX43 to CD8⁺ T cell mediated chlamydial pathogenesis is currently under investigation in our laboratory.

This work was supported by Midwestern University Faculty Start-up Fund and NIH Grant 1R03AI088342 to AKM.
Centhaquin antinociception in mice is mediated by $\alpha_{2A}$ and $\alpha_{2B}$ but not $\alpha_{2C}$ adrenergic receptors

Shaifali Bhalla, Izna Ali, Shridhar V. Andurkar and Anil Gulati

Department of Pharmaceutical Sciences, Chicago College of Pharmacy

Midwestern University, Downers Grove, IL 60515, USA

Background: The use of clonidine as a primary and adjuvant analgesic is well-documented. It is known that imidazoline and $\alpha_2$-adrenergic receptors are involved in clonidine antinociception. Clonidine also produces antihypertensive actions mediated through the central nervous system. We have reported that centhaquin, a centrally acting anti-hypertensive drug, produces its hypotensive effect through a mechanism similar to that of clonidine. Centhaquin has also been shown to possess significant antinociceptive activity which is partially blocked by yohimbine, idazoxan, and naloxone. However, the involvement of specific adrenergic receptor subtypes ($\alpha_{2A}$, $\alpha_{2B}$, or $\alpha_{2C}$) in centhaquin antinociception is unknown.

Objective: The present study was conducted to determine antinociceptive properties of centhaquin citrate, a water soluble salt of centhaquin, and involvement of $\alpha_{2A}$-, $\alpha_{2B}$-, or $\alpha_{2C}$-adrenergic receptors in mice.

Methods: BRL-44408 ($\alpha_{2A}$-adrenergic receptor antagonist), imiloxan ($\alpha_{2B}$-adrenergic receptor antagonist) and JP-1302 ($\alpha_{2C}$-adrenergic receptor antagonist) were used to determine the involvement of $\alpha_{2A}$-, $\alpha_{2B}$-, or $\alpha_{2C}$-adrenergic receptors, respectively. Antinociceptive responses were determined by the tail-flick and hot-plate latency methods in male Swiss-Webster mice treated with centhaquin citrate alone and in combination with BRL-44408, imiloxan, or JP-1302. Parameters were measured for 360 min and expressed as Mean±S.E.M. N=8 per group.

Results: Centhaquin citrate produced significant antinociceptive responses in mice (P<0.05) which were blocked by BRL-44408 (tail-flick test: 49.75% decrease, P<0.05; hot-plate test: 49.12% decrease, P<0.05) and imiloxan (tail-flick test: 46.98% decrease, P<0.05; hot-plate test: 46.42% decrease, P<0.05). Centhaquin citrate antinociception was not affected by JP-1302 in both tail-flick and hot-plate latency tests over the 6-hour observation period.

Conclusion: This is the first report demonstrating centhaquin citrate antinociception and its blockade by BRL-44408 and imiloxan. We conclude that $\alpha_{2A}$ and $\alpha_{2B}$ but not $\alpha_{2C}$ adrenergic receptors are involved in centhaquin antinociception in mice.
Alteration in the brain ET$_B$ receptor binding characteristics following cerebral ischemia

Shaifali Bhalla, Mary Leonard, Seema Briyal and Anil Gulati

Department of Pharmaceutical Sciences, Chicago College of Pharmacy;
Midwestern University, Downers Grove, IL 60515, USA

Background: Stimulation of endothelin ET$_B$ receptors by IRL-1620 has been shown to provide neuroprotective effect in middle cerebral artery occlusion (MCAO) model of cerebral ischemia in rats. However, the involvement of ET$_B$ receptors in cerebral ischemia is not established. It is not known whether characteristics of ET$_B$ receptors in the brain are altered following cerebral ischemia.

Objective: We have therefore conducted the present study to determine changes in binding characteristics of ET$_B$ receptors in the rat brain, 1 and 7 days following right MCAO.

Methods: MCAO was produced in male Sprague Dawley rats using a 4.0 monofilament guided through the right external carotid artery to the middle cerebral artery. Binding studies were performed using [$^{125}$I]-IRL-1620 (specific activity 2200 Ci/mmol) as the radioligand and cold IRL-1620 (0-32 nM) as displacer. Non-specific binding was determined using 1 µM concentration of IRL-1620. $K_d$ and $B_{max}$ values were calculated using GraphPad Prism version 5.00 for Windows (GraphPad Software, San Diego, CA, USA). A level of $P<0.05$ was considered significant. The sample size was $N=4$ per group.

Results: On day 1 and day 7, MCAO rats displayed marked neurological and motor function deficit as evidenced by a high foot fault error (60±16% and 35±7%, respectively; $P<0.01$) and a reduced ability to remain on the rota rod ($P<0.05$). No deficits were observed in sham-treated animals. The infarct volume of MCAO rats was 126±40 mm$^3$ and 153±22 mm$^3$ on day 1 and day 7, respectively. Binding characteristics ($K_d$ and $B_{max}$) were not altered at 24 hours post MCAO. However, a significant decrease in $K_d$ values of ET$_B$ receptor binding in both left and right hemispheres was observed 7 days post MCAO. The decrease in $K_d$ in the right (ischemic) hemisphere was significantly ($P<0.001$) greater compared to left (non-ischemic) hemisphere. $B_{max}$ was increased in both left and right hemispheres with the right (ischemic) hemisphere showing a significantly ($P<0.001$) greater increase compared to the left (non-ischemic) hemisphere.

Conclusion: The density and affinity of ET$_B$ receptors is increased only on the 7$^{th}$ day of cerebral ischemia. It is speculated that this increase in ET$_B$ receptor binding is an attempt to provide neuroprotection to prevent excessive damage to the brain.
Endothelin B Receptor Agonist, IRL-1620, Enhances Angiogenesis and Neurogenesis Following Cerebral Ischemia in Rats

Mary G. Leonard and Anil Gulati

Midwestern University Chicago College of Pharmacy, Downers Grove, IL 60515

Background: Endothelin B (ETB) receptor agonist, IRL-1620, has been shown in previous studies, conducted in our lab, to provide significant neuroprotection at both 24 hours and 1 week following permanent cerebral ischemia. It is possible that IRL-1620 may be neuroprotective due to angiogenesis and neurogenesis. However, the effect of IRL-1620 on neurovascular remodeling following cerebral ischemia has not been established. The present study was conducted to determine the effect of IRL-1620 [Suc-[Glu9,Ala11,15]-Endothelin-1(8-12)] on astrocytes, neurons, and vascular endothelial cells after the induction of cerebral ischemia.

Methods: Male Sprague-Dawley rats undergoing permanent middle cerebral artery occlusion (MCAO) received three intravenous injections of either vehicle or IRL-1620 (5 µg/kg) at 2, 4, and 6 hours post occlusion. Brain tissues of animals euthanized at 24 hours or 7 days post occlusion were processed for immunofluorescent labeling of ETB receptors, astrocytes, neurons, and vascular and neuronal growth factors.

Results: At 24 hours post occlusion, IRL-1620 treatment increased ETB receptor expression and preserved neuronal numbers in the cortex, striatum and subventricular zone (SVZ) of the ischemic rat brain. IRL-1620 also enhanced the number of blood vessels labeled with vascular endothelial growth factor (VEGF) when compared to vehicle treatment. By 1 week following MCAO, VEGF-positive vessels/30 µm brain slice in the IRL-1620 group numbered 11.33±2.13 versus 4.19±0.79 in the vehicle group (P<0.01), indicating an increase in angiogenesis. Additionally, animals receiving IRL-1620 displayed an increased number of proliferating cells (P<0.0001) and cells positively staining for nerve growth factor (NGFP<0.0001) in the infarcted brain. NGF-positive cells in the cortex, striatum and SVZ of IRL-1620 treated animals numbered 2.29±0.31, 2.08±0.26, and 3.05±0.38 per 100 µm², respectively, demonstrating a significant increase in neurogenesis as compared to the vehicle group, which averaged less than 1 NGF-positive cell per 100 µm². Pretreatment with ETB antagonist, BQ788, blocked the effects of IRL-1620 treatment, confirming the role of ETB receptors in the neurovascular remodeling actions of IRL-1620.

Conclusions: Results of the present study indicate that IRL-1620, administered on the day of infarct, is neuroprotective and enhances angiogenic and neurogenic remodeling following cerebral ischemia.
Sean M. Mirk, PharmD, Jen Phillips, PharmD, BCPS, and Huzefa Master, PharmD, BCPS
Department of Pharmacy Practice, Midwestern University, Downers Grove, IL

Title: Evaluating the Effectiveness and Student Perceptions of On-line Interactive Learning Lectures

Objectives: This is a two phase IRB-approved study to evaluate the effectiveness, perception and opinions of an interactive on-line lecture format.

Methods: Storyline (Articulate Global, Inc; New York, NY) was used by faculty members to create interactive on-line learning modules (OLMs) in separate courses. In the first phase (Phase 1) of this project two faculty members created OLMs for an elective course offered to third-year professional pharmacy students. The OLMs were mandatory and took the place of a traditional live lecture (TLL). Each OLM focused on a different disease state. After completing each OLM, students completed a survey that assessed their level of satisfaction with the on-line format and their opinions on how the on-line format compared to a TLL. Results from Phase 1 were used to improve the development of the OLMs for the second phase (Phase 2). In Phase 2, first-year professional pharmacy students enrolled in a required course who agreed to participate were randomized into two separate groups. One group completed an OLM and the other group attended a TLL. A survey was administered to both groups to assess their opinions. Quiz and final exam questions pertaining to the subject matter were used to assess impact on short and long-term learning. Student participation in both phases was voluntary and consent was obtained.

Results: In Phase 1, both OLMs were completed by all students enrolled (n = 27). The response rate for the survey following each OLM was 66.7% and 40.7%, respectfully. After the first OLM, most students either strongly agreed or agreed that the OLM was effective at achieving the learning objectives (77.8%) and provided a practical application of the subject matter (88.9%). In addition, most strongly agreed or agreed that the OLM helped them to apply the information taught to a patient case (83.3%) and enhanced their understanding of concepts and principles related to the topic (72.2%) better than a TLL. After the second OLM, similar results were seen. A majority of students also felt that the number of on-line lectures, as part of this course, should increase. Phase 2 results are pending.

Implications: Student perceptions and opinions toward an interactive on-line lecture format are positive and most felt the number of OLMs should increase. Similar results were seen regardless of subject matter or lecturer. Results were used to improve the development of the OLM for Phase 2. The results from Phase 2 will be analyzed to compare the effectiveness of an interactive on-line lecture format to a TLL.

This research was supported in part by the Scholarship of Teaching and Learning Grant
Effect of centhaquin resuscitation on coagulation in a rabbit model of uncontrolled hemorrhagic shock

Gwendolyn Pais¹, Nora Mulloy², Zhong Zhang¹ and Anil Gulati¹

Department of Pharmaceutical Sciences, Chicago College of Pharmacy¹ and Biomedical Sciences Program, College of Health Sciences², Midwestern University, Downers Grove, IL 60515

Background: It is known that aggressive resuscitation with crystalloids following hemorrhagic shock induces coagulopathy. Centhaquin is a cardiovascular active agent, which has been found to be effective in resuscitation of hemorrhagic shock. However, its effect on coagulation is not known.

Objective: To determine the effect of resuscitation with centhaquin on blood coagulation in a rabbit model of uncontrolled hemorrhagic shock using thromboelastography (TEG).

Methods: Male New Zealand white rabbits were anaesthetized and a laparotomy was performed and hemorrhage was induced by a single puncture to the abdominal aorta. Resuscitation with normal saline or centhaquin (0.05 mg/kg) was carried out after 15 minutes of aortic puncture to maintain the mean arterial pressure (MAP) at 45 mmHg for 60 minutes (hypotensive resuscitation). Each rabbit was then observed for an additional 60 minutes. In another group normal saline was infused at a higher rate to maintain MAP at 60 mmHg (normotensive resuscitation). The effect of centhaquin on arterial blood gases was determined using a blood gas analyzer, volume of infusion and blood loss were measured and coagulation was monitored by TEG.

Results: Hypotensive resuscitation by saline required a volume of 207±9 mL to maintain MAP at 45 mmHg which was significantly (p=0.001) more than centhaquin (133±11mL). Volume (377±11 mL) of saline needed for normotensive resuscitation (60 mm Hg) was markedly (p<0.0001) greater compared to hypotensive resuscitation. Blood loss was similar in saline (40±3 mL) and centhaquin (38±2 mL) hypotensive resuscitation, however, it was significantly (p<0.05) more with normotensive resuscitation. TEG parameters at baseline were R=11.4±0.6 min, K=2.9±0.1 min, α=54.0±0.8°, MA=65.6±0.5 mm. Hemorrhagic shock produced a decrease in R, K, MA and an increase in α. TEG did not differ significantly between groups at end of hemorrhage. Hypotensive resuscitation with saline produced no change in R, decreased K and MA, and increased α. Hypotensive resuscitation with centhaquin produced no change in R, K and α, compared to saline, however, MA increased significantly (p<0.02). Normotensive resuscitation with vehicle produced no change in R, increased α (p<0.001), decreased K (p<0.01) and decreased MA (p<0.03) compared to centhaquin.

Conclusion: TEG parameters are altered following resuscitation but less affected when hypotensive resuscitation is performed with centhaquin.
Immediate Loading of Implants in the Atrophic Edentulous Maxilla Without Bone Augmentation: 5-Year Clinical Outcomes
J. Toljanic, R. Baer, K. Ekstrand, A. Thor

Recent clinical studies have demonstrated that predictable integration can be achieved for implants immediately loaded with fixed restorations in the maxilla. Less data exist describing outcomes for this treatment modality when used in atrophic maxillae. In this prospective study, long-term clinical outcomes were measured for subjects with atrophic edentulous maxillae who underwent implant placement without bone augmentation combined with immediate fixed provisional restoration.

A total of 51 subjects diagnosed with atrophic edentulous maxillae (based on Lekholm and Zarb criteria bone quality 3 or 4; bone quantity C, D, or E) were recruited from 2 independent centers. Each subject received 6 implants (OsseoSpeed™, Astra Tech Implant System) with screw-retained fixed provisional restorations placed within 24 hours of implant surgery. No bone augmentation procedures were performed. Definitive screw-retained fixed restorations were placed 20 – 24 weeks after surgery. Subjects were annually assessed both clinically for implant integration and restoration function and radiographically for changes in crestal bone height over a follow-up interval of 5 years.

Forty subjects remained under follow-up and were assessed at 5 years. Data obtained at this 5-year interval revealed 232 implants remained in function for a 93% implant survival rate (Kaplan-Meier survival analysis). Mean marginal bone loss was found to be 0.44 mm. Thirty-nine of 40 subjects continued to function with their fixed restoration while the remaining subject was functioning with a removable complete maxillary denture not retained by the remaining implants.

The results of this study indicate that individuals with atrophic edentulous maxillae may be successfully restored using an implant rehabilitation protocol that includes immediate loading with fixed provisional restorations without the inclusion of bone augmentation procedures. Predictable long-term outcomes may be anticipated under these conditions.

This study was supported by DENTSPLY Implants.